Glucagon Use in Paediatric Type 1 Diabetic Patients:

An Innovative Approach to Improve Outcomes

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DEDICATION

I dedicate this research to the people who mean the world to me: my parents for being the best role models I could have ever asked for and for always giving us the best; my fiancé who supports me and believes in me no matter what I do; my sisters who are always there with their unconditional love; my grandparents Mary Ann and Joseph, Paula and John, who always provided encouragement.

ABSTRACT

Hypoglycaemia is the most common acute complication and is considered a major problem amongst children with type 1 diabetes mellitus. Hypoglycaemia is very often undetected, under-reported and poorly understood by the patients and their carers. This lack of confidence in detecting, reporting and understanding hypoglycaemia puts patients at risk of consequences of untreated hypoglycaemia which can range from seizures to premature death.

The aim of this research was to develop and evaluate the impact of educating carers of paediatric patients suffering from type 1 diabetes mellitus, on the emergency use of glucagon in hypoglycaemia in a safe and effective way.

A Glucagon Tool Kit was developed in both Maltese and English, consisting of information on hypoglyceamia, a chart and a video on how to reconstitute and use glucagon. This was disseminated to all pharmacists and a questionnaire was completed to analyse the knowledge and confidence on the use of glucagon before and after the intervention. The same Glucagon Tool Kit was given to carers of children with type 1 diabetes mellitus. Carers were recruited after their visit to the outpatients' clinic with the medical consultant. A questionnaire was completed at baseline to assess carers' knowledge on glucagon. Carers were given the Glucagon Tool Kit and four weeks after intervention, carers were contacted by phone to complete the questionnaire again to reflect the impact of the intervention.

The 'Pharmacist Glucagon Assessment Questionnaire' was completed by 139 pharmacists. Using the Wilcoxon sign test a significant difference was noted in both confidence and knowledge of use on glucagon when before to after intervention is compared ($p < 0.001$).

One hundred and forty patients with type 1 diabetes mellitus attend the paediatric diabetes outpatients service at Mater Dei Hospital. Of these 80 were successfully interviewed. A statistical significant difference ($p < 0.001$) was noted when comparing before intervention to after intervention for confidence and knowledge on reconstituting glucagon.

The educational material developed had a significant impact on the knowledge and confidence the pharmacist and carers have on the use and reconstitution of glucagon. This will empower pharmacists with better tools to educate patients and to instill confidence in carers to make use of glucagon appropriately when required.

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GLOSSARY

Carer	The person/s who is principally taking care of the type 1 diabetic child or a diabetic patient.
Glucagon	Medication used when the patient develops severe hypoglycaemia and is unable to take anything by mouth due to unconsciousness[1].
Glucagon Injection	The kit (product itself) that is presented to the patients which includes the vial with medication and the water for injection vial for reconstitution.
Glucagon Tool Kit	This is the Tool Kit developed consisting of the information sheet, chart on how to reconstitute glucagon and the video clip.
Hyperglycaemia	Characterised by high blood sugar levels. Range for normal blood sugar levels are 4-7mmol/l.
Hypoglycaemia	This event occurs when blood sugar levels are less than or equal to 3.9mmol/l[2].

[1] American Diabetes Association (ADA). [American Diabetes Association Workgroup on Hypoglyceamia] Defining and reporting Hypoglycaemia in Diabetes. *Diabetes Care.* 2005; 28(5): 1245-1249

[2]American Diabetes Association (ADA). [American Diabetes Association Workgroup on Hypoglyceamia] Defining and reporting Hypoglycaemia in Diabetes. *Diabetes Care.* 2005; 28(5): 1245-1249

Intervention	The intervention refers to the dissemination of Glucagon Tool Kit as an educational tool.
Paediatrics	The cohort of patients is between the age of 0 – 16 years of age.
Pink Card or Schedule Five Entitlement	Approvals patients are granted to enable them to be given medication for free via the national health system.
Reconstitution	The mixing of the powder in the vial with the sterile liquid in the injection to form the medication required to treat patient.
Type 1 Diabetes Mellitus	A disorder whereby the pancreas ceases to produce insulin as a result of complete beta cell destruction. Due to this patient has to rely on insulin treatment and constant monitoring to mimic the body, and maintain a physiological blood glucose level as much as possible[3].

[3] American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care.* 2010; 33(1): S62-S69

ABBREVIATIONS

ADA: American Diabetes Association

DKA: Diabetic Ketoacidosis

EMA: European Medicines Agency

HL: Health Literacy

IDF: International Diabetes Federation

MDH: Mater Dei Hospital, Malta

NICE: National Institute of Health and Care Excellence Guidelines

PIL: Patient Information Leaflet

SIGN: Scottish Intercollegiate Guidelines Network

SPC: Summary of Product Characteristics

T1DM: Type 1 Diabetes Mellitus

WHO: World Health Organisation

CHAPTER 1

INTRODUCTION

1.1. DIABETES MELLITUS

Diabetes mellitus is defined by World Health Organisation and International Diabetes Federation as a group of metabolic diseases distinguished by hyperglycaemia manifesting with a fasting blood glucose level of more than 7mmol/L or glucose levels of more than 11mmol/L two hours after a meal. Hyperglycemia results due to defects in insulin secretion, insulin action or both (WHO, 2006). This definition is widely adopted to describe diabetes mellitus in international guidelines such as the Scottish Intercollegiate Guidelines Network and American Diabetes Association guidelines (American Diabetes Association,2010; Scottish Intercollegiate Guidelines Network, 2014).

1.1.1. TYPES OF DIABETES MELLITUS

Diabetes mellitus does not involve only one pathogenic process. It ranges from autoimmune destruction of the beta cells in the pancreas, leading to insulin deficiency, resistance of insulin action which is brought about by inadequate insulin secretion and/or decreased tissue response to insulin at any point in the complex hormone action pathways (American Diabetes Association, 2010).

Type 1 diabetes mellitus is distinguished as absolute deficiency of insulin secretion very often requiring insulin therapy whereas type 2 diabetes mellitus is caused by a combination of both resistant insulin action and inadequate insulin production (American Diabetes Association, 2010). Type 2 diabetes mellitus can be due to genetic defects in the beta cells, or in insulin actions, resulting from infections or viruses. It can also develop as a result of other genetic syndromes such as Prader Willi Syndrome or Down Syndrome and can be drug induced or due to disease of the exocrine pancreas (American Diabetes Association, 2010).

As stated by Cameron and Wherrett (2015) although type 1 diabetes mellitus is the most common form of diabetes in children, this is not the only form that children can be diagnosed with. Other types of diabetes a child can develop include type 2 diabetes mellitus, with age of diagnosis being at puberty but rarely younger than 10 years. Neonatal diabetes mellitus develops in children, younger than 6 months of age, while type 2 diabetes mellitus is diagnosed from 6 months of age to 18 years. Type 1 diabetes mellitus can be diagnosed at any age in childhood, however the peak onset is 5-7 years of age and at, or close to puberty (Atkinson et al, 2014). All can present with diabetic ketoacidosis apart from maturity-onset diabetes in the young, which occurs at age younger than 25 years (Cameron and Wherrett, 2015).

This dissertation will focus on paediatric patients with type 1 diabetes mellitus.

1.2. Incidence of type 1 diabetes mellitus

Type 1 diabetes mellitus (T1DM) is one of the most common chronic disorders in paediatric patients in the United States and Europe (Formosa et al, 2012; Freeborn et al, 2013; Cameron and Wherrett, 2015). An analysis carried out on a European population based registry between 1989 and 2003 in children younger than 15 years of age, revealed a 3.9% increase per year in the incidence of this type of diabetes mellitus (Cameron and Wherrett, 2015). Incidence rates of type 1 diabetes mellitus have been on the increase for decades in many countries (Atkinson et al, 2014; Cameron and Wherrett, 2015). In Europe, the most marked increase has been noted in paediatric patients younger than 5 years of age (Formosa et al, 2012; Freeborn et al, 2013; Atkinson et al, 2014). Predictions estimate that the incidence of type 1 diabetes mellitus will double in patients under the age of 5 years by the year 2020 (Todd, 2010; Freeborn et al, 2013). This shift of increase in type 1 diabetes mellitus diagnosed in the younger age group was also confirmed in

Malta. A study carried out by Formosa et al, in 2012 on Maltese paediatric patients highlighted a marked increase in incidence of type 1 diabetes mellitus in patients aged 0-9 years. The SWEET project carried out in 2009 places Malta's current incidence in children in 5th place within the European Union, in close proximity to the United Kingdom and Denmark (Formosa et al, 2012).

1.3. UNDERSTANDING TYPE 1 DIABETES MELLITUS

The etiology and pathology behind type 1 diabetes mellitus is aptly documented in various textbooks. In this section of the dissertation a brief overview of type 1 diabetes mellitus is given in order to present a holistic concept of the condition.

The pancreas, Islet of Langerhans, are made up of 4 different cells, all secreting peptide hormones namely beta cells which produce insulin and amylin, A cells producing glucagon, D cells responsible for producing somatostatin and PP cells having pancreatic polypeptide function. In a nondiabetic patient, insulin is released depending on the glucose concentration, if glucose concentration increases then insulin is released to act on liver, muscle and fat, as an anabolic hormone. It also inhibits the action of glucagon amongst other things. Glucagon on the other hand is the opposite of insulin. It is released when low concentrations of glucose and fatty acids are present in the blood, it is inhibited when these are high (Rang and Dale, 2012).

Type 1 diabetes mellitus is caused by an auto-immune mediated disorder that destroys the insulin-producing pancreatic beta cells (Atkinson et al, 2014; Cameron and Wherrett, 2015). Risk factors implicated in type 1 diabetes mellitus include strong genetic susceptibly and environmental factors such as enterovirus infections, hygiene hypothesis and sanitation as well as diet (Todd, 2010; Atkinson et al, 2014; Tamayo et al, 2014; Cameron and Wherrett, 2015). Although environmental pollution is not adequately

evaluated to link it to type 1 diabetes mellitus, preliminary evidence suggests that there might be a link between chemical exposure and type 1 diabetes mellitus (Peng and Hagopian, 2006; Howard et al, 2011; Howard and Lee, 2012).

1.4. Manifestation and Diagnosis of type 1 Diabetes mellitus

The classic symptoms associated with type 1 diabetes mellitus onset are: polydipsia, polyphagia, and polyuria, along with overt hyperglycaemia which remains the hallmark in diagnosing type 1 diabetes mellitus in children and adolescents, less so in adults (Silverstein et al, 2005; Atkinson et al, 2014). The National Institute of Health and Care Excellence (NICE) guidelines also indicate that a child can feel excessive tiredness (2005).

Diabetic Ketoacidosis (DKA) which carries with it a mortality rate of 0.15-0.30% in Europe and North America in type 1 diabetic paediatric patients, is also the initial presentation in 15-67% of paediatric patients Europe and North America. This was also documented to be significantly high amongst Maltese paediatric population (Formosa et al, 2012).

Diabetes mellitus should be identified and treated immediately (Silverstein et al, 2005). A fasting blood glucose test result greater than 7mmol/L (126mg/dL) indicates the patient is diabetic. Other tests which can be done include random blood glucose test with results higher than 11.1mmol/L (200mg/dL) and abnormal result of 2-hour oral glucose tolerance test indicate patients having diabetes mellitus (Silverstein et al, 2005; Atkinson et al, 2014).

The American Diabetes Association modified their guidelines to include also the use of HbA1c as a test that can be performed. In this case, the glycated haemoglobin gives an

average blood glucose concentration over the past 3 months. A result of greater or equal to 6.5% indicates that the patient is diabetic (Atkinson et al, 2014).

1.5. Pharmacotherapy of Type 1 Diabetes Mellitus

The discovery of insulin in the 1920s was a breakthrough in the history of type 1 diabetes mellitus (Atkinson et al, 2014). Insulin dosage regimen is usually based on body weight, age and pubertal status (Silverstein et al, 2005).

Insulin therapy can be individualised in three basic types of insulin regimen as specified in The National Institute of Health and Care Excellence guidelines (Table 1.1). The Scottish Intercollegiate Guidelines Network guidelines and American Diabetes Association also refer to these regimens. The main aim is to maintain near normoglycemia as much as possible (Scottish Intercollegiate Guidelines Network 2014; National Institute of Health and Care Excellence,2015). In Malta, multiple daily dosing is used as mainstay of treatment for peadiatric type 1 diabetes mellitus patients.

Table 1.1 Different Insulin Therapies as per NICE Guidelines (2015)

A) Multiple daily dosing of insulin or basal-bolus insulin regimen (used in Malta): Short- acting insulin or rapid-acting insulin analogue before a meal e.g.: Aspart (NovoRapid®) or Human Regular Insulin (Humulin S®) Followed by one or more separate doses of intermediate- acting insulin or long-acting insulin e.g.: Insulin Glargine (Lantus®)
B) Continuous subcutaneous infusion: Gives regular or continuous supply of insulin, via subcutaneous route
C) From one to three insulin injections daily: These are short acting insulin or rapid insulin analogue mixed with intermediate-acting insulin e.g.: Human Isophane Insulin (Humulin I®)

Oral medication such as metformin with insulin therapy is used in type 1 diabetes mellitus patients who are within research studies, since the effect of this combination is uncertain. Other anti-diabetic oral treatment such as sulphonylureas and acarbose, with insulin should be avoided since they increase the risk of hypoglyceamia without any benefit (The National Institute of Health and Care Excellence, 2015).

The Scottish Intercollegiate Guidelines Network (SIGN) guidelines (2014) give a grade B to the statement stating that '*Children and adolescents may use either insulin analogues (rapid-acting and basal), regular human insulin and NPH preparations or an appropriate combination of these'*. Grade B recommendations mean that recommendations are based on a body of scientific evidence including studies classified

as high-quality systematic reviews of cohort or case and control studies with low risk of bias and high likelihood of establishing a fundamental relationship. It shows that the recommendation is directly relevant to the target population of the guideline and highly consistent with each other, or the scientific evidence inferred from studies classifies as high quality studies with very little or low risk of bias (1++, 1+) (Scottish Intercollegiate Guidelines Network, 2014).

A grade, more robust evidence and stronger recommendation, is given to pump/ continuous subcutaneous infusion given to children with limited improvements to glucose control and those unable to achieve targets. It is also suggested with a grade B, for those patients experiencing severe hypoglycaemia (Scottish Intercollegiate Guidelines Network, 2014).

Insulin available on the Maltese Formulary used in regimens for type 1 diabetes mellitus peadiatric patients are listed in Table 1.2.

Table 1.2 Types of Insulins Available on the Maltese Government Formulary List

Active ingredient	**Type of insulin**	**Regimen taken**
Insulin Aspart	Rapid Acting insulin	Given immediately before a meal If used patient cannot take soluble insulin concomitantly[4]
Soluble Insulin	Rapid Acting Insulin	Taken 20-30 minutes before meals[5]
Human Isophane Insulin	Intermediate acting insulin	Basal insulin and is usually given twice a day[6]
Insulin Glargine	Long Acting Insulin	This insulin is used only once a day, at the same time each day[7]

1.6. ACHIEVING GOOD GLYCEMIC CONTROL

To achieve desired glycemic control, dietary intake, blood glucose levels and administration of insulin have to be monitored closely (Freeborn et al, 2013; Cameron and Wherrett, 2015; The National Institute of Health and Care Excellence, 2015). Strict targets attempting to reach a glycated haemoglobin level very near to normal range is

[4] Summary of Product Characteristics for NovoRapid. Novo Nordisk A/S, 2009. Accesses via Internet: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000258/WC500030372.pdf on 20.8.16

[5] Humulin S Cartridge Summary of Product Characteristics. Eli Lilly and Company Limited. 2015. Accessed via Internet: http://www.medicinesauthority.gov.mt/medicine-details?id=85756 on 20.8.16

[6] Humulin I Cartridges Summary of Product Characteristics. Eli Lilly and Company Limited, 2015. Accessed via Internet: http://www.medicinesauthority.gov.mt/medicine-details?id=85755 on 20.8.16

[7] Lantus Summary of Product Characteristics. Sanofi Aventis, 2015. Accessed via Internet: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000284/WC500036082.pdf on 20.8.16

suggested so as to reduce the risk of patients developing long term complications (Atkinson et al, 2014; The National Institute of Health and Care Excellence, 2015). The strict control may cause stress and challenges on patients with type 1 diabetes mellitus, effecting their quality of life (Freeborn et al, 2013).

1.7. COMPLICATIONS OF DIABETES MELLITUS IN PAEDIATRIC PATIENTS

One of the major threats diabetes mellitus poses for its patients is that of long term damage, dysfunction and failure of different organs in the body, mostly the eyes, kidneys, nerves, heart and blood vessels (American Diabetes Association, 2010; Freeborn et al, 2013). Long term complications in children may be asymptomatic at first, however, conditions such as retinopathy have been noted in paediatric patients as early as 3.8 years of being diagnosed with diabetes mellitus (Benitez-Aguirre et al, 2011). Thus, glucose control in children with type 1 diabetes mellitus is of outmost importance for preventing or delaying these complications (Freeborn et al, 2013; Atkinson et al, 2014).

The International Diabetes Federation (IDF) considers diabetes mellitus as one of the most challenging health problems in the 21st century in the International Diabetes Federation Europe Region, because the above mentioned macro- and microvascular complications give rise to increased disability which in return, result in a huge financial constraint on an already decreasing working age population (Tamayo et al, 2014).

In type 1 diabetes mellitus, short term complications can be very serious. Two of which are *hypoglycaemia* and *extreme hyperglycaemia / DKA (Diabetic Ketoacidosis)* (Freeborn et al, 2013; Cameron and Wherrett, 2015). Both complications are a critical limiting factor for optimizing glycaemic control in patients (American Diabetes Association, 2005).

Hypoglyceamia was noted by clinicians during the development of insulin treatment, in 1922, and despite the improvement through time, it still remains a critical major burden in diabetic patients (American Diabetes Association, 2010).

Hypoglycaemia in type 1 diabetes mellitus is the most common acute complication and is considered a major problem amongst children with type 1 diabetes mellitus (Yardley et al, 2011; Sundberg and Forsander, 2013; Kalra, 2014; Ly et al, 2014). It is also the most common side effect of insulin treatment and impinges on everyday activities (Graveling et al, 2014). Hypoglycaemia is very often undetected, under-reported and poorly understood by the patients and their carers (Kalra, 2014). This lack of confidence in detecting, reporting and understanding hypoglycaemia puts the patients at risk of consequences of untreated hypoglycaemia which can range from seizures to premature death.

The American Diabetes Association (ADA) defines hypoglycaemia as *'any abnormally low plasma glucose concentration that exposes the subject to potential harm.'* As quoted in the American Diabetes Association, 2005, the Whipple's triad documents this clinical syndrome as one that exhibits symptoms when low concentrations of glucose are present and relief of these symptoms when the low plasma glucose is corrected. The American Diabetes Association and the European Medicines Agency (EMA) recommendations for threshold vary when defining hypoglycaemia. American Diabetes Association propose a threshold of <70mg/dL or 3.9 mmol/L while the European Medicines Agency set the threshold at <60mg/dL or 3.3 mmol/L (Kalra, 2014).

Hypoglycaemia can be classified as asymptomatic or biochemical depending on the presence or absence of symptoms together with glucose monitoring (Kalra, 2014). Hypoglycaemia can also be classified depending on the severity of hypoglycaemia

(American Diabetes Association, 2005; Kalra, 2014). There are five categories of hypoglycaemia namely:

i. Severe Hypoglycaemia where another person is required to assist the patient and administer carbohydrate, glucagon or other resuscitative actions. Severe hypoglycaemia can lead to seizures and coma.

ii. Documented symptomatic hypoglycaemia where typical symptoms of hypoglycaemia along with measures of plasma glucose less than or equal to 70mg/dL (<3.9mmol/L)

iii. Asymptomatic Hypoglycaemia consisting of measures of plasma glucose less than or equal to 70mg/dL (<3.9mmol/L) but no symptoms of hypoglycaemia

iv. Probable Symptomatic hypoglycaemia, typically consisting of symptoms of hypoglycaemia which are not accompanied by a plasma glucose determination but assuming that patient has low plasma concentration [measures of plasma glucose less than or equal to 70mg/dL (<3.9mmol/L)]

v. Relative Hypoglycaemia or Pseudohypoglyceamia whereby patients with diabetes mellitus experiences any typical symptoms however measuring plasma glucose concentration is greater than 70mg/dL (>3.9mmol/L) but approaching that level.

1.7.1. Symptoms and Complications of hypoglycaemia

Symptoms of hypoglycaemia are divided into those related to pathophysiology mechanism and those related to time of occurrence such as nocturnal hypoglycaemia (Kalra, 2014). The pathophysiology mechanism symptoms of hypoglycaemia are further subdivided into neurogylcopenic symptoms such as behavioural changes, difficulty to think, confusion, neuroglycopenic manifestations such as seizure, coma and even death

and neurogenic (adrenergic counter regulation) such as palpitation, tremor, hunger, sweating (American Diabetes Association, 2005; Graveling et al, 2014; Kalra, 2014).

In children, hypoglycaemia can also be noted when the child changes behaviour and becomes naughty or irritable (Graveling et al, 2014). Literature reviews indicate that hypoglycaemic episodes increase the risk of death by a six-fold factor, increase the cost of medical care and also loss of productivity (Kalra, 2014). Recurrent untreated hypoglycaemia leads to a vicious cycle of hypoglycaemia unawareness while frequent mild hypoglycaemia puts the child in risks for severe hypoglycaemic events with coma and seizures (Sundberg and Forsander, 2013). In children, hypoglycaemia can go unnoticed due to the age-appropriate cognitive immaturity and also the difficulties in understanding body sensations at such an age. Better tools and strategies, such as frequent testing of glucose levels, need to be implemented if neither the child nor the parent can recognise the hypoglycaemic episodes (Sundberg and Forsander, 2013). Severe prolonged hypoglycaemia can lead to coma, seizures and, death (Ly et al, 2014). Impaired concentration, behavioural changes and life threatening events are all reasons why prevention of hypoglycaemia is of utmost importance (Ly et al, 2014). Although the effect of type 1 diabetes mellitus and brain development remains controversial, and are not consistent across studies, repeated severe hypoglycaemia has been reported to effect long term memory, attention, and verbal IQ (Ly et al, 2014). Anxiety and morbidity are linked with nocturnal hypoglycaemia. Patients with type 1 diabetes mellitus are much less likely to be awakened due to nocturnal hypoglycaemic episode than non-diabetic patients. This leads to prolonged hypoglycaemia which may result in seizures and occasionally death (Ly et al, 2014).

1.8. BIO-PSYCHOSOCIAL EFFECTS OF HYPOGLYCEAMIA: FEAR

Hypoglycaemia is a biological effect which may have psychological implications. It is noted that hypoglycaemic events cause fear not only in children themselves but also in parents and carers (Haugstvedt et al, 2010; Haugstvedt et al, 2015). Studies, as quoted by Haugstvedt et al, in 2010, show that there is a positive association between parental fear of hypoglycaemia and episodes of severe hypoglyceamia, which lead to higher blood glucose levels being reported in children (Haugstvedt et al, 2010). Gonder-Frederick et al in 2006, report a relationship, that may play a part between the carers belief that the child has an emergency glucose constantly at hand and less fear of the hypoglyceamia. It was also noted that the parents fear causes negative health effects, long-term amongst type 1 diabetic children (Haugstvedt et al, 2015).

Another form of fear is parents sending children to school. The inadequate understanding of the disease and the fact that school personnel tend to underestimate the problems, cause parents and carers to lack confidence in the school's ability for the child to be managed should anything happen (Pinelli et al, 2010).

1.9. GLUCAGON: LIFESAVING PHARMACOTHERAPY

Glucagon is a single-chain polypeptide amino acid synthesized in the A cells of the islet cells. It is a fuel mobiliser which increases blood glucose and stimulates protein breakdown in muscle. Glucagon is stimulated by low concentration of glucose and fatty acid in plasma and inhibited by high concentration of glucose and fatty acid in plasma. Once released it will increase blood sugar and also increases the force of contraction of the heart. The two main actions of glucagon are increasing glycogenosis and increases gluconeogenesis (Rang and Dale, 2012). When used in diabetic patients, glucagon

mobilises hepatic glycogen which in return is released in the blood as glucose. It will have minimal to no effect in patients who have lost liver glycogens. Hence glucagon has no effect in patients who have been fasting for a long period of time, are suffering from adrenal insufficiency, have chronic hypoglycaemia and on alcohol induced hypoglyceamia[8]. Glucagon inhibits the tone and motility of the smooth muscles of the gastrointestinal tract and unlike adrenaline has no effect on muscle phosphorylase.

1.9.1. DOSING OF GLUCAGON[9]

The half-life of glucagon in blood is approximately 3-6 minutes, with the onset of action occurring within 5-15 minute of intramuscular dosing. This action lasts for around 10-40 minutes depending on the dose. Glucagon is available as 1mg/ml syringe for subcutaneous or intramuscular use. In children, the dose to be administered depends on the weight of the child. Children weighing more than 25kg, or older than 6 to 8 years should be administered 1mg (1ml) glucagon. Children weighing less than 25kg, or younger than 6 to 8 years should be administered 0.5mg glucagon. Patients can experience vomiting as a side effect. Once the patient has regained consciousness, a snack high in sugar should be administered to replenish the liver glycogen and prevent recurrence of hypoglycaemia. If the patient has not regained consciousness within 10 minutes, medical assistance should be sought and intravenous glucose administered.

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[8] Patient Information Leaflet, GlucaGen, Novo Nordisk A/S 2015. Accessed via internet https://www.medicines.org.uk/emc/medicine/4257 on 18.12.15

[9] Summary of Product Characteristics: GlucaGen, Novo Nordisk A/S 2015. Accessed via internet https://www.medicines.org.uk/EMC/medicine/4258/SPC/GlucaGen+Hypokit+1+mg/ on 18.12.15

1.9.2. AVAILABILITY OF GLUCAGON

In Malta glucagon injection is available on the government formulary list and is available as free medication to all patients who suffer from Type 1 Diabetes Mellitus, Type 2 Diabetes Mellitus, Gestational Diabetes and have a Pink Card or Schedule Five Entitlement.[10] In Malta glucagon injections are available as 1ml syringe together with one vial. The brand available is NovoNordisk[11]. Community pharmacies do not stock glucagon on the private market since all diabetic patients have access to free glucagon available on the Government Formulary List.

Mini-dose glucagon rescue is available in other countries. In this scenario, small doses of glucagon are delivered to the patient with an insulin syringe, to treat mild to moderate hypoglycaemia which is associated with gastroenteritis or decrease food intake (Hartley et al, 2006).

In the USA, both the mini-dose glucagon and the glucagon injection, comprising of a vial with powder and a syringe with water for injection to reconstitute glucagon, are available. Hartley et al in their article in 2006 state that the normal glucagon has a large needle, which leads to parents of children with type 1 diabetes mellitus, feeling reluctant to use. This led to the development of 'mini-dose glucagon rescue'. This treatment is used to treat mild or impending hypoglycaemia that is linked with gastroenteritis or patients

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[10] The Government Formulary List. Accessed via internet https://health.gov.mt/en/pharmaceutical/Pages/formulary/formulary.aspx on 11.1.16

[11] Medicine's Authority. Accessed via Internet: http://www.medicinesauthority.gov.mt/search-medicine-results?modSearch=sim&field=A0CAB2899E64C5CD on 30.8.16

refusing to eat. This low dose of glucagon is given subcutaneously with an insulin syringe. Carers are advised to keep a glucagon dose together with an insulin syringe. If child will be hypoglycaemic due to not eating food or gastroenteritis, the glucagon is diluted as per package information leaflet and draw up the solution into an insulin syringe. Unlike the glucagon injection, where dose administered is 1ml or 0.5ml depending on weight, patients here are administered in units (micrograms) as follows: patients who are less than 2 years of age are given 20 micrograms, from age of 2-15 years, dose is one unit (10 micrograms) per year of age. Maximum dose being 15 units.

If blood levels remain lower than 4mmol/l after 20 minutes, glucagon is re-administered, this time double the original dose. Blood glucose levels should be checked every 1-2 hours and if necessary the dose of glucagon is repeated every 2-3 hours as needed. Meanwhile the child is encouraged to take sugary drinks if possible (Hartley et al, 2006).

1.9.3. ADMINISTERING GLUCAGON

Administering glucagon is not straight forward and a series of steps need to be carefully followed in order to ensure safe technique and administration. For this reason, the aspect of empowering carers of young patients to develop better knowledge and confidence on the use of glucagon was identified as the focus of this dissertation.

The carer has to follow these steps:

I. Open the hard container and remove caps from the vial and needle

II. Insert the needle through the rubber stopper within the marked circle of the small vial

III. All liquid must be injected and the needle must be kept in the vial

IV. While holding both the syringe and the vial together, the vial is gently shaken until all the white particles are dissolved

V. One has to ensure that the plunger is completely down

VI. Once all solution is clear, the plunger is slowly withdrawn so all the solution is back in the syringe

VII. Care should be taken so the plunger does not come off from the syringe

VIII. The small vial is removed

IX. With the needle pointing upwards the syringe is tapped softly with your fingers so any air bubbles collect to the top of the syringe

X. Very gently, the plunger is pushed until all air is removed- this is noted since a small amount of liquid is pushed out

XI. Once this is done the syringe in injected into a muscle, such as the thigh.

1.9.4. STORAGE CONDITIONS AND STABILITY OF GLUCAGON INJECTION

Ensuring appropriate storage conditions of glucagon is of utmost importance to ensure efficacy of the drug. The glucagon injection container should be stored at a temperature of +2 to +8 degrees Celsius. It can be stored at room temperature (25 degrees Celsius) for up to 18 months as long as the expiry date is not exceeded. Freezing is not an option and

if the reconstituted solution produces signs of insoluble particles this should be discarded immediately[12] (National Institute for Health Care and Excellence, 2015).

Current glucagon preparations are acidic, lyophilised formulations. Once it is reconstituted, preparation must be used immediately to decrease the risk of aggregation (Steiner et al, 2010; Caputo et al, 2014). Two major reasons why glucagon does not exist as a pre-filled syringe is due to the aggregation that can form and the chemical degradation that happens after the reconstitution is made and solution is allowed to settle (Caputo et al, 2014). The stability is dependent on temperature, conformation and the interactions both at solid state and in solution (Steiner et al, 2010). Aggregated glucagon is cytotoxic at high concentrations and also has delayed actions when compared to fresh glucagon in vivo. When aggregation happens the solution forms insoluble gel particles that impart cloudiness in the solution. Various ways have been tested to find a preparation that can remain stable. Caputo et al, 2014 tested solutions such as increasing the pH of the solution to pH 9, this showed significant loss of potency, however when same solution was added to cumin-stabilised formulation difference was not significant when compared to a fresh solution, in live pigs (in vivo). This resulted in a solution that was stable for 7 days. A limitation in this research was that the study lacked experiments on shelf-life stability for long term stability (Caputo et al, 2014).

Steiner et al, 2010, concluded that the solution tested from their end presented 90% of the original glucagon for more than 10 days at the temperature of 37 degrees Celcius.

[12] Summary of Product Characteristics: GlucaGen, Novo Nordisk A/S 2015. Accessed via internet https://www.medicines.org.uk/EMC/medicine/4258/SPC/GlucaGen+Hypokit+1+mg/ on 18.12.15

Both mentioned papers have looked into glucagon use in pumps and not for long term shelf life of glucagon preparations.

1.10. Management of hypoglycaemia at Mater Dei Hospital- hypoglycaemia Management Guideline

Hypoglycaemia can be triggered by many factors such as excess insulin dosing; less food consumption, exercise, sleep and in older children alcohol. Risk increases when patients are of a younger age (less than 6 years) since it is difficult to predict the food consumption and physical activity (Ly et al, 2014). Patients with longer duration of diabetes mellitus and those patients who suffered from previous severe hypoglycaemia pose a higher risk for hypoglycaemia. Early warning signs should be noted immediately and appropriate treatment used. Equipment to measure blood glucose must be accessible for confirmation and safely manage hypoglycaemia (Ly et al, 2014). A source of glucose must always be available to all children suffering from diabetes mellitus, for immediate use in case of hypoglycaemic episode (Ly et al, 2014).

Mild hypoglycaemia associated with mild symptoms and signs consisting of mild adrenergic and cholinergic symptoms such as sweating, pallor, tremors, and occasionally headaches and behaviour changes relating to neuroglycopenia. This is generally treated with 15g of an easily absorbed carbohydrate followed by a protein containing snack (Silverstein et al, 2005). Glucose levels, when tested with a glucose meter, will be at 3.3-3.9 mmol/l. The grams of carbohydrates required vary depending on the weight of the patient, the type of insulin therapy and timing (Ly et al, 2014).

Symptoms of moderate hypoglycaemia include aggressiveness, drowsiness and confusion and are evident together with autonomic symptoms with blood levels documented at less than 4.4 mmol/l. Management of moderate hypoglycaemia requires

oral treatment of 20-30g of glucose in order to restore the blood glucose levels. Very often the oral treatment is used however it is administered by someone other than the patient (Silverstein et al, 2005). The type of carbohydrate needs to be selected carefully since 40g of carbohydrate in the form of juice is required to give the same rise in blood glucose as 20g in the form of glucose tablets. Sucrose requires more grams when compared to glucose for the same rise. Milk, chocolate and other fatty foods will cause glucose to be absorbed more slowly and are to be avoided in the initial management of hypoglyceamia. After this is given to the patient, retesting of blood glucose levels are necessary after 10-15 minutes to determine if the response is adequate or not. If no response or inadequate response, oral intake is repeated. Complex carbohydrates, such as fruit, bread, cereal or milk, can be consumed to prevent further episodes of hypoglycaemia (Ly et al, 2014).

In severe hypoglycaemia, when the patient is unconscious and or unable to take oral treatment due to disorientation, glucagon is administered intramuscularly or subcutaneously (American Diabetes Association, 2005). Harris et al, (2001) concluded that glucagon administration is not as simple as it seems and that hands-on education is better than mere demonstration.

The guidelines at Mater Dei Hospital which are not only specific to children, define hypoglycaemia as blood glucose levels less than 3.0mmol/l. First line investigations stated include random blood glucose, blood glucose monitoring, urea+ electrolytes and creatine. Management is in line with the above guidance whereby if patient is conscious and able to swallow, glucose or sugary drink is given orally. If patient is unconscious a health care professional, in hospital has two options. The first option is to administer aliquots of 100ml of 10% Dextrose IV over 5-10minutes. This can be repeated as

necessary and is then followed by 10% dextrose IVI plus a snack after patient is consciously awake.

The second option is to give 1mg of glucagon intramuscularly plus 5% dextrose IVI followed by a snack when consciousness regained.

Blood glucose monitoring is a must at 15 minutes, 30 minutes and 60 minutes interval[13].

1.11. RAISING AWARENESS AND PROVIDING EDUCATION

Holistic education about diabetes mellitus including how to identify symptoms and knowing signs of hypoglycaemia are imperative (Freeborn et al, 2013; National Institute of Health and Care Excellence, 2015). Freeborn et al, (2013) concluded that interventions and education must address prevention along with management of hypoglycaemia while promoting regular childhood activities.

The National Institute of Health and Care Excellence guidelines published in August 2015 include the importance of education about detecting and managing hypoglycaemia (National Institute of Health and Care Excellence, 2015). Educating parents or carers who have children with type 1 diabetes mellitus, on management of the disease, is essential to minimise the impact of hypoglyceamia (Martin et al, 2012; Seaquist et al, 2013). If the child is a toddler one might not recognise the symptoms of hypoglycaemia due to lack of communication- change in behaviour such as loss of temper is what one must note as signs of hypoglyceamia. Puberty on the other hand is associated with insulin resistance while patients tend to give less attention to diabetes leading to increasing the risk for

[13] MDH guidelines on Hypoglyceamia Management Guideline. Department of Medicine. April 2010. MED/02/GUIDE/2009/v01.1 Accessed via KURA on 20.6.16

hypoglyceamia. As the child is growing, wide fluctuations of activities throughout the day lead to patient being placed at risk of hypoglycaemia (Seaquist et al, 2013).

Evidence based studies indicate that education and intensive diabetes case management in children with type 1 diabetes families, and close telephone contact with the diabetes team are related to decreased hospitalisation and emergency room visits (American Diabetes Association, 2005; Silverstein et al, 2005). This in return is more cost saving (American Diabetes Association, 2005). Ly et al, 2014, stress the importance of education on hypoglyceamia, playing a key role in diabetes care. Patients and families should be educated on the causes, effects, treatments and prevention of hypoglycaemia. Awareness should be incorporated in routine clinical reviews, since as stated previously impaired hypoglycaemia awareness increases risk of severe hypoglycaemia, significantly. Emphasis of education on administration of glucagon was highlighted while carers are to be trained on how and when to use it (Ly et al, 2014). The National Institute of Health and Care Excellence guidelines also state that carers should be adequately informed and trained to give intramuscular glucagon for severe hypoglycaemic episodes (2015). Harris et al, 2001 concluded that glucagon administration is not as simple as it seems and that hands-on education is better than mere demonstration.

1.12. HEALTH LITERACY

Health literacy (HL) is described as: ‘the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate heath decisions’ (Pulgaron et al, 2013).

In diabetes mellitus health literacy can be summarized as reproduced in Table 1.3.

Table 1.3 Health literacy in Type 1 Diabetes Mellitus [14]

Reading Skills	Understanding written text and management plans are important
Numeracy skills	This is especially important to manage dosing and monitoring of blood glucose together with diet and activities carried out
Navigation skills	Accessing resources amongst them being the clinic, clinician and other services

Risk factors for HL comprise of age, genetics, language, educational status, environment (Ferguson and Pawlak, 2011). In the USA, it is estimated that only 12% of the 228million US adults have the necessary skills to be able to manage their own healthcare appropriately (Ferguson and Pawlak, 2011). While nearly half of all adult Americans, have difficulty understanding and taking action on health information (Ferguson, 2012). Health Literacy is described as the 'currency' whereby the quality of US health, healthcare and health outcomes are improved (Ferguson and Pawlak, 2011). Poor HL effects health behavior, decisions and outcomes (Ferguson, 2012).

Health literacy is of outmost importance since it has been noted that parents' health literacy is associated with better management of diabetes mellitus. In other words, if parents have low HL correlates with poorer glyceamic control in school aged children. It

[14] Adapted from Pulgaron E.R., Sanders L.M., Patino-Fernandez A.M., Wile D, Sanchez J, Rothman RL, et al. Glyceamic control in young children with diabetes: The role of parental health literacy. *Elsevier.*2014; 94: 67-70

is hypothesized based on the adult HL literature, that if parent have low HL this will result in children having poorer glyceamic control (Pulgaron et al, 2013).

Pictograms can be used for medication counseling to reduce medication errors and improve adherence amongst patients who have low health literacy (Ferguson and Pawlak, 2011). These interventions help improve patients understanding. Decreasing health literacy will in return increase better health outcomes (Ferguson, 2012).

1.12.1. Material used to support Health Literacy

Educational material and leaflets with pictures in conjunction with a short video will improve comprehension of complex topics (Ferguson, 2012). Research suggests that the knowledge and understanding by patients can be increased by using visual images and words in video technology (Ferguson, 2012). Besides use of simple to the point pictures with short texts explaining the picture also allow low health literacy people to understand well and enhances better communication of instructions (Kripalani et al, 2007; Peregrin, 2010). This is also noted by Hill- Briggs and Smith, in their paper in 2008, where it states that individuals with low literacy themselves pinpoint brochures or books as the primary source from which they obtain information, with printed materials proving effective as an intervention tool (Hill-Briggs and Smith, 2008).

A video in conjugation with leaflets that helps highlight the key points in simple terms together with pictures can be very effective to improve patient education (Hill-Briggs and Smith, 2008; Ferguson, 2012). Video is an underutilized medium that can be helpful as an educational tool. According to Krouse, quoted by Ferguson in 2012, it mentions that three major uses for a video are to assisting with making decisions, to decreasing anxiety about the procedures and to teaching self-care practices. Using video with written text

and pictures together with spoken text increase attention, understanding and recall of health information. It enables patients to visualize better and thereby understand more the information given (Ferguson, 2012). The combination of visual together with written printed information can increase memorization of health information (Houts, 2006; Peregrin, 2010; Ferguson, 2012). One needs to also keep in mind that people with low health literacy tend to concentrate only till around 8 minutes, therefore if a lot of information is given to them it can actually have an opposite effect (Ferguson, 2012).

1.13. PATIENT AND CARER EMPOWERMENT

Holistic education about diabetes mellitus, including how to identify symptoms and knowing signs of hypoglycaemia, is vital (Freeborn et al, 2013; The National Institute of Health and Care Excellence, 2015). Freeborn et al (2013) concluded that interventions and education must address prevention along with management of hypoglycaemia while promoting regular childhood activities. The National Institute of Health and Care Excellence (NICE) guidelines published in August 2015 include the importance of education about detecting and managing hypoglycaemia (The National Institute of Health and Care Excellence, 2015). Educating parents and or carers who have children with type 1 diabetes mellitus on the management of the disease is crucial to minimise the impact of hypoglycaemia (Martin et al, 2012; Seaquist et al, 2013). If the child is a pre-verbal toddler, the symptoms of hypoglycaemia may not be immediately recognised due to lack of communication- change in behaviour, such as loss of temper, is what one must note as a possible, but not definite, sign of hypoglycaemia. Puberty, on the other hand, is associated with insulin resistance while patients tend to give less attention to diabetes. As the child is growing, wide fluctuations of activities throughout the day lead to patient placed at risk of hypoglycaemia (Seaquist et al, 2013).

The American Diabetes Association issued a statement stressing that studies indicate that education and intensive diabetes mellitus care management in families with children with type 1 diabetes mellitus, together with close telephone contact with the diabetes team are related to decreased hospitalization and emergency room visits (Silverstein et al, 2005). This in return is actually cost saving (American Diabetes Association, 2005). Ly et al (2014) stress the importance of education sessions on hypoglycaemia, playing a key role in diabetes care. Patients and families should be educated on the causes, effects, treatments and prevention of hypoglycaemia (Freeborn et al, 2013; Ly et al, 2014). Hypoglycaemia awareness should be incorporated in routine clinical reviews, since impaired hypoglycaemia awareness significantly increases risk of severe hypoglycaemia (Ly et al, 2014). Furthermore, Ly et al, (2014) emphasise the importance of education on administration of glucagon. Carers are to be trained on how and when to use it.

1.13.1. BARRIERS TO EFFECTIVE GLUCAGON USE

Tamayo et al, 2014, have pointed out four barriers to effective care. These barriers are:

a. The patient

One important barrier is the patient lacking basic information. Pharmaceutical interventions can motivate the patient to change behaviour or adhere to treatment.

b. The individual professional

Another barrier may be the individual professional, such as inadequate knowledge of guidelines decreasing effective interventions that can be done and lack of motivation. Employing the right communication skills and appropriate interventions these barriers can be eliminated.

c. The health care team

This barrier is due to the lack of communication which is present between the different members of the healthcare team.

d. The organisation of the health care system

Barriers such as lack of disease registers and lack of guidelines impact effective care.

1.14. PHARMACEUTICAL CARE

Since 1969 the American Pharmacists Association's code of ethics highlighted the duty of the pharmacist, *'to extend all of their abilities to the patient'* (Cruthirds et al, 2013). The knowledge and expertise of the pharmacist must be used to ensure that patients' health takes first priority. Cruthirds et al, (2013) continue by quoting Hepler and Strand, were in 1990 the latter defined pharmaceutical care as being '*instrumental in advocating a more patient-centred role within pharmacy practice models'*. A study carried out in 2000 showed that there was 78% decrease in the rate of preventable adverse drug events when a pharmacist was included in the rounding team (Cruthirds et al, 2013). Apart from this many documentation stress the benefits of pharmacist-provided medication education, which lead to decreased costs and better patient satisfaction (Goldstone et al, 2015). Lack of information to the patients, together with lack of understanding are barriers to non-adherence by the patient. Clifford et al (2006) in their article *'Patient centred advice is effective in improving adherence to medication'* highlight that when a pharmacist provides information about newly started medication for chronic disease, a significant reduction in patients non-adherence is seen. The patients also altered their beliefs about the medicine taken- the risk benefit ratio beliefs was shifted more towards benefits and reduction in medicine related problems noted (Clifford et al, 2006). The

pharmacist is in a position to provide medication education and target this adherence to help reduce hospitalization and costs (Goldstone et al, 2015). Pharmacists in a clinical setting are primary source of advice and information on safety of medication appropriate use and cost effective treatment (Sabre and Samar, 2014).

Another pivotal intervention the pharmacist can make, is that of creating and providing prints or online material to both patients and other healthcare professionals on topics such as optimal medication use and general health as underlined by the American Society of Hospital pharmacist[15].

1.15. AIM

The aim of this research was to develop and evaluate the impact of educating carers of paediatric patients suffering from type 1 diabetes mellitus, on the emergency use of glucagon in hypoglycaemia in a safe and effective way.

1.15.1. OBJECTIVES

The objectives were to:

i. Assess the knowledge and perception of carers of type 1 diabetes mellitus patients on hypoglycaemia and on its management with a special reference to use of glucagon

[15] ASHP Guidelines on the pharmacist's Role in providing Drug Information. Medication Therapy and Patient Care: Specific Practice Areas- Guidelines. Accessed via internet http://www.ashp.org/DocLibrary/BestPractices/SpecificGdlMedInfo.aspx on 11.1.16

ii. Implement pharmacist-led education and counselling sessions on the safe use and administration of glucagon in order to optimise glucagon pharmacotherapy targeting patients and their carers

iii. Increase the awareness and education amongst healthcare professionals on the use of glucagon and to analyse the outcomes and satisfaction of a pharmacist-led service offered

1.16. THE SETTING

Currently there are 140 paediatric type 1 diabetes mellitus patients till the age of 16 who visit the outpatient's paediatric diabetic clinic at Mater Dei Hospital. Once patients are above this age they are then transferred to an adult diabetologist of their preference.

Generally, if well controlled these paediatric patients visit the consultant paediatric endocrinologist approximately every 3 months. Appointments are mainly booked either every Tuesday or every Friday from 12.30 to 3.30 pm. Blood tests namely HbA1c are taken for monitoring factors. During their visit parents/carers present a diary with readings of the blood sugar levels throughout the past 3 months and it is discussed if the treatment taken is giving optimum desired control of blood sugar and whether other factors are influencing the results obtained. The treatment the child is on is also noted. The child is weighed and the dosage of insulin is recalculated accordingly to ensure that the child is taking the required dose based on weight.

CHAPTER 2

METHODOLOGY

2.1. METHODOLOGY

The research methodology is based on two phases. Phase 1 consisted of the development of the Glucagon Tool Kit, which contains material complied by the researcher to suit the Maltese population. The Glucagon Tool Kit consisted of the information leaflet, video and chart along with the questionnaires required to carry out the pharmacist-led education on glucagon use. This Glucagon Tool Kit was evaluated during the implementation study phase (phase 2) involving carers of type 1 diabetes mellitus children attending the diabetes clinic, and pharmacists.

2.2. LITERATURE REVIEW

Extensive literature review was carried out to bring to light the published studies and previewed articles assessing glucagon use by carers of paediatric type 1 diabetic patients.

Arrays of databases were searched using variety of word combinations. Some keywords and phrases used while researching were: 'type 1 diabetes mellitus', 'glucagon use', 'glucagon use in type 1 diabetic children', 'hypoglycaemia and glucagon use', 'fear of using glucagon', 'improving health literacy'. The major databases used were: Science Direct, Elsevier, HyDi- Hybrid Discovery, MEDLINE, Google Scholar. Journals which were an important source of reference are Paediatric Diabetes, Diabetes Care, Lancet, Journal of Paediatrics and Child Health, Journal of Clinical Nursing, Practical Diabetes International. Guidelines which were referred to were the latest relevant NICE guidelines and American Diabetes Association together with SIGN guidelines and those used at Mater Dei Hospital. Information on glucagon was obtained from the summary of product

characteristics (SPC)[16] and product information leaflet(PIL), Up-to-date and Micromedex database.

2.3. Development of Glucagon tool kit required for pharmacist-led education sessions

Phase 1 of this research consisted of the development of the Glucagon Tool Kit for carers of children with Type 1 Diabetes Mellitus (T1DM). The material developed consisted of:

1) Development of pharmaceutical advice in the form of a leaflet (Appendix 2E)
2) Development of a video on reconstitution of glucagon (Appendix 2F)
3) Development of a chart on reconstitution of glucagon (Appendix 2G)

2.3.1. Development of Leaflet

Upon reviewing the material that was provided to patients it was noted that advice on how to reconstitute glucagon was lacking. Pharmaceutical advice was designed to provide carers with a holistic approach on this phenomenon from when blood glucose levels decrease to just below 3.9mmol/litre, to moderate hypoglycemia, and severe hypoglycemia.

Special focus was given on how to reconstitute glucagon, how to store it and dosage regimen, together with any other relevant information.

[16] Summary of Product Characteristics: GlucaGen, Novo Nordisk A/S 2015. Accessed via internet https://www.medicines.org.uk/EMC/medicine/4258/SPC/GlucaGen+Hypokit+1+mg/ on 18.12.15

Information was mostly obtained from the SPC and simplified. This material was provided in both Maltese and English. The pharmaceutical advice leaflet was validated by a panel of experts made up of pharmacists, doctors and a Bachelor of Science graduate.

Suggestions put forward were taken into consideration and the final version of the information was developed. The information was kept short, concise and to the point. As much as possible jargon used was kept simple. Since information given to patients, about what hypoglycemia is, was already given to parents and carers by the nurses at the diabetes clinic, this was not included. Another reason this was not included is so that focus is on the preparation and use of glucagon.

Advice on what to do after glucagon administration was also highlighted and emphasized by placing it in a box and using bold font:

Once the patient has regained consciousness a snack high in sugar should be administered to restore the liver glycogen and prevent another episode from occurring. If patient has not regained consciousness within 10 minutes, then intravenous glucose should be administered or medical assistance sought.

After validation, the phrase was compressed and simplified to:

Once the patient has regained consciousness a snack high in sugar should be administered to prevent another episode from occurring. If patient has not regained consciousness within 10 minutes, then medical assistance is sought.

A cover with title was selected. Clear legible format was chosen, with font 12 and double line spacing. The document was also referenced.

To explain better the 6 months' decrease when the glucagon injection is stored at temperature above 8 degrees Celsius the phrase was amended by adding an example.

In other words, you should reduce 6 months from the expiry date written on the box. Example: if the expiry date states 5.2018, reduce this to 11.2017

This example was based on the new glucagon injection that the researcher had to display.

2.3.2. Development of video

A professional videographer was contacted in order to create a video capturing the steps of how to administer the glucagon. The video was kept concise and short in order to facilitate its use. Filming took place on a white backdrop using special equipment so every detail will be captured. Voice was then recorded and editing done to come up with a final product. Length of the video was kept to approximately 1 minute 40 seconds.

The validation of the video in Maltese and English was carried out by a panel of experts consisting of pharmacists, doctors and a Bachelor of Science graduate and non-medical people, in order to ensure that it is clear and understandable. A common comment lead to the addition of the glucagon injection itself being injected, to make the video complete.

Availability of the video to all patients was also an issue that had to be tackled. The video was made available online such that it is freely accessed from literally anywhere and anytime by anyone. Relatives can therefore easily access the link at any point in time. Vimeo.com was the site chosen. This site also gave the ability for one to alter the URL so to make it easier for users to access it and remember the link. A version of the video in both Maltese and English were uploaded on link shown in Figure 2.1.

Figure 2.1 Internet Link to Video on Reconstitution of Glucagon.

http://vimeo.com/glucagon/1

http://vimeo.com/glucagon/2

2.3.3. Development of a chart on reconstitution of glucagon

A chart (Appendix 2G) was developed in order to enable carers to have a complete guide on how to use glucagon. The main aim of the chart was that parents will keep it in a place that will be easily accessible if the child develops a hypoglycemic attack and can be followed if necessary. The chart compiled in both Maltese and English was supplied back to front and consisted of 6 images taken from the video with short explanations written underneath each image. The video URL was also included in the chart. This chart was printed in full colour and laminated so that it will remain intact.

2.4. Development of questionnaires

Three questionnaires were developed in total, two for use with carers of type 1 diabetic patients, to be used one before and one after intervention, and the third questionnaire for use with the pharmacists.

A glucagon assessment questionnaire for before educational intervention [17] and a glucagon assessment questionnaire for after the educational intervention with carers of patients with type 1 diabetes mellitus were designed. The aim of these questionnaires was to get an understanding of what patients know about hypoglycaemia and of the use and reconstitution of glucagon. A comparison between before intervention and after the intervention was made to identify the impact the information given by the pharmacist had. The aim of this questionnaire was to analyse the use of glucagon amongst

[17] The educational intervention consists of dissemination of the Glucagon Tool Kit, which is made up of the Information Sheet, Video and the Chart.

pharmacist, together with looking into the outcome and satisfaction of the pharmacist led service.

2.4.1. DESIGNING OF THE QUESTIONNAIRES

The importance of educating and training carers of paediatric patients with type 1 diabetes mellitus on the emergency use of glucagon in hypoglycemia, in a safe way was observed from the literature review and also upon spending time with the clinical team at Mater Dei Hospital.

The first questionnaire entitled 'Glucagon Assessment Questionnaire Before Intervention' (Appendix 2C) was developed. Section A of this questionnaire, entitled Demographics Data Sheet (Appendix 2B), allows for the below data to be collected:

A. Carer: Gender, age, level of education, diabetic or if carer has ever dealt with any other person who was diabetic and on insulin treatment.
B. Child: Gender, age, year of onset of diabetes and how it was discovered.
C. How informed carers think they are about: meal planning, medications taken, hyperglycemia, hypoglycemia, support for the disease.
D. Medications taken by child and how long child has been taking this treatment
E. If carer is satisfied with the glycemic control at the moment and the HbA1c reading
F. If child suffers from any other condition and any other medications taken
G. If they have glucagon injection at home

Section B of the 'Glucagon Assessment Questionnaire Before Intervention' (Appendix 2C), was designed to obtain all information that the carer knows on hypoglycemia and the use and preparation of glucagon itself. The aim was to collect carer's knowledge

before the intervention, this being considered as control at baseline.

This questionnaire enables the below information to be collected and evaluated:

a) Introduction, questions 1,2,3 gather information on if child has ever experienced a hypoglycemic attack, and if so its severity. If the child was ever hospitalized due to this and if glucagon was ever administered by the carer.
b) Evaluation on the carer's knowledge – definition of hypoglycemia, mode of action of glucagon, why glucagon is used, is looked into by questions 4, 5, 6.
c) Symptoms the child experiences when hypoglycemic, are sought in question 7.
d) Use of glucagon-if they have glucagon injection at home and if it is carried around with them, where glucagon injection is stored and what happens if they take it out of the fridge. This section also evaluates if the carer was ever thought on how to administer and use glucagon and if they consider themselves informed well. Question 14 requests the carer to shortly explain how the glucagon is prepared and question 15 follows with some statements that are important to follow. Here carers are questioned how important, from 1(being the least important) to 5(most important) the statements are. This section also questions the dose that the carer would give to the child, question 16.
e) Fear and confidence on administration of glucagon – this aspect is also looked into by question 18, 19, 20, 21,22. Fear of use of glucagon, fear of leaving child with other people, fear that child will develop hypoglycemia and what actions are taken to avoid this.
f) Advise by carer to other carers and assistants in school on the use of glucagon is also evaluated.

To facilitate analysis of question number 14, a sample answer was noted and the researcher gave the carer a grade during questioning to be able to compare the before and after reply. This was due to the question being an open-ended reply and so a quantitative approach was used.

The sample answer was:

1) Inject the syringe into the vial with powder
2) Mix – holding both the syringe and vial together
3) Withdraw the liquid once dissolved
4) Remove air
5) Inject into muscle

This question carried 5 marks depending on how many of the above points are mentioned as a reply. Each point carrying 1 mark.

The second questionnaire entitled: 'Glucagon Assessment Questionnaire After Intervention' (Appendix 2D) was developed by applying alterations to the first questionnaire, used before intervention. The Glucagon assessment questionnaire After intervention (Appendix 2D) was used with the same cohort of patients four weeks after the intervention. It was used to evaluate if, with the intervention patients gained more knowledge than what they previously knew.

Some questions were removed to ensure that the questionnaire is to the point and those questions that were not subject to change were removed. These are questions: 7, 12, 20, 21A, 22B, 23.

Addition of questions 20 – 25 help analyse the usefulness of the material provided. Questions looked into how useful the material provided was, if the material provided was

used and if the confidence level on use and administration of glucagon increased. Carers were then asked to state if they think they required any other information they wish to receive.

The third questionnaire created was that for pharmacists (Appendix 2H). This short questionnaire is used to gauge the pharmacists' perspective on the use and administration of glucagon and on the usefulness of the material provided. All information created was incorporated in the questionnaire created and supplied to pharmacists via email via the Pharmacy Council database. Google Forms was used to create the questionnaire. In this way, all pharmacists registered with the pharmacy council received the information and so resulting in more accessibility. This allows also to divide the questionnaire into sections. Since the information provided, the Glucagon Tool Kit, was incorporated in the questionnaire, at the end of the questionnaire, email address of the researcher was supplied so if the material was required, soft/hard copy will be provided.

Two sections were used. A covering letter was also written as an introduction to the questionnaire. This was followed by section One on general information. It consists of area of practice, gender and age. It then moved on to general questions to gauge if the pharmacist has any personal experience with diabetes and insulin via relatives or close family or even the pharmacist him/herself. The questionnaire also analyses if the pharmacist has ever used glucagon, provided advice or had any requests for advice for glucagon. If advice was given the frequency was also noted.

Before the Glucagon Tool Kit was supplied to the pharmacist a fundamental question was asked with regards to the expiry date of the medication in question and what happens if the glucagon injection was stored at room temperature.

All material – Glucagon Tool Kit (information sheet, chart and video link) were uploaded for all pharmacists. Following this, questions to rate knowledge and confidence on use administration of glucagon before and after the information provided and if the pharmacist thinks there is adequate awareness on glucagon were requested.

To close off the questionnaire pharmacists were asked to rate, how informative and useful the Glucagon Tool Kit was and how concise the video clip was.

2.5. VALIDATION OF QUESTIONNAIRES AND RELIABILITY TESTING

Table 2.1 gathers all questionnaires created and the testing done to validate questionnaire and ensure reliability. All were reviewed by a panel of experts.

Table 2.1 Validation and Reliability Testing of the Questionnaire

<table>
<tr><th colspan="2"><u>Questionnaire</u></th><th><u>Validation</u></th><th><u>Reliability testing</u></th></tr>
<tr><td rowspan="2">1) Glucagon Assessment Questionnaire Before the intervention</td><td><u>Section A:</u> Demographics</td><td rowspan="3">Carried out by panel of 10 experts: Paediatric Consultant Endocrinologist,

5 pharmacists amongst them Medical practitioner, graduates in Science, two non-medically associated people.</td><td rowspan="2">Inter-rater reliability test used: Carried out on 8 diabetic patients and 2 carers of type 1 diabetic patients; patients were questioned by researcher then same person was re-questioned by another researcher, results obtained were then compared.</td></tr>
<tr><td><u>Section B:</u> Glucagon Assessment Questionnaire</td></tr>
<tr><td>2) Glucagon Assessment Questionnaire After the Intervention</td><td><u>Section B:</u> Glucagon Assessment Questionnaire</td><td>Carried out by 5 pharmacists. Test re- test method after 2 weeks was used.</td></tr>
<tr><td colspan="2">3) Pharmacist Glucagon Assessment Questionnaire</td></tr>
</table>

2.5.1. ALTERATIONS MADE TO QUESTIONNAIRES AFTER VALIDATION

No major alterations were done to Section A of the glucagon assessment questionnaire before intervention, the demographics section. It was noted that all basic information was gathered to help give an insight to the carer being interview.

After validation, section B of the glucagon assessment questionnaire before intervention, was altered to help make it more patient friendly and uniform in the way it looks. Such as grouping together, where possible, the same style of questions. E.g. open ended, yes/no or Likert Scale questions.

When a Likert scale was used, it was reduced to 1-5 not 1-10 since it was simpler and the same outcome obtained.

Table 2.2 gathers how questions 4, 5, 6 were proposed initially before the validation of the questionnaire, and how the final version was presented to patients in the questionnaire.

Table 2.2 Changes done to questions in the questionnaire before and after validation

Proposed questions before validation	**Finalized questions after validation**
4) How can hypoglycemia be best described? Blood sugar levels drop below 4mmol/l □ True □ False □ Do not know	4) Hypoglycemia is best described as a blood sugar level below 4mmol/L □ True □ False □ Do not know
5) How does glucagon work? It unlocks glucose in the liver so it will increase blood glucose □ True □ False □ Do not know	5) Glucagon works by unlocking glucose in the liver so it will increase blood glucose □True □ False □ Do not Know
6) When is glucagon used? __ Low sugar levels ___ high sugar levels ___Do not Know	6) Glucagon is used when blood sugar levels are low □True □ False □ Do not Know

Question 9 queried if glucagon injection is kept in another place other than at home. Additional questions were added to question 9 to analyze if patients carry glucagon injection with them, when and where it is carried around and if no why and what do they do if it is not with them and they need to use it.

Question number 11 was changed from 'If you store glucagon at room temperature, does it expire as stated on the label or do you have to change the expiry date?' to more simple wording 'If you store glucagon at room temperature, what will happen to its expiry date?'.

Furthermore, if carers selected the option that the expiry date is shortened, a sub question to how much you would reduce the expiry date to, was added.

Question number 23 states if teachers at school are informed on what happens if hypoglycaemia occurs, more questions were added to investigate the reason why school is not informed about the use of glucagon, and what is done if the child develops a hypoglycemic episode in this case.

Since the glucagon assessment questionnaire after four weeks was based on the glucagon assessment questionnaire, were applicable same alterations were made.

The 'Pharmacist Glucagon Assessment Questionnaire' was kept as simple and brief as possible, while still gathers relevant information on the use and administration of glucagon.

All areas of practice were listed as much as possible in question 1, where pharmacists are asked to tick their principal employment.

Question number 4 and 5 were initially one as follows: '*Are you or any member of your close family, diabetic?'*

It was however suggested that these questions are divided into two and 'diabetic' was further specified to 'insulin dependent diabetic'.

Question on glucagon storage was also changed from a yes or no question, asking if glucagon can be stored at room temperature, and if so will the expiry date change, to a more professional question. The version presented stated phrases which the pharmacist has to select as being the correct phrase.

2.6. Approvals for research

University Ethics Approval was sought and granted (Appendix 1A; Appendix 1B; Appendix 1C).

2.7. Patient consent form and study information sheet

All carers who agreed to participate in the research were given a study information sheet (Appendix 2A) and asked to sign a consent form (Appendix 1D). The carer had the option to choose between English or Maltese version. The consent form made clear that the patients' identity was safeguarded together with complete confidentiality. Patient was given explanation on the research itself via the study information sheet (Appendix 2A).

Patient's participation was a selective one. Carers were eligible to participate in the research if the patients satisfied the inclusion criteria in Table 2.3. Patients were excluded from the research if they were newly diagnosed type 1 diabetes mellitus patients.

Table 2.3 Inclusion Criteria

Carers of pediatrics who are type 1 diabetic
Children with T1DM who are under the care of the participating clinician
Able to understand English or Maltese
Not suffering from mental illness or impaired cognition
Carer is above the age of 18 years
Able to converse with the investigator
Willing to participate in the research and sign the consent form

2.8. Implementation of Glucagon Tool kit at the Diabetes Clinic

Figure 2.2 shows a general overview of how the intervention was carried out. Once patient was recruited, glucagon assessment questionnaire before intervention (Appendix 2C) was filled in. This helps to gauge the information the patient's carer had on glucagon and the experience they had with this medication. This questionnaire was considered as control. It was decided that patients will not be divided into control or intervention between themselves since we are dealing with information for children and parents talk between themselves. In order to eliminate any discrimination that can occur it was decided that the same patient is both control and intervention.

The questionnaire was filled in by the interviewer, who was sitting next to the carer, whereby carers replied to the questions read by the interviewer verbally and then noted down.

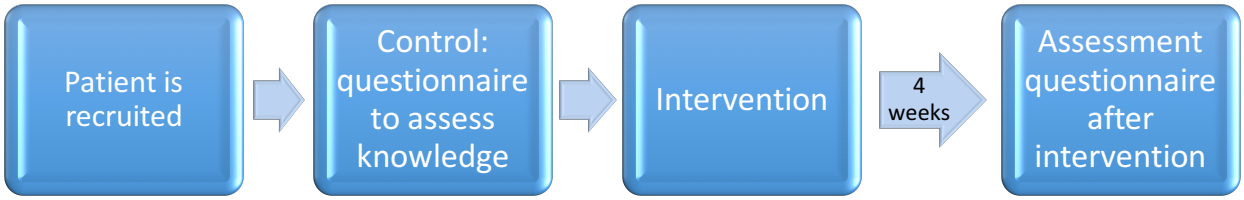

Figure 2.2 General overview of how the intervention was carried out.

Ten patients were recruited as pilot study. During this phase, no alterations were required to be done to both the Glucagon Tool Kit and the questionnaires since all material provided was clear and concise. Researcher thereby proceeded to recruit further patients.

2.8.1. Intervention: Using Glucagon Tool Kit

Hundred forty patients with type 1 diabetes mellitus (up to 16 years of age) attend the paediatric diabetes outpatients service at Mater Dei Hospital. The researcher visited the clinic 28 times to recruite patients. This was done between beginning of June 2016 – end of September 2016.

During these visits, 10 patients refused to be interviewed and approximately 17 patients rescheduled their appointment, 2 patients were admitted to hospital and 82 patients were recruited. Of these 82 patients 2 did not complete the final questionnaire and therefore were eliminated from the research.

The intervention consisted of a discussion whereby the Glucagon Tool Kit was provided. The information leaflet was explained to the carers. The importance that a source of sugar should be carried with them was highlighted so severe hypoglycaemia is avoided as much as possible.

A demonstration of how to mix glucagon was shown to the patient on a real glucagon injection. Two glucagon injections were available during each individual intervention- one showing how the glucagon injection is when opened (a new glucagon injection) and another glucagon injection that was used to show how in reality it is actually used. This demonstration enabled carers to actually query researcher on any problems they may encounter. The steps on the information sheet were also followed step by step.

Side effects of this medication were discussed giving rise to highlighting the importance of giving a source of glucose and/or a snack immediately once child regains consciousness.

Dosage given to the child was also discussed. Temperature variation with regards to if the glucagon injection can be carried around and the maximum temperature that it can reach were issues tackled. It was emphasized that in order to carry the glucagon injection above 8 degrees Celsius one must decrease 6 months from the total shelf life and also maintain temperature within 25 degrees Celsius.

Link to the video clip was printed on the back of the information sheet. Both Maltese and English links were available.

Together with the demonstration and the information above, a chart with the most important 6 steps of the whole process was created from the video. Screen shots were taken and short precise instructions were written under each image captured. This was used as a re-enforcement on how to mix glucagon. It was explained that this chart can be

placed in a handy place for emergency use. It was laminated so as to keep it intact. The video link was also typed at the corner of each side, Maltese or English version, so the video clip could be easily accessible.

After all this the carers are asked if they have any queries on how to use it.

Carers were also advised that if they had an expired glucagon injection at home they can actually try out the whole process on this expired glucagon injection, so they can be confident on the use of this medication, if the real need arises.

To conclude this session, carers were shown the one minute and a half, video clip. All material was then given and any questions answered.

Eight patients were selected at random and given the glucagon injection to try out after viewing the video. This will shed light on how effective viewing the video was – patients were given points and the issues encountered were noted by the researcher.

2.8.2. GLUCAGON ASSESSMENT QUESTIONNAIRE AFTER INTERVENTION

The second assessment which took place four weeks after baseline was done via phone since questionnaire only took approximately 5 to 7 minutes so to avoid causing inconvenience to the carer to visit the hospital again.

During these conversations carers were asked if they found any difficulties with regards to the use and administration of glucagon. Same questions as the baseline questionnaire were assessed to evaluate the answers given now that they were given educational material.

Carers were asked how to mix the glucagon injection again and marks were allocated to the answer given depending on the basic steps mentioned. Same marking scheme was

maintained as the previous questionnaire i.e. sample answer:

1) Inject the syringe into the vial with powder
2) Mix – holding both the syringe and vial together
3) Withdraw the liquid once dissolved
4) Remove air
5) Inject into muscle

5 marks were also allocated to this question.

All participants were advised not to discard their expired glucagon injection but to keep them and use it to train with. In this way when in actual need it will be easier to manage.

2.9. PHARMACIST INTERVENTION

Pharmacists were recruited by email. This was sent to pharmacists via the local Pharmacy Council database. A total of 588 pharmacists received the email. Google Forms was used to create and send the questionnaire. The questionnaire (Appendix 2H) was divided into two sections. In the first section, the pharmacist was assessed on the current knowledge on glucagon. Subsequently the Glucagon Tool Kit was provided and the second part of the questionnaire used to analyse the impact the Glucagon Tool Kit on the pharmacist. The response was automatically recorded anonymously on Gmail and accessed by the researcher.

2.10. DATA HANDLING AND STATISTICAL ANALYSIS

Statistical analysis of the questionnaire before and after the intervention for carers and the questionnaire for pharmacists was conducted using Statistical Package for the Social Service (SPSS) software version 24. This was suggested after a meeting held with

Statistics and Operations Research Faculty of Science Head of Department Professor Liberato Camilleri, at the University of Malta.

CHAPTER 3

RESULTS

3.1. Evaluation of Glucagon Tool Kit by Carers

The results gathered and analysed will focus on the demographics of both carers and children with type 1 diabetes mellitus, the glucagon assessment questionnaire before and after intervention, together with the demonstration test.

3.1.1. Demographics

From the carers interviewed 23.75% were male and 76.25% were female. When questioned on nationality, 92.5% were Maltese while 7.5% were not Maltese. Figure 3.1, depicts the age group of the carers of the children recruited.

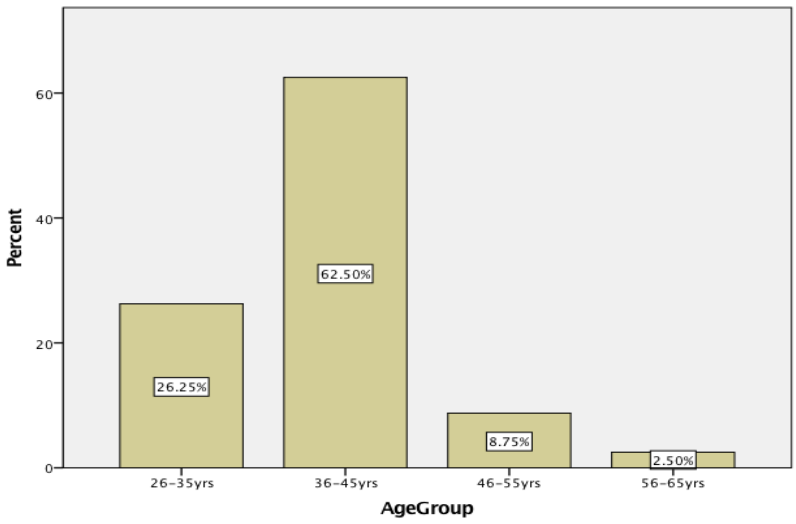

Figure 3.1 Age of The Carers Participating in Study (N=80)

All carers had secondary education, with 23.75% going on to post-secondary and another 23.75% of the carers having tertiary education.

Only 2 carers had diabetes mellitus, one carer being on oral treatment while the other carer was taking insulin treatment. The rest of the carers (78) were not diabetic. Nevertheless 81.25% are dealing with type 1 diabetes mellitus for the first time and 18.75% have dealt with diabetes mellitus in the past.

The age children had when interviewing the carers ranged from 2 years to 16 years of age with a mean age of 10 years. Thirty-two children were females while 49 were male. Two children, one girl and a boy, were twins therefore they were considered as one since carers were interviewed once.

The mean age of onset in children recruited was 5.75 years, ranging from age 0.16 years (2months) to 14 years. The most common presentation was the usual characteristics a child presenting with, thirst, weight loss and polyuria (60 children). Fifteen children interviewed presented initially as sick or unwell, leading to the diagnosis of type 1 diabetes mellitus (Figure 3.2).

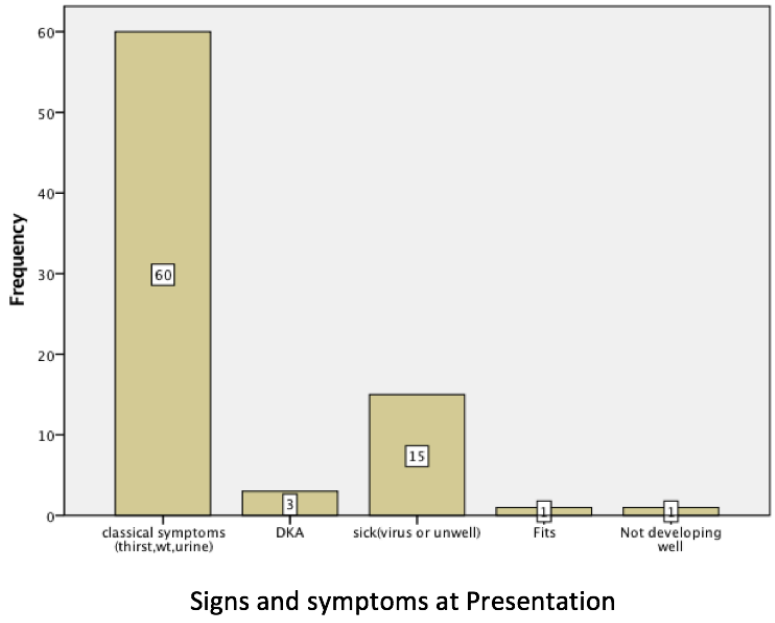

Figure 3.2 A Graph of Frequency and Signs and Symptoms at Presentation of T1DM (N=80)

Carers were asked to rate how informed they think they were on selected issues. These selected issues were meal planning, medications taken by child, hypoglyceamia and hyperglyceamia together with whether the necessary support was given from Mater Dei Hospital. Results are summarised in Figure 3.3, where 1 is the least informed and 10

being most informed. When asked to rate the support carers find with regards to type 1 diabetes mellitus, 7 carers gave a score of 8, 13 carers a score of 9 while the rest, 60 carers of the 80 interviewed gave a score of 10.

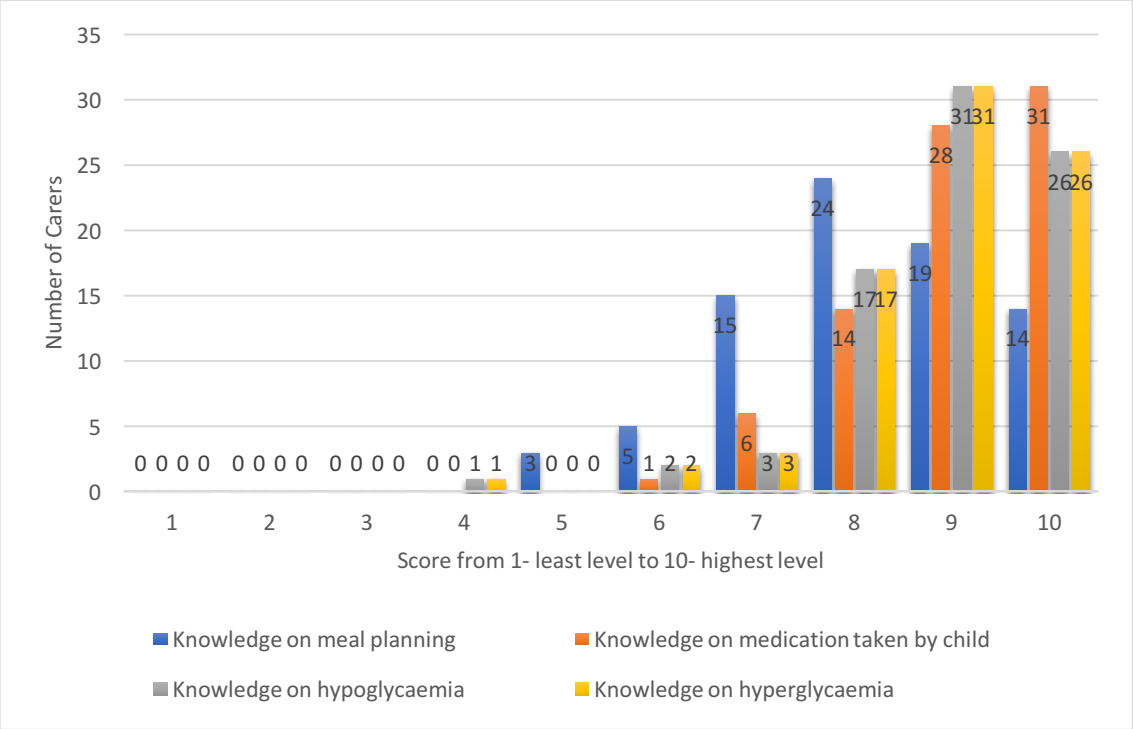

Figure 3.3 Carers Score on Knowledge of Issues Related to Type 1 Diabetes Mellitus

The majority of the children are prescribed Lantus®, Novo Rapid® (90%, n=70). Fifty-five of these 70 children were prescribed Humulin S® in addition, as an alternative to the NovoRapid®, to be used during school hours. The other 10% of the total cohort of patients were prescribed insulins such as Humulin S® and Humulin I® as an alternative to Lantus® (Figure 3.4).

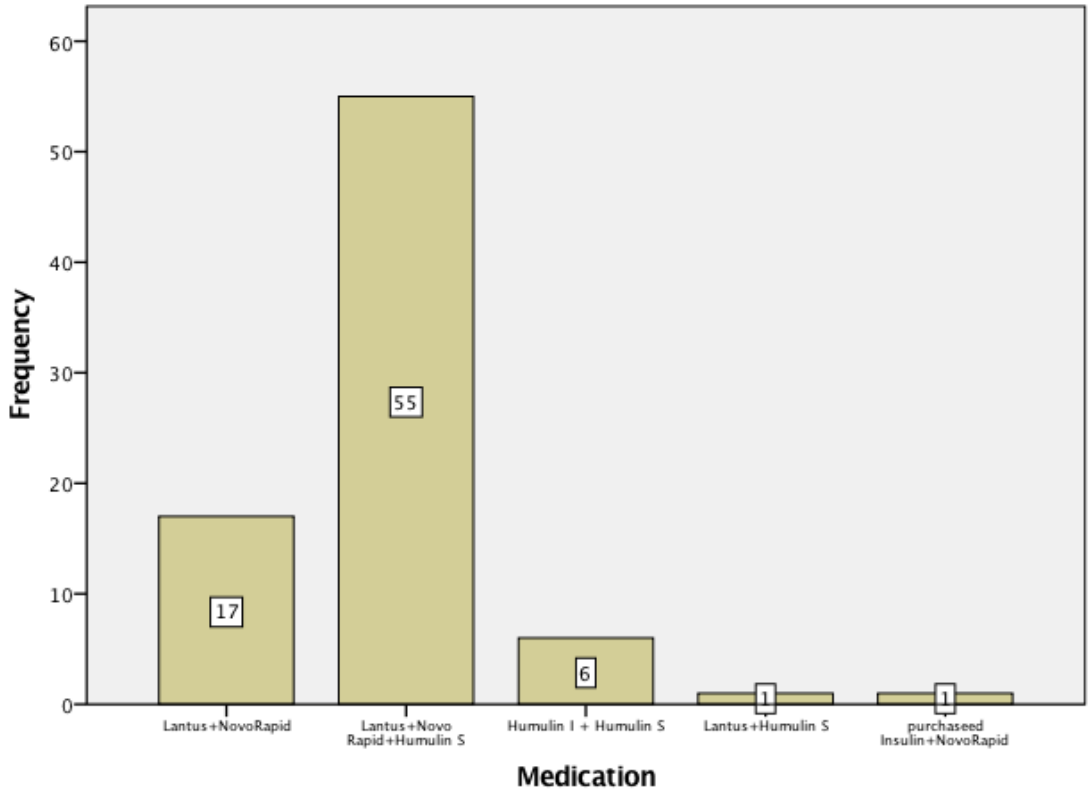

Figure 3.4 Diabetic Medications Participants are currently taking (N=80)

When carers were questioned if they were satisfied with the child's glycemic control, 68.75% (55 carers) stated they were satisfied. Fifteen carers, 18.75% were not satisfied, and 12.5% (10 carers) are neither satisfied nor not satisfied.

When questioned about other medical issues, 61 children did not have any other condition other than type 1 diabetes mellitus, 8 had celiac disease while 11 other children suffer from other disease not just type 1 diabetes mellitus. Only 8 of the 80 children took medication other than that for diabetes mellitus. When questioned if they had glucagon at home all carers stated yes.

Figure 3.5 shows the frequency that the child or carer tests blood glucose levels through the day, with a mean of 5.4 times.

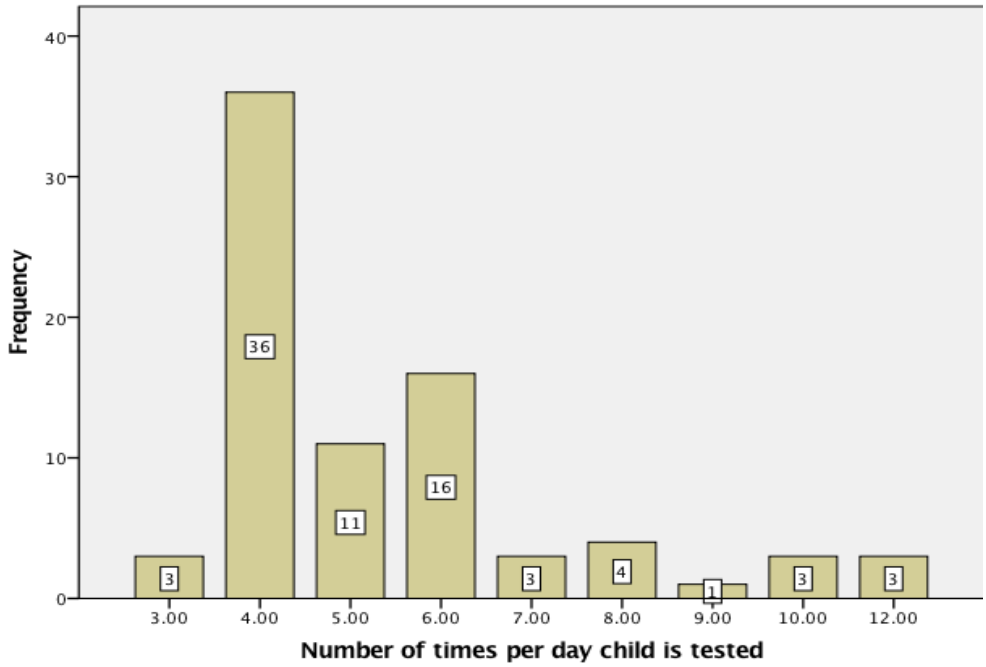

Figure 3.5 Number of Times Child is Tested for Blood Sugar Levels per Day (N=80)

Carers were asked to provide the researcher with the latest HbA1c of the child. A mean score of 7.63 was recorded (Figure 3.6).

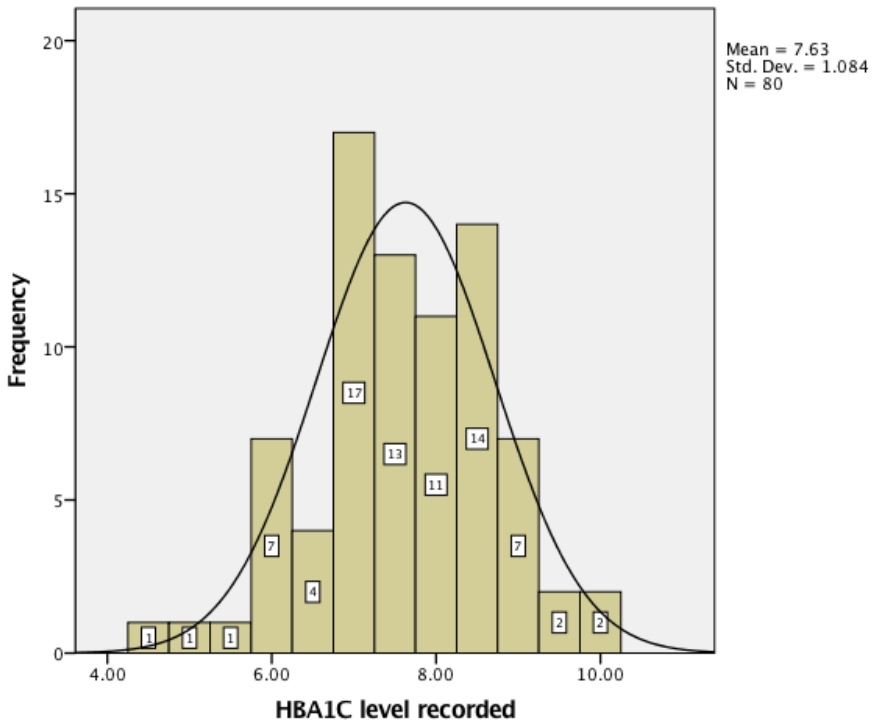

Figure 3.6 Level of HbA1c Recently Recorded (N=80)

3.1.2. GLUCAGON ASSESSMENT QUESTIONNAIRE BEFORE INTERVENTION

The carers were questioned if their child ever developed hypoglycaemia and 91.3% of carers stated yes while only 8.8% stated that this had not happened so far.

The severity of the hypoglyceamic attack was also analysed, with 41.3% stating that the child acts normal (Figure 3.7). Figure 8 describes the symptoms esperienced by children when hypogylceamic.

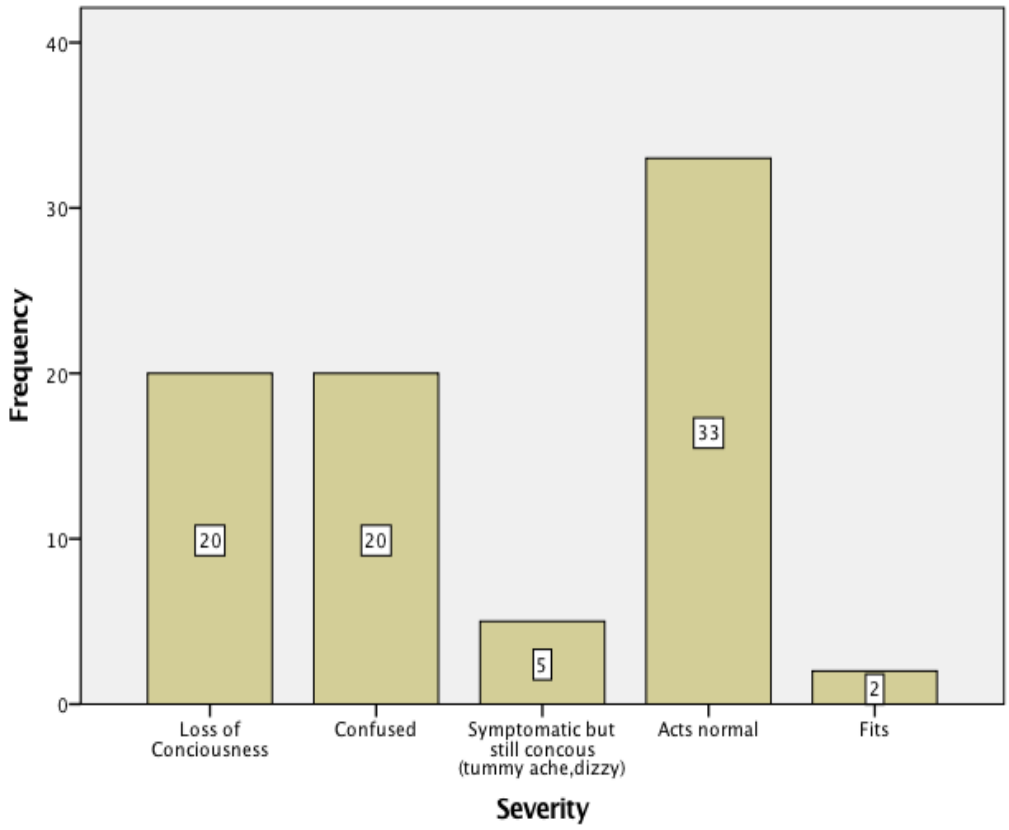

Figure 3.7 Signs and Symptoms of Hypoglyceamia which Reflect Severity (N=80)

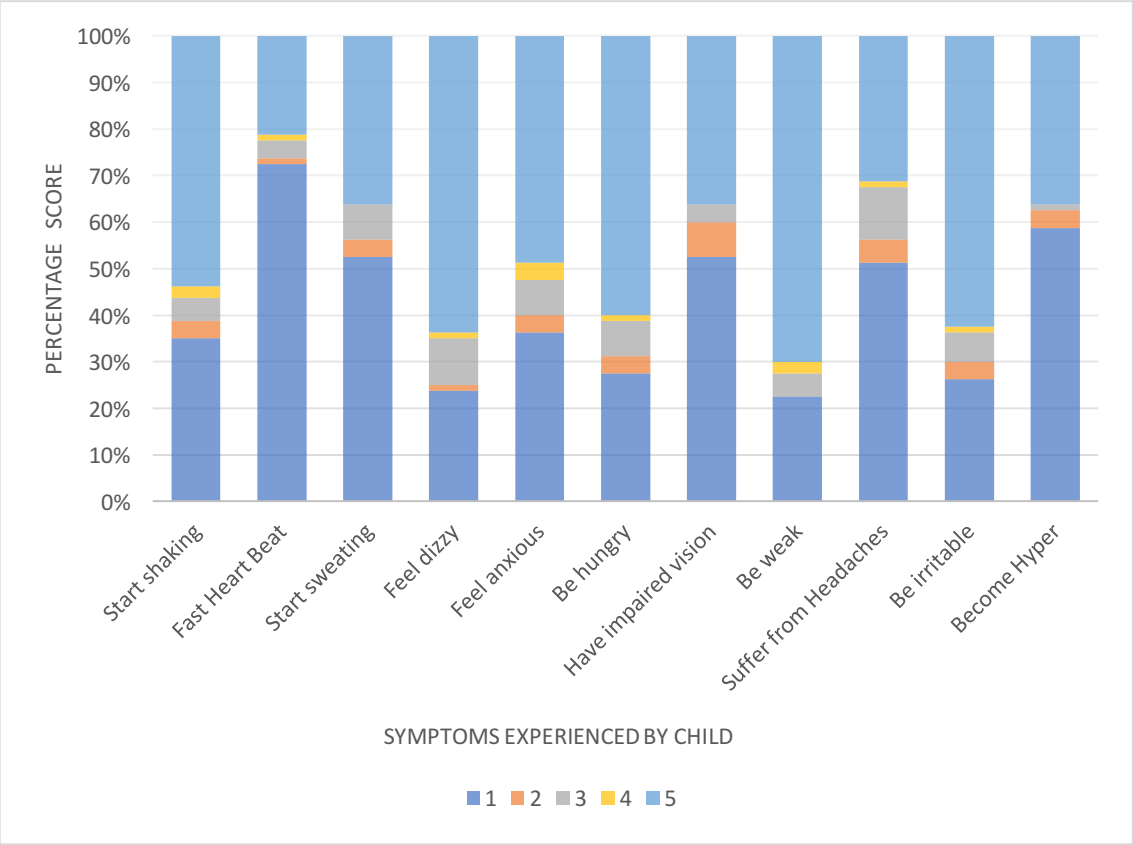

Figure 3.8 Score From 1(Least Felt) to 5 (Most Felt) Symptoms when Child Experiences a Hypoglyceamic Episode (N=80)

Eighteen children out of 80 (22.5%) interviewed, were hospitalized at some point in the past. Only 3 children had an occurrence of hypoglycemia that lead to hospitalization in the past year (2015), the rest of the children, 15 in all, were hospitalized 1-3 times when they were younger.

When questioning the use of glucagon 20 of the carers (25%) used glucagon on their children. Out of these 11 of them used it only once, 2 carers used it twice, 3 carers used it three times, 1 carer 4 times and 3 carers 5 times. The other 75% of the carers never used glucagon in their life.

When carers were asked to define hypoglyceamia and why it is used, all carers (100%) replied correctly. When asked to state if the mode of action is correct as per statement in

questionnaire, 73.8% answered correctly, 6.3% stated that the mode of action described in question 5 is wrong and 20% did not know the mode of action of glucagon.

3.1.2.1. GLUCAGON USE BEFORE INTERVENTION

All participants stated that they have glucagon injection at home. However only 42.5% stated that they have glucagon in another place other than at home. The majority, 61.3% do not carry the glucagon injection with them. Approximately, 21.3% state that glucagon injection was too bulky to keep it cool so they do not carry it around. Thirty percent carried glucagon injection around when they go too far from home or abroad. All participants stated that they stored glucagon injection in the fridge. Figure 3.9 shows what is done as an alternative to not taking glucagon. Those who carry juice were 23.8 %.

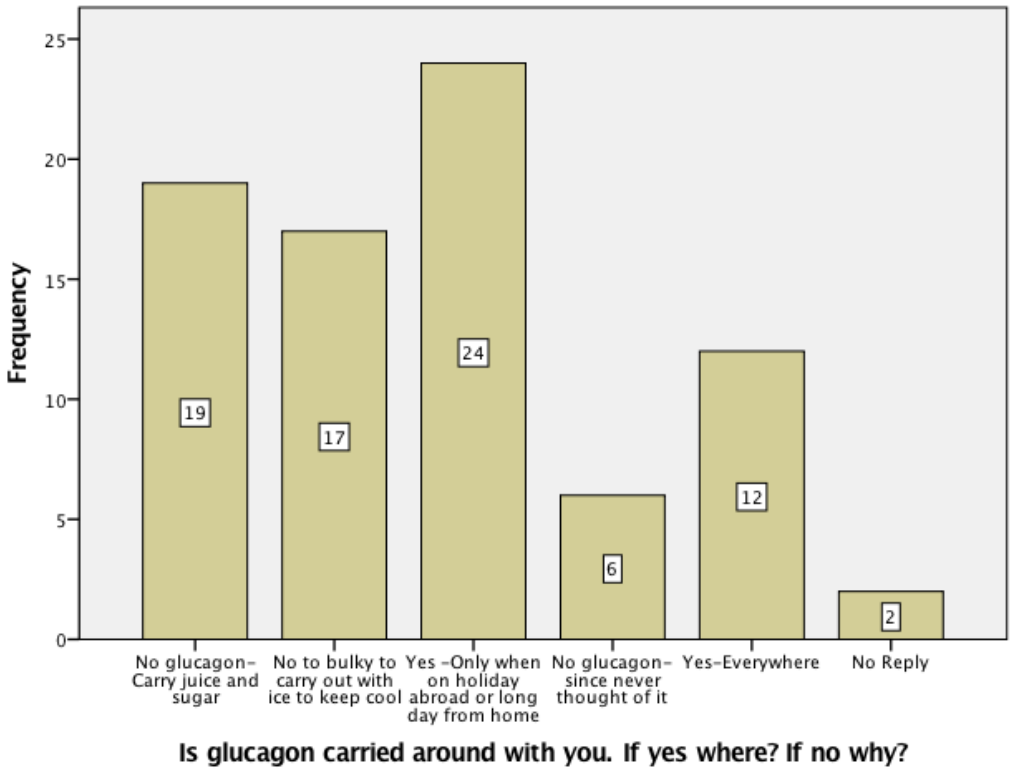

Figure 3.9 Analysis of carrying Glucagon around (N=80)

When queried about what happens to the expiry date if the glucagon injection is taken

out of the fridge, 36.3% stated that it should be discarded, 27.5% stated it shortens the date but do not recall by how much, 26.3% correctly state that it shortens by 6 months, while 10% do not know.

The majority of the participants, 87.5% recall previously being informed on use of glucagon, while 12.5% stated they were not informed. Carers were asked to state how informed they think they are, with 48.8% think they are informed, followed by 35% thinking they are not so informed, 11.3% feel they are very informed and 5% not informed at all.

Carers were told to state how the glucagon injection is used, based on predetermined scoring system as explained in the methodology. The carers are given a score from 0- no idea on how to use glucagon to 5- excellent knowledge on use of glucagon. Twenty-five percent of the participants obtained a zero score, 10% scored 1, 8.8% a 2, and only 21.3% and 26.3% scored a 4 and 5 respectively (Figure 3.10).

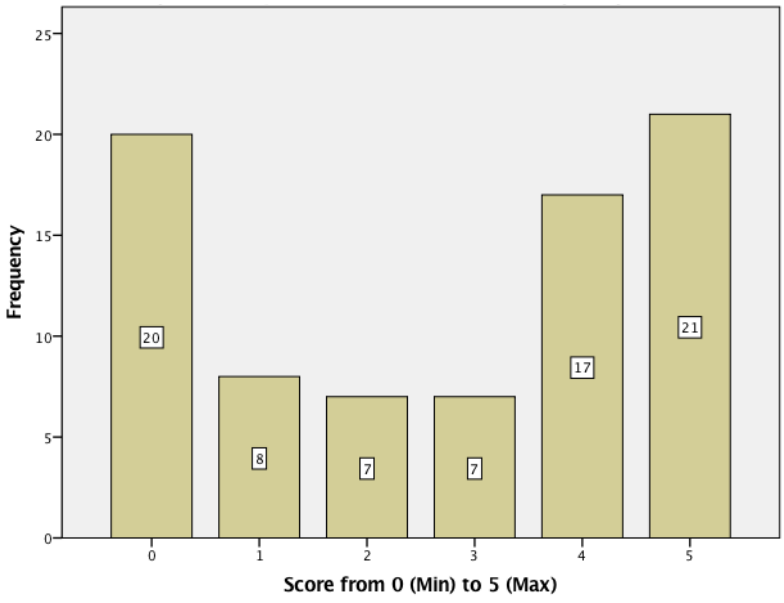

Figure 3.10 Analysis on how Well the Carers know how to use Glucagon (N=80)

Important points when mixing glucagon were selected and carers were asked to rate from 1 (the least important) to 5 (important). Table 3.1 summarises these results.

Table 3.1 A Table Depicting How Carers Responded Prior to Intervention on the Key Points One Needs to Keep in Mind When using Glucagon (N=80)

	0	**1**	**2**	**3**	**4**	**5**	**Do not know**	**Total**
All white powder must be dissolved	18	0	0	0	1	57	4	80
When mixing, the needle must be kept in bottle	22	17	1	0	1	34	5	80
Air should be removed before injecting	21	0	1	1	0	54	3	80

Questioned what dose should be administered, 62.5% stated the dose correctly, 6.3% did not state the dose correctly, while 31.3% did not know.

Confidence and fear were also rated (Figure 3.11 and 3.12). Only 14 carers felt they were very confident on the use of glucagon (Figure 3.11).

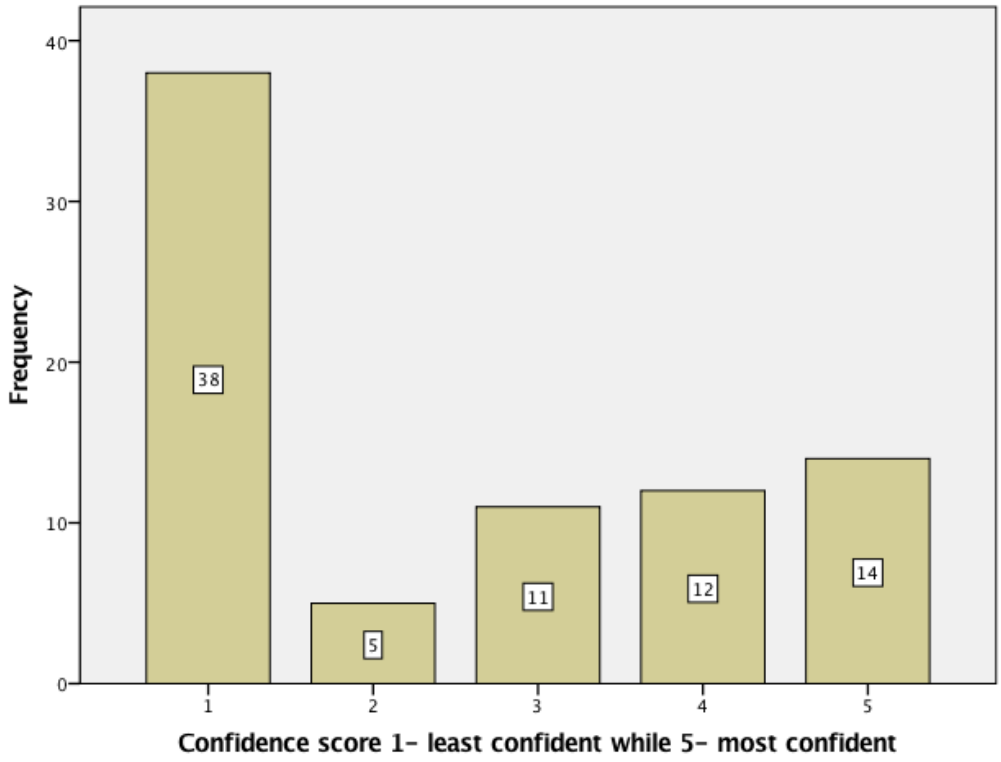

Figure 3.11 Likert Scale used to Measure Confidence of Carers to use Glucagon (N=80)

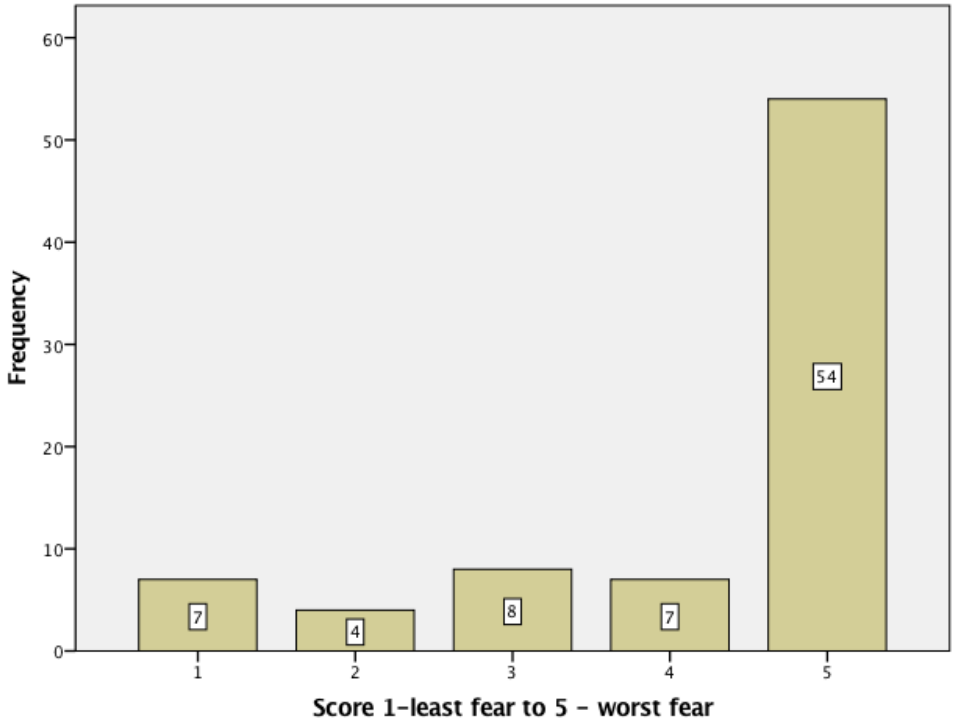

Figure 3.12 Carer's Fear of Use of Glucagon Injection. Score of 1 Depicts Least Fear While Score of 5 Shows Worst Fear (N=80)

The majority of the carers felt they were afraid to use the glucagon injection (Figure 3.12). Parents were asked what actions they take to avoid the child getting hypoglycaemia. Those who stated that they monitor blood glucose levels and give only adequate sugars were a total of 97.5%. A small percentage of 1.25% stated they give sugar before bed and another 1.25% stated they give sugar at school.

On being asked whether other carers of your child are knowledgeable of the glucagon administration process in case you are not available, 31.3% stated yes while 65% stated no and 3.8% did not know. A total of 37.5% of carers are not so confident with leaving children with other carers and 43.8% are just confident, while 12.5% are not confident at all. The minority 6.3%, are very confident.

More than half, 62.5% of the carers do not explain how to use glucagon when they leave the child under someone else's care, 16.3% rarely do so too, and only 20.0% do so initially. While 1.3% rarely explain glucagon to other carers.

Ninety-five percent of the carers never left the child under someone else's care and experienced a hypogylceamic episode.

School is where the child spends half his day, hence carers were asked if they ever explained use of glucagon in hypoglyceamia to school members. The majority, 56.3% stated that school was informed but 41.3% stated that they did not inform school. About 2.5% were too young for school.

Approximately 31.3% of the carers stated that the school refused to use glucagon. Of the total carers interviewed 2.5 % stated that they do not have a nurse or learning support assistant (LSA) at school whereas another 2.5% assumed that the nurse should know how and when to administer. Ambulance and calling the parents were the most frequent actions school should take if glucagon is not used.

3.1.3. GLUCAGON ASSESSMENT QUESTIONNAIRE FOUR WEEKS AFTER INTERVENTION

Four weeks after disseminating the Glucagon Tool Kit, the carers were contacted again by phone. When questioned if the child developed hypoglyceamia in the past four weeks, 62.5% stated that yes.

Only 1 child lost consciousness while the majority 46.3% acted normally. 7.5% of the children felt confused. No child was hospitalized and no one used glucagon injection.

Carers were asked to define hypoglyceamia and the mode of action of the glucagon medication, together with why glucagon injection is used. Almost all carers, 98.8% ticked the correct definition of hypoglyceamia and 97.5% stated that the mode of action of glucagon in description is correct. Only 1.3% of the carers did not know the definition of hypoglyceamia while 2.5% of carers did not know the mode of action of glucagon. All carers knew why glucagon is used.

3.1.3.1. GLUCAGON USE AFTER INTERVENTION

Fifty-five percent of the carers have glucagon injection in another place other than at home, while 45% only have it at home. Sixty-five percent stated they carry glucagon injection around now while 35% still stated they do not carry glucagon injection with them.

Twenty-seven carers carry glucagon only when on holiday abroad or when they are staying for a long day away from home, while 20 carers do not carry glucagon since they carry juice and sugar. Sixteen carers stated they carry glucagon everywhere they go. The rest of the carers gave reason as found in Figure 3.13.

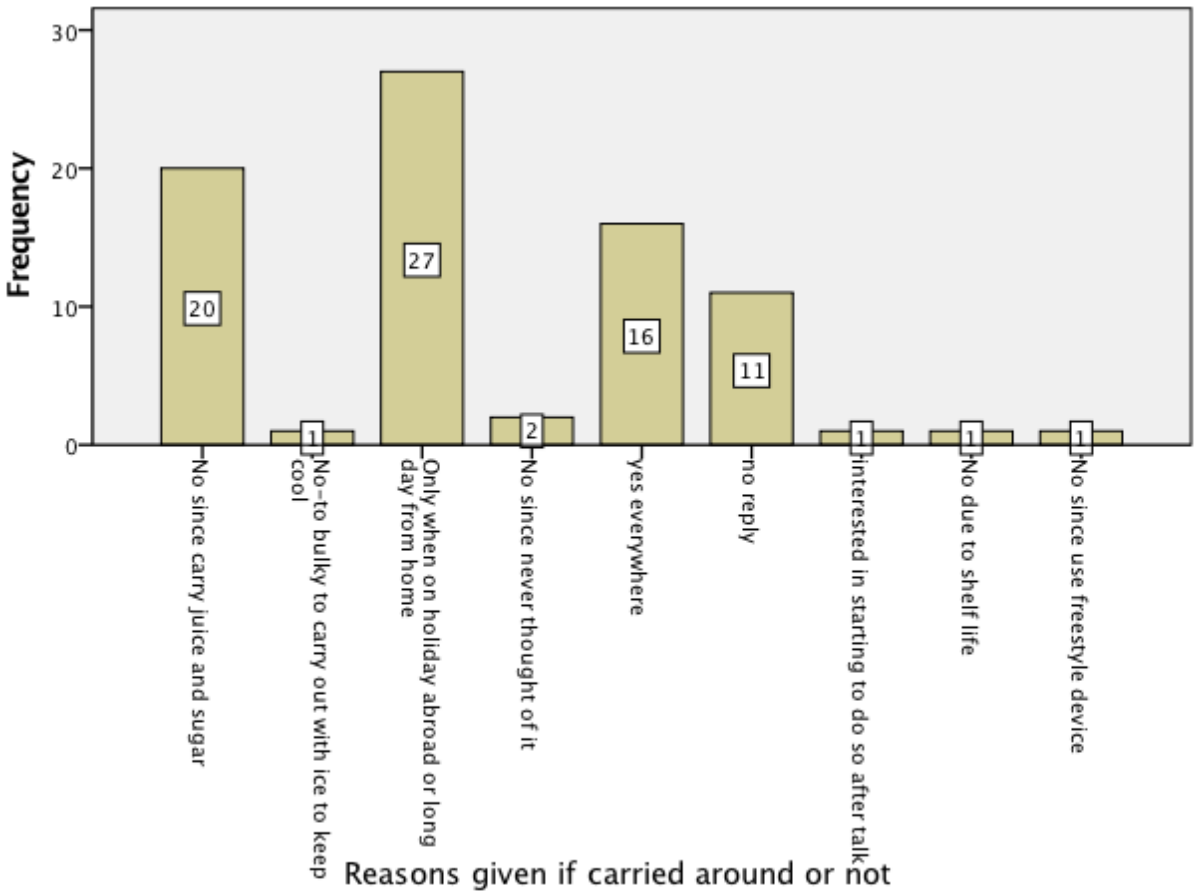

Figure 3.13 Reasons on Whether or not the Glucagon Injection is Carried Around with the Child if he/she go out (N=80)

All carers keep glucagon injection stored in fridge. After the pharmacist's intervention through the Glucagon Tool Kit 85% of the carers correctly stated that the expiry of the glucagon injection shortens by 6 months if left out the fridge, 13.8 % recall that it shortens but forgot the duration by which it shortens, while only 1.3% (1 carer) did not know the answer.

Figure 3.14 shows how informed carers feel about glucagon post intervention of the Glucagon Tool Kit.

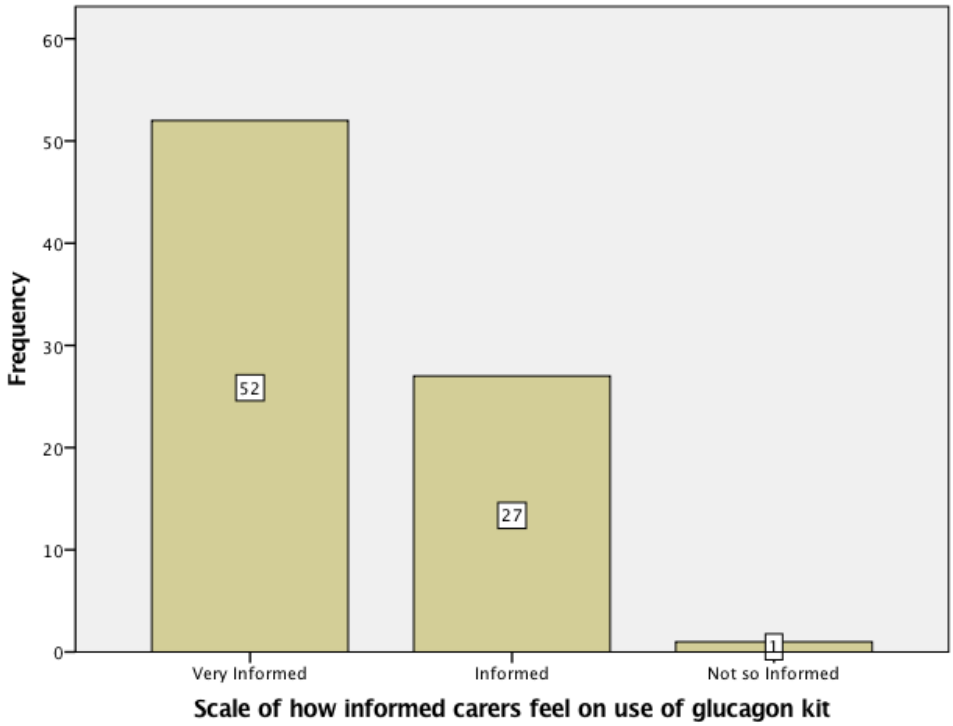

Figure 3.14 Graph Showing How Informed Carers Feel after the Intervention on use of Glucagon Injection (N=80)

Carers were again asked how to use glucagon injection (Table 3.2).

Table 3.2 The Score Carers Obtained After They Were Asked to State How They Use Glucagon Injection (N=80)

	Score					
	0	1	2	3	4	5
Frequency	0	0	1	1	16	62
Percentage	0%	0%	1.3%	1.3%	20%	77.5%

Zero means that the carer does not know how to use glucagon, while 5 means that the carer knows exactly how to use glucagon.

All carers gave a score of 5 (very important) to the statement in question 13.

In response to question 15, which queried if other carers know how to use glucagon when the child is let under their care, 42 carers stated no, while 37 stated yes. Only one participant did not know. Confidence and fear of using glucagon was measured again in this interview, with a score of 1 to 5, 1 being the least confident and 5 the most confident (Table 3.3).

Table 3.3 Analysis of level of confidence and level of fear carers score on the use of glucagon

	Score				
	1	2	3	4	5
Confidence	1.3%	2.5%	23.8%	35%	37.5%
Fear	1.3%	0%	3.8%	5%	90%

Twenty- eight carers out of the 80 participants, explain the use of glucagon to other potential carers initially when the child will be left under their care. Eight carers do so every now and then while 15 carers rarely explain the use of glucagon to other. Another 29 carers never explain the use of glucagon to other carers.

3.1.4. Assessing the impact of the Glucagon Tool Kit

The percentage of carers that rated the Glucagon Tool Kit information as 5, very informative, were 93.8%, while the other 6.3% gave it a score of 4 out of 5. Approximately 88% of the carers used the material given with 11.3% not finding time to use it.

The video was reviewed by 72.5% of the carers, 12.5% did not use the video and 15% did not state if they used it.

The majority, 43 of the carers, placed the reconstitution chart with other diabetes information (Figure 3.15).

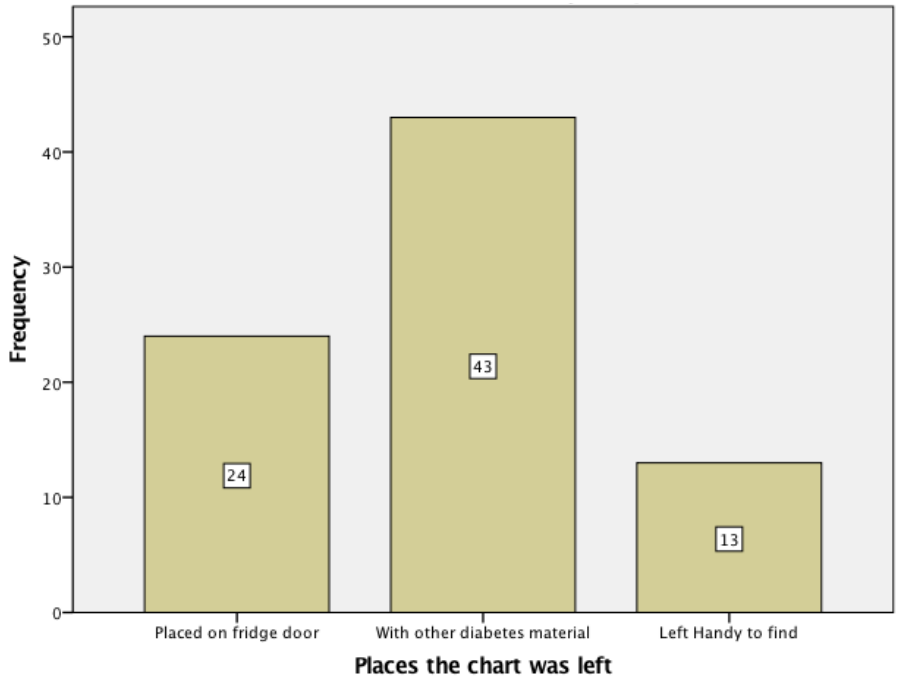

Figure 3.15 A Graph Showing Where the Carer's Placed the Chart Given by the Interviewer (N=80)

The majority of carers, 96.3% of those interviewed felt that their confidence increased after the intervention, while 3.8% did not feel an increase in confidence.

Carers were finally asked if they think they require some other kind of information and 75% stated no. Of the other 25 %, 13.75% (11 carers) wanted more revision sessions, 6.25% (5 carers) requested general knowledge sessions on e.g.: diet, carbohydrate counting and use of pump. Five percent wanted increased awareness and education on glucagon in schools. One participant did not put forward any suggestions.

A random eight carers were given a glucagon injection and asked to demonstrate how glucagon injection is used. The same scores used during the questionnaire to grade the carers were used. Four carers scored 5 out of 5. The other four scored a 4 out of 5 since the withdrawal part was the most difficult part of the demonstration for them to complete.

3.1.5. COMPARISON OF GLUCAGON ASSESSMENT QUESTIONNAIRE DATA BEFORE AND AFTER INTERVENTION

When all the below data (Table 3.4), before and after intervention, were tested, both the Kolmogorov-Smirnov test and the Shapiro-Wilk test gave a p-value of 0.001. Due to this being less than 0.05 level of significance the alternative hypothesis was accepted and thereby all data is not normally distributed. In this regards non-parametric tests were used.

Table 3.4 Test for Normality to Identify How Parameters Will be Analysed with Regards to Parametric or Non-Parametric Tests (N=80) (P< 0.001)

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Fear of use Before	.400	80	.000	.640	80	.000
Fear of use After	.513	80	.000	.323	80	.000
Confidence of Use Before	.298	80	.000	.783	80	.000
Confidence of Use After	.226	80	.000	.834	80	.000
Explain how to use Before intervention	.218	80	.000	.834	80	.000
Explain how to use After Intervention	.460	80	.000	.524	80	.000
Do you carry glucagon around? Before Intervention	.398	80	.000	.618	80	.000
Do you carry glucagon around? After Intervention	.417	80	.000	.603	80	.000
Knowledge on dose administration Before intervention	.397	80	.000	.640	80	.000
Knowledge on dose administration After intervention	.538	80	.000	.144	80	.000
Knowledge of Expiry Date if left above 8 degrees Celsius Before Intervention	.227	80	.000	.864	80	.000
Knowledge of Expiry Date if left above 8 degrees Celsius After Intervention	.495	80	.000	.409	80	.000
How informed do you feel- Before Intervention	.275	80	.000	.845	80	.000
How informed do you feel- After intervention	.412	80	.000	.636	80	.000
a. Lilliefors Significance Correction						

3.1.6. Assessing Significant differences: Wilcoxon Signed Ranks test

The Wilcoxon Signed ranks test was used to compare mean rating scores before and after an intervention. It is a non-parametric alternative to the paired sample t-test. The rational

of using this test was that the responses are not metric but have an ordinal categorical scale.

The null hypothesis specifies that the mean rating scores after intervention was comparable to the mean rating scores before, i.e. intervention was not effective. This is accepted if the p-values exceeds the 0.05 level of significance.

The Alternative hypothesis specifies the mean rating score after the intervention was significantly higher than the mean rating score before, i.e. the intervention was significantly higher than the mean rating score before and was effective. This is acceptable if the p-value is less than the 0.05 criterion.

When used to test for confidence of use in carers of type 1 diabetic mellitus children, the alternative hypothesis was accepted, meaning that the mean rating score after the intervention was significantly higher than the mean rating score before, i.e. the intervention was significantly higher than the mean rating score before and was effective, since p-values was 0.001 with mean rising from 2.48 before intervention to 4.05 after intervention.

The same can be said when fear of use, before and after, was compared ($p< 0.001$) mean before was 4.21 and after intervention mean was 4.82. Also, when 'how to use glucagon' was questioned before and after ($p< 0.001$) mean before was 2.70 after was 4.73, resulting in statistical significant difference.

3.1.7. Assessing Significant differences: Chi Squared test

The Chi Squared test was used to assess the association between two categorical variables. One of these categorical variables indicated whether the response was provided before or after intervention. The other indicated the opinion of participants. In this

research, Chi Squared test was used to assess before and after intervention for:

1) The dosage given to children (Table 3.5)
2) Knowledge of what happens to expiry date of glucagon if left out of the fridge (Table 3.6)
3) If patients increased taking glucagon injection out with them (Table 3.7)
4) How informed the carers feel (Table 3.8)

Table 3.5 Chi Square Test Results, Comparing Before Intervention to After on the Dose Administered (N=80)

			Intervention		Total
			Before	After	
Q16Dose	Dose stated is correct	Count	50	78	128
		Percentage	62.5%	97.5%	80.0%
	dose not stated correctly	Count	5	0	5
		Percentage	6.3%	0.0%	3.1%
	Do Not Know	Count	25	2	27
		Percentage	31.3%	2.5%	16.9%
Total		Count	80	80	160
		Percentage	100.0%	100.0%	100.0%

$X^2(2) = 30.718$, $p < 0.001$

After intervention, the percentage of correct replies increased from 62.5% to 97.5%, while the percentage of incorrect replies decreased from 6.3% to 0.0%. Moreover, the percentage of non-replies decreased from 31.3% to 2.5%.

Since the p-value is less than 0.05 level of significance then it follows that the intervention was statistically significant in effectively improving knowledge in dose to be given to children by carers.

Table 3.6 Chi Square Test Results Comparing Before Intervention to After on what Happens to the Expiry Date if Glucagon Injection is kept at Temperature above 8 Degrees Celcius (N=80)

			Intervention		Total
			Before	After	
Expiry Date	Shortens By 6months	Count	21	68	89
		Percentage	26.3%	85.0%	55.6%
	Shortens but does not recall by how much	Count	22	11	33
		Percentage	27.5%	13.8%	20.6%
	Discard	Count	29	0	29
		Percentage	36.3%	0	18.1%
	Do Not Know	Count	8	1	9
		Percentage	10.0%	1.3%	5.6%
Total		Count	80	80	160
		Percentage	100.0%	100.0%	100.0%

$X^2(3) = 62.931$, $p < 0.001$

After use of the Glucagon Tool Kit, the percentage of replies that correctly stated that glucagon must be shortened by 6 months once out of the fridge increased from 26.3% to 85.0%, while the percentage of those who stated that it must be discarded decreased from 36.3% to 0.0%. A decrease was also noted from 10.0% to 1.3% for those patients who do not know what happens. Moreover, the percentage of those who remembered it must be

shortened but do not know the exact months by how much to shorted decreased from 27.5% to 13.8%.

Given that the p-value is less than 0.05 level of significance the use of Glucagon Tool Kit was statistically significant in improving knowledge on shortening expiry date once the glucagon injection is no longer below 8 degrees Celsius.

Table 3.7 Chi Square Test Results, Comparing Before Intervention to After on whether Glucagon Injection is Carried Around with Children When not at Home (N=80)

			Intervention		Total
			Before	After	
Do you carry glucagon with you	Yes	Count	31	52	83
		Percentage	38.8%	65.0%	51.9%
	No	Count	49	28	77
		Percentage	61.3%	35.0%	48.1%
		Total Count	80	80	160
		Total Percentage	100.0%	100.0%	100.0%

$X^2(1) = 11.041$, $p < 0.001$

After intervention, the percentage of carers that stated they carry glucagon injection with them increased from 38.8% to 65.0%, while the percentage of those who do not decreased from 61.3% to 35.0%.

Since the p-value is less than 0.05 level of significance, the use of the Glucagon Tool Kit was statistically significant in improving awareness that the glucagon injection is to be used in emergency and therefore should be carried around with the child.

Table 3.8 Chi Square Test Results, When Comparing How Informed Carers Felt Before Intervention to After Intervention (N=80)

			Intervention		Total
			Before	After	
How Informed do you feel	Very Informed	Count	9	52	61
		Percentage	11.3%	65.0%	38.1%
	Informed	Count	39	27	66
		Percentage	48.8%	33.8%	41.3%
	Not so informed	Count	28	1	29
		Percentage	35.0%	1.3%	18.1%
	Not Informed at all	Count	4	0	4
		Percentage	5.0%	0.0%	2.5%
Total		Count	80	80	160
		Percentage	100.0%	100.0%	100.0%

$X^2(3) = 61.631$, $p < 0.001$

After intervention, the percentage of patients who feel very informed increased from 11.3% to 65.0%, while the percentage of those who feel not so informed decreased from

35.0% to 1.3%. Moreover, the percentage of those who feel not informed at all decreased from 5.0% to 0.0 %.

Since the p-value is less than 0.05 level of significance the use of the Glucagon Tool Kit was statistically significant in improving how well informed that carers feel.

3.2. Evaluation of the Glucagon Tool Kit For Pharmacists

Hundred thirty- nine pharmacists submitted a response. Out of these 69.1% were female (n= 96) and 30.9% were male (n=43).

More than half of the pharmacists, 52.5% were within the age group of less than 35 years of age (Table 3.9).

Table 3.9 Age of Participants (N=139)

Age Range	**Percentage**
23-25years	13.7% (n=19)
26-35 years	38.8% (n=54)
36-45 years	23.7% (n=33)
46-55 years	20.9% (n=29)
56 years +	2.9% (n=4)

Of the 139 pharmacists interviewed, 14.4% worked in hospital pharmacy as their principal employment while 43.9% worked in community. The remainder of the pharmacists who participated in the research practiced in another sector (Table 3.10).

Table 3.10 Principal Employment each Participant Practices in (N=139)

Sector	**Percentage**
Hospital	14.4% (n=20)
Community	43.9% (n=61)
Regulatory Affairs	11.5% (n=16)
Industry	6.5% (n=9)
Academia	2.2% (n=3)
Medical Representative	7.9% (n=11)
Procurement Section	7.9% (n=10)
Other	6.5% (n=9)

Table 3.11 shows the overall response obtained for the questions the researcher asked to gain insight on the pharmacist and their experience with diabetes mellitus and glucagon.

Table 3.11 Insight to Pharmacist's Experience with Diabetes and Glucagon (N=139)

	Yes	No	Don't know
Are you insulin dependent diabetic?	1	138	0
Any member of your close family is insulin dependent diabetic?	25	114	0
Have you ever used Glucagon Injection	1	138	0
Did you ever provide advice on the use of glucagon	47	88	4
Have you ever had requests for information about use of glucagon	42	93	4

When questioned on advice given to patients on glucagon, 7.1% of the pharmacists claimed to give advice yearly and 7.1% give advice monthly (Figure 3.16).

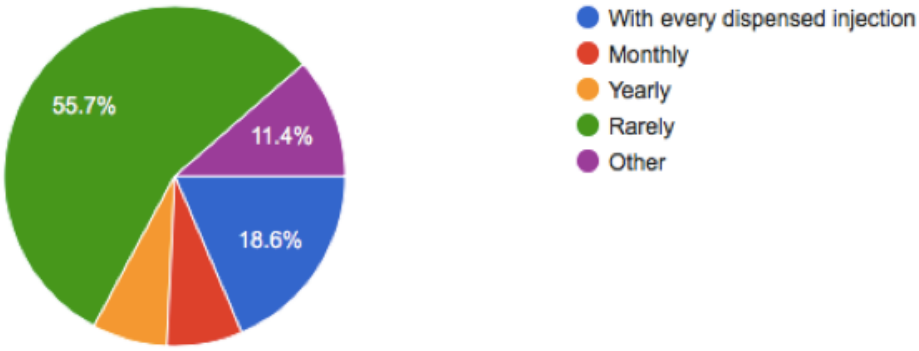

Figure 3.16 Frequency of Advice Given on Glucagon (N=139)

Pharmacists were also asked to indicate what will happen if glucagon is stored at room temperature (not exceeding 25 degrees). With the majority (33.1%) stating that expiry date has to be decreased (Figure 3.17).

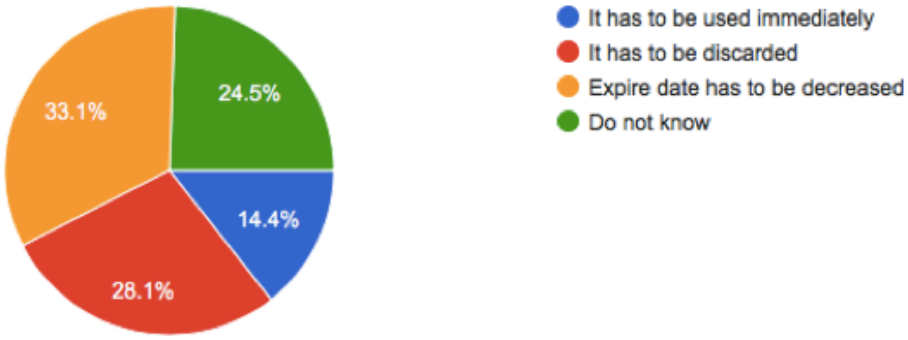

Figure 3.17 Expiry of Glucagon Injection if Stored at Room Temperature (N=139)

3.2.1. Evaluation of Intervention

Figure 3.18 summarises the perception of pharmacist on the level of awareness there is on glucagon reconstitution and use, amongst carers of pediatric Type 1 diabetic patients.

A scale of 1 – 5 was used with 1 being the least awareness and 5 being the most with 50 pharmacists scoring a level of awareness at a score of 3.

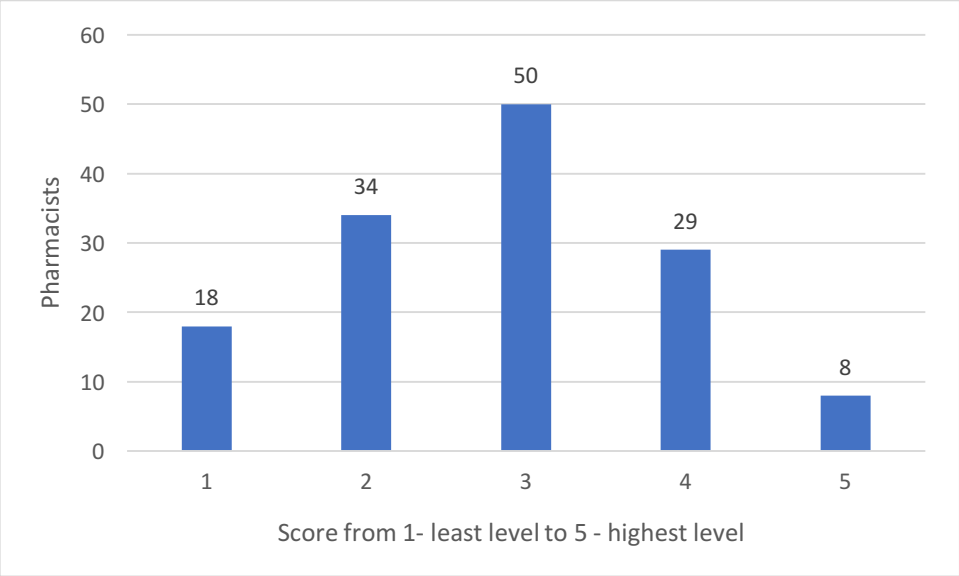

Figure 3.18 Pharmacist's Perception on Awareness on Glucagon reconstitution and use (N=139)

Pharmacists were also asked to rate their own knowledge on glucagon reconstitution and use prior to viewing the Glucagon Tool Kit provided. This same question was asked after the Glucagon Tool Kit was administered (Figure 3.19).

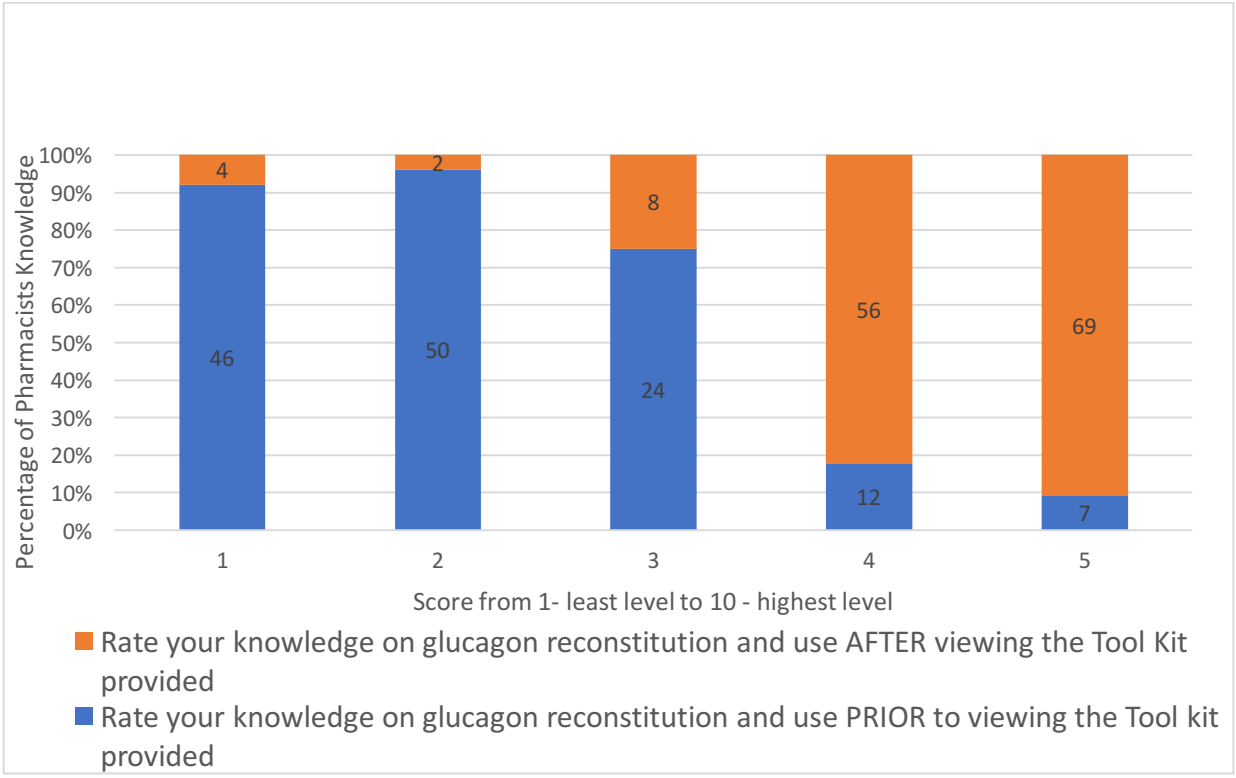

Figure 3.19 Pharmacist Knowledge on Use of Glucagon (N=139)

Confidence was also measured in the same way. Pharmacists were asked to rate the level of confidence on the use and administration of glucagon prior to, and after the intervention. A scale of 1 to 5 was used with 1 being the least and 5 the most confident (Figure 3.20).

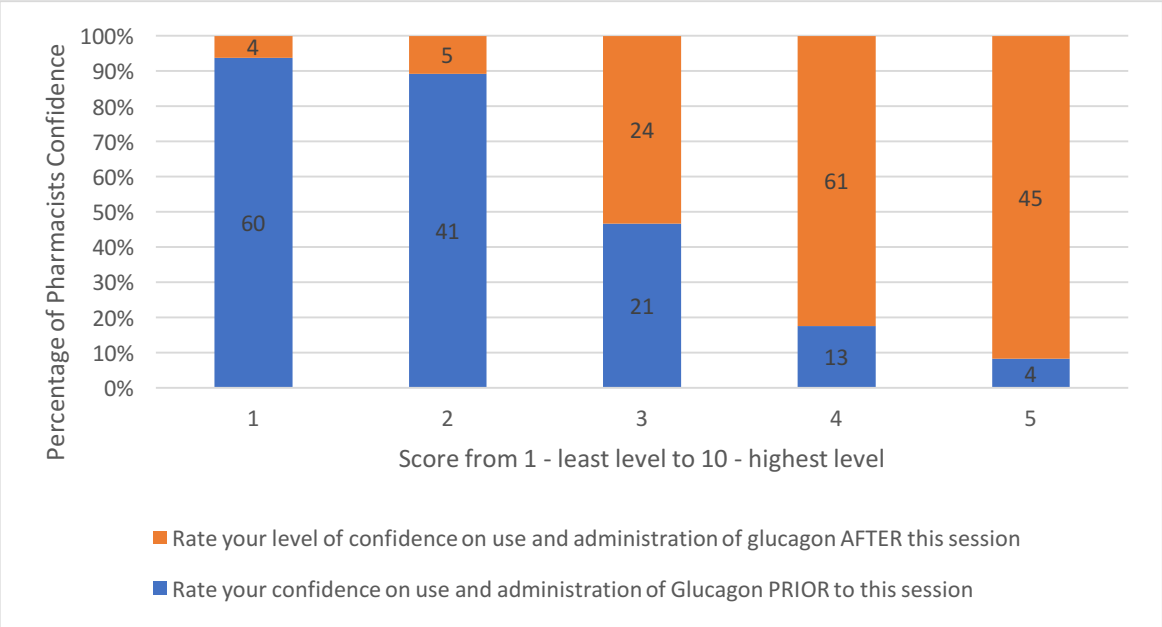

Figure 3.20 Pharmacist Level of Confidence on Use of Glucagon reconsitution and use (N=139)

In the last section of the questionnaire, pharmacists were requested to rate from 1 to 5, how informative the Glucagon Tool Kit is, how concise the video is and the usefulness of the Glucagon Tool Kit. A Likert Scale was used, were 1 was the least useful and 5 was the most useful. As the majority, 90- 92% of the participants, rated the Glucagon Tool Kit as informative and Glucagon Tool Kit as useful (rating of 4 or 5) (Table 3.12).

Table 3.12 Rating by Pharmacists on Glucagon Tool Kit

	1	**2**	**3**	**4**	**5**	**total**
How informative is the Glucagon Tool Kit provided?	0	4	9	48	78	139
How concise is the video in the Glucagon Tool Kit provided?	0	4	7	46	82	139
Rate the usefulness of the Glucagon Tool Kit	0	1	10	35	93	139

3.2.2. STATISTICAL INTERPRETATION

When confidence and knowledge of use of glucagon, before and after the provision of the Glucagon Tool Kit, were tested for normality, both the Kolmogorov-Smirnov test and the Shapiro-Wilk test gave a p-value of 0.001. Due to this being less than 0.05 level of significance the alternative hypothesis was accepted and thereby all data was not normally distributed. In this regards non-parametric tests was used.

The mean rating score ranges from 1-5 where the larger the score, the higher the knowledge or confidence. The Wilcoxon Signed ranks test was used to compare mean rating scores before and after an intervention.

The null hypothesis specifies that the mean rating scores after intervention was comparable to the mean rating scores before, i.e. intervention was not effective. This was accepted if the p-values exceeds the 0.05 level of significance.

The alternative hypothesis specifies the mean rating score after the intervention was significantly higher than the mean rating score before, i.e. the intervention was significantly higher than the mean rating score before and was effective. This was acceptable if the p-value was less than the 0.05 criterion.

With respect to both the pharmacist level of confidence and knowledge it was noted that after the use of the Glucagon Tool Kit there was a statistically significant improvement in confidence with glucagon use and less fear with glucagon use (p-values are both 0.001) (Table 3.13).

Table 3.13 Determining Statistical Significant Difference between Before to After Intervention for Pharmacists (N=139)

Statistical parameter measured	**Mean before**	**Mean after**	**Wilcoxon Sign ranks test**
Confidence of use	1.9928	3.94781	0.001
Knowledge on use	2.1655	4.3237	0.001

CHAPTER 4

DISCUSSION

4.1. DISCUSSION

Hypoglycaemia is linked with significant morbidity, decreased quality of life and risk of mortality (Kedia, 2011; Freeborn et al, 2013; Ly et al, 2014). Glucagon is the first line medication that is used for severe hypoglycaemia and is designed to be administered by a non-medical person (Kedia, 2011).

An audit report carried out at Mater Dei Hospital, Malta, between October 2015 to January 2016, assessed parents' knowledge on managing hypoglycaemia. When caregivers were questioned which aspect, they felt least confident in, with regards to hypoglycaemia management, 77.8% (91 carers out of 117) stated that using glucagon was something they felt least confident. Thereby the authors proposed an introduction of a hands-on training session in the use of glucagon [18](Unpublished audit report, 2016). This background led to the development of this research with the aim of developing resources that could be used to support community pharmacists and caregivers in the use of glucagon and hypoglycaemia in paediatric type 1 diabetes mellitus patients in Malta.

Amongst the results obtained in this research, carers were asked how many times a child gets tested for blood glucose levels daily and the mean score of 5.4 times was recorded. This is in line with the advice given by the clinician who stresses the importance of testing blood glucose levels at least four times a day.

Despite having 91.3% of the carers stating that their child experienced some level of hypoglycaemia at some point in their life, 75% of the interviewed have never made use

[18] Sapiano K., Torpiano P., Torpiano J., Audit Report: Assessing parents' knowledge of how to manage suspected hypoglycaemia in their child. January 2016

of glucagon in their life. This is in tandem with published literature, where Kedia in 2011 and Kalra in 2014 stated that glucagon remains underappreciated and underused.

Despite this underuse, as per correspondence via email in February 2017, with Central Procurement and Supplies Unit, consumption of glucagon injections by the various government entities, is of 4,693 vials per year at the cost of 19.87euros each. This includes the use for both the adult and the paediatric diabetic population, amounting to 93,250.00 euros per year. This research has limitations to allow one to analyse this pharmaco-economically since adults are not included in this research. However, Kedia (2011) stated that glucagon, if used well, gives economic advantages by reducing the number of patients who are admitted to hospital. The American Diabetes Association also supports this cost saving by stressing on education. In Malta, further studies in assessing the cost of hypoglycaemia and glucagon use can be looked into. Besides one can also investigate cost of the current scenario where patients are given the glucagon injection and self-administer. One can include cost of an education and support system for these caregivers versus cost it would take for one to go directly to a hospital or get ambulance if hypoglycaemic.

The underuse of glucagon can be attributed to various factors. Infrequent use, fear, lack of education, lack of confidence which were all parameters that were measured in this research before and after intervention.

Fear is a cofounding factor, not just for the child but also for their caregivers (Haugstvedt et al, 2010; Haugstvedt et al, 2015). The fear of future hypoglycaemic episodes is noted to be one of the underlying factors, which leads to inappropriate diabetes control and suboptimal glycaemic management (Kedia, 2011). Fear was very evident in this research, where before the intervention, 67.5% of those interviewed gave the highest score of 5,

when questioned how scared they are of the child suffering from a severe hypoglycaemic attack. The researcher went on to question what actions are taken to avoid this from happening. The majority, 97.5%, stating that they give appropriate amounts of sugar but monitor constantly. After providing the Glucagon Tool Kit and giving information on the use of glucagon injection to caregivers, the highest score of 5, given by carers was now 90%.

HFS- Hypoglycaemia Fear Survey is a tool used to assess parents' worries and their behaviours to hypoglycaemia. In a study by Haugstvedt et al (2010), the survey was adopted for parents. The HFS is a 25-item survey, of which 10 criteria assess behaviour such as inappropriate behaviour due to hypoglycaemia, example: giving children large meals before going to bed to avoid hypoglycaemic episode at night or allowing the child to have levels of blood glucose higher than required to be safe that hypoglycaemia does not occur. The other 15 items assess worry, such as anxiety-provoking aspects of this phenomena. A Likert Scale is used and a score is obtained- high scores indicate fear among patients (Haugstvedt et al, 2010).

One would need to investigate further if, in the Maltese population, there is an association between parental fear of hypoglycaemia and episodes of hypoglycaemia together with higher blood glucose levels being reported, as highlighted by Haugstvedt et al in 2010. The scope of this research was to educate on the use of glucagon, therefore this aspect was not explored.

Sending children to school is another fear (Pinelli et al, 2010). This is also evident from the results obtained. Of all the respondents, 56.3% only stated that the school is informed of glucagon in the case of a hypoglycaemic episode, while 41.3% did not inform the school. Of these 41.3%, 31.3% state that school will not use glucagon if an episode

occurs, therefore this is why the school was not notified. One can thereby recommend the development of tool kits and workshops that can be addressed to school teachers and heads, to ensure safe environment for children and ensure peace of mind to the parents. In fact, when asked if there is any other information that the carers wish to receive, of the 25% who said yes, 5% want increased awareness and education on glucagon given to schools. This is also proposed by Kedia, 2011, where it is stated that introducing training on the use of glucagon injection for schools, sports coaches, also extended to nurses and any other person, healthcare professional or not, who works in close contact with children, will benefit from short and long term management of diabetes.

The dilemma with schools is the current controversial stand where educators do not take responsibility to administer chronic or emergency medications to children. If they receive formal training about glucagon, educators may feel empowered and confident to administer this medication so as to limit morbidity and hospitalisation of the child as a result of hypoglycaemia.

Education is the key to better diabetes control (Freeborn et al, 2013; The National Institute of Health and Care Excellence, 2015), Kedia in 2011 is even more specific, and states that to improve management of severe hypoglycaemia, cooperation between patients, families and health care providers need to be established, together with provision on better information and continued education. Increased frequency of glucagon use will also benefit the child, for both short-term and long-term benefits (Kedia, 2011). The research being carried out in this dissertation proves that education does help on various levels, such as increased confidence and also increased knowledge. Caregivers themselves expressed the wish to be educated. When asked if there is any other information that can the carers wish to receive, of the 25% who said yes, 13.75% said they wish to have more

revision sessions and 6.25% requested information on general knowledge related to diabetes.

Lack of awareness of hypoglycaemia is a key factor that increases risks of severe hypoglycaemia. This leads to these patients having nine times the risk of having severe hpyoglyceamic episodes than those who are aware of the condition (Kedia, 2011). The reason for this being that signs and symptoms will not be noted earlier and therefore one cannot treat and correct the low blood sugars before it has aggravated (Kedia, 2011). Young age in itself is also a risk factor for hypoglycaemia. (Bulsara MK et al, 2004; Gonder-Fredrick L et al, 2008; Clarke et al, 2009; Kedia, 2011) When questioned on the symptoms of severity the child shows when hypoglycaemic, 41.25% of participants stated that the child acts normal. In view of this, during the development stages of the Glucagon Tool Kit it was decided that a holistic approach is taken and hypoglycaemia in general is briefly explained to serve as a revision for carers. This was assessed by questioning what hypoglycaemia means at the start of each questionnaire. All participants correctly selected that hypoglycaemia is best defined as a blood sugar level below 4mmol/L.

Before the intervention one can note that 61.3% of the caregivers' state that they do not carry glucagon injection around with them, one of the main reasons (21.25%) being that it is too bulky to carry around and keep cool with an ice pack. This scenario changed after the intervention with only 35% of the carers not carrying glucagon injection around at all.

The change in expiry date is another educational point that the researcher focused on. Prior to the intervention, 36.3% of the participating caregivers, would discard the glucagon injection if taken out of the fridge, while only 26.3% gave the correct answer. Ten percent did not know what to do at all. After provision of the Glucagon Tool Kit 85% of the carers gave the correct reply when re-tested, hence they stated that the expiry

decreases by 6 months if the glucagon injection is left out of the fridge up to a temperature of 25 degrees Celsius. Only 1.3% did not know the answer and the rest (13.8%) were unsure of the period of time the expiry date has to be decreased.

Before the analysis of how one should use and administer glucagon the carers were asked how informed they feel on the use and administration of glucagon. Thirty-nine of the 80 (48.75%) participants stated they feel informed, 35% feel not so informed and 5% do not feel informed at all, while 11.25% feel very informed. This situation improved after the intervention and provision of the Glucagon Tool Kit. A statistical significant difference is in fact noted ($p<0.001$), with 65% of the carers feeling very informed, 33.75% feeling informed and the minority 1.25% feeling not so informed.

Another educational point was related to reconstitution and administration of glucagon. This was both demonstrated verbally and by a dummy glucagon injection in front of the caregiver. The video was also viewed. As with the other interventions this resulted in a statistically significant difference, where ratings before intervention range from 20 caregivers getting a score of zero, 8 carers scoring 1, 7 scoring 2 and another 7 carers scoring 3, 17 scoring 4 and only 21 carers out of 80 scoring 5, full marks. After the intervention scores were shifted to 62 carers scoring 5 and the rest 16 carers,1,1, scoring 4, 3, 2 respectively.

During development of the video it was ensured that it will be produced in Maltese and English to help optimise educating all carers. It was also vital to keep it as short as possible, thereby the length of the video is approximately 1.3 minutes. Same principles were also applied to the chart developed. The chart was created to ensure that the carer will be fully equipped with how to use the medication especially during use. Six important images were selected and short phrases written underneath each one to explain in brief

what needs to be done. This is in line with what Ferguson and Pawlak, 2011 suggests – to use pictures, focus on a central message, emphasise key points and use lots of white space, with font size 12 or larger. In another paper by Ferguson, 2012 it states that a video accompanied by a leaflet to highlight the key points will be very effective in aiding patient education.

Videos are an underutilised medium that assists in education. It enables patients to visualise and better understand since it provides complex information in a visual format instead of having it only written (Ferguson, 2012).

The carers found the information provided via Glucagon Tool Kit very informative since 93.8% of the interviewed gave it full scores. The video was viewed by 72.5% of the carers. The chart was placed with the fridge door by 30% of the participants, while 53.75% placed it with other diabetic notes and 16.25% left it in a handy place to find immediately. This proves that the aim of the video and material created have been reached. The results of increased knowledge and confidence also highlight this.

To aid accessibility and sharing of the video provided to everyone, the video was uploaded on vimeo.com website which gives the option to change the URL of the link to a simpler and catchier URL to enable one to memorise it better.

Confidence is another issue that needs to be dealt with in order to optimise use of glucagon. Hands on practice with glucagon is recommended (Harris et al, 2001; Kedia, 2011) As highlighted in paper by Kedia, 2011, this research also stressed on the use of an expired glucagon injection to practice on with saline water. This enables caregivers to build confidence if a real emergency had to happen.

Confidence was also tested by means of a Likert scale in this research. It is evident that education provided together with the demonstration and video on how to use glucagon

all help achieve a positive statistically significant difference in confidence amongst the participants. When participants were questioned if they feel that their confidence increased, 96.3% stated that confidence did increase.

The Glucagon Tool Kit was also extended to pharmacists. When asked if information on glucagon was ever provided by the pharmacist to carers of patients with type 1 diabetes mellitus 33.8% of those interviewed stated yes, while 30% state that they (the pharmacists) received requests to provide information on glucagon. It was not specified if those who were given information or requested information were for use in T1DM in adults or children. Besides this, upon analysing results it was noted that the Glucagon Tool Kit provided, statistically significantly increased knowledge of the pharmacists on glucagon, together with a statistical significant increase in confidence to use glucagon. This intervention helps to decrease one of the four barriers that Tamayo et al (2014) speaks of in their article. Tamayo et al (2014), states that the individual professional barrier can be eliminated by interventions on guidelines and adequate provision of knowledge. This in turn will increase the effective care to the caregivers.

4.2. LIMITATIONS OF STUDY

Intervention with patients was re-assessed only four weeks after the intervention due to time limitations. Barely any literature focuses on glucagon use in paediatric T1DM in Malta. Sampling children population was investigated so the power of the sample with regards to patients and carers has a Confidence Interval of 7.2 with sample size of 80 for the patients interviewed. In parallel to interviewing patients, pharmacists were also being interviewed so this could have influenced patients in their response if pharmacists were to share the knowledge gained. Above all, timing of year of the intervention could have affected the results from patients since it was summer, turn out at doctor's clinic was not

to the maximum- patients reschedule due to going abroad and due to other events, that they may have.

Although the response given was highly statistically significant, the population of pharmacists who responded to the questionnaire was too small when compared to the total pharmacist population. Due to time limitations, a one to one contact could not be held with pharmacists. This would have helped increase the response rate.

4.3. Recommendation for further studies

Extend this research to schools and teachers and other healthcare professionals in Malta who aid diabetic patients benefit from the use of glucagon. The economic impact of overall use of glucagon and hypoglycaemia on the health care's budget and the benefits of education versus the patient being admitted to hospital is to be researched further. Another suggestion is to extend this research to adult population. A fourth suggestion would be to assess the impact of the Glucagon Tool Kit by looking at patient outcomes whereby the occurrence of hypogylceamic episodes in this patient population after the pharmacist led intervention is assessed. Studying the duration of the education empowerment and at what point carers and patients would require re-enforcement through a live session may be explored.

4.4. Conclusion

This research has led to the development of a Glucagon Tool Kit which was shown to be concise, informative and useful is now being used for service provision. Nurses, doctors and pharmacists together with other healthcare professionals, in both hospital and community settings, are using the Glucagon Tool Kit to educate type 1 diabetes mellitus patients on the safe and effective use of glucagon. The availability of the developed

Glucagon Tool Kit makes it easy for carers to go through the kit whenever they need to refresh their memories. The Glucagon Tool Kit contributes to increased patient safety in managing hypoglycaemia in type 1 diabetes mellitus paediatric patients.

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APPENDICES

APPENDIX 1: APPROVALS

APPENDIX 1A

APPLICATION TO UREC

Applicant's email: danika.agius-decelis.08@um.edu.mt Index No:

UNIVERSITY OF MALTA

UNIVERSITY RESEARCH ETHICS COMMITTEE

Check list to be included with UREC Proposal Form

Please make sure to tick **ALL** the items. Incomplete forms will not be accepted

		YES	NOT APP.
1a.	Recruitment letter/ information sheet for subjects, in English	☒	☐
1b.	Recruitment letter/ information sheet for subjects , in Maltese	☒	☐
2a.	Consent form, in English, signed by supervisor, and including your contact details	☒	☐
2b.	Consent form, in Maltese, signed by supervisor and including your contact details	☒	☐
3a.	In the case of children or other vulnerable groups, consent forms for parents/ guardians, in English	☐	☒
3b.	In the case of children or other vulnerable groups, consent forms for parents/ guardians, in Maltese	☐	☒
4a.	Tests, questionnaires, interview or focus group questions, etc in English	☒	☐
4b.	Tests, questionnaires, interview or focus group questions, etc in Maltese	☒	☐
5a.	Other institutional approval for access to subjects: Health Division, Directorate for Quality and Standards in Education, Department of Public Health, Curia...	☒	☐
5d.	Other institutional approval for access of data: Registrar, Data Protection Officer Health Division/ Hospital, Directorate for Quality and Standards in Education, Department of Public Health...	☒	☐
5c.	Approval from Person Directly responsible for subjects: Medical Consultants, Nursing Officers, Head of School	☒	☐

Received by Faculty Office on	
Discussed by Faculty Research Ethics Committee on	
Discussed by University Research Ethics Committee on	

UNIVERSITY OF MALTA

Request for Approval of Human Subjects Research

Please type. Handwritten forms will not be accepted.

FROM: (*name, address for correspondence)* Danika Agius Decelis *Joselove Triq il- Merill Mosta MST4611*	PROJECT TITLE: Glucagon use in Paediatric Type 1 diabetic Patients: An innovative Approach to Improve outcomes.
TELEPHONE: 79415960	
EMAIL: danika.agius-decelis.08@um.edu.mt	
COURSE AND YEAR: Doctorate in Pharmacy (Pharm D) 2015-2017	
DURATION OF ENTIRE PROJECT: From 01/03/2016 To 01/03/2017	FACULTY SUPERVISOR'S NAME AND EMAIL: Professor Lilian M.Azzopardi and Dr Louise Grech lilian.m.azzopardi@um.edu.mt; louise.grech@um.edu.mt

ANTICIPATED FUNDING SOURSE: *(Include grant or contact number if known)* *N/A*

1. Please give a brief summary of the purpose of the research, in non-technical language. The aim of this research is to develop and evaluate the impact of educating carers of paediatric patients with type one diabetes mellitus on the emergency use of glucagon in hypoglycaemia, in a safe way.
2. Give details of procedures that relate to subjects' participation (a) How are subjects recruited? What inducement is offered? (*Append copy of letter or advertisement or poster, if any.)* *Carers of patients having type 1 diabetes mellitus and attending the out patients clinics of the participating consultants will be given a study information sheet(Appendix 1) to read. Any quesries will be answered by the pharmacist –researcher who will be present. After having read and understood the sheet, the carers will be asked if they are willing to participate in the research. Those accepting to participate in the research will be given the Consent Form(Appendix 2) and asked to sign it. No inducement is offered. The participationg carers will be offered educational sessions run by pharmacist-researcher in order to educate on the safe and important use of glucagon in emergency hypoglyceamia.*
(b) Salient characteristics of subjects – number who will participate, age range, sex, institutional

affiliation, other special criteria:
Approximately 100 carers of children who have type 1 diabetes will be asked to participate. Criterias for inclusion in the research:Carers of children suffering from Type 1 diabetes Mellitus; Are under the care of participating clinician; Able to understand English or Maltese; Not suffering from Mental illnesses or impaired cognition

(c) Describe how permission has been obtained from cooperating institution(s) – school, hospital, organization, prison, or other relevant organization (*append letters).* Is the approval of another Research Ethics Committee required?
Approval have been sought and granted from: Chairman of the Department of Paediatrics, participating consultants, Data Protection Officer at Mater Dei Hospital and Chief Executive Officer at Mater Dei Hospital. Approval attached (Appendix 3)

(d) What do subjects do, or what is done to them, or what information is gathered? (*Append copies of instructions or tests or questionnaires)* How many times will observations, test, etc., be conducted? How long will their participation take?
Educational sessions on the correct and safe use of glucagon pen will be provided to the carers of the patietns by the pharmacist- researcher. Educational material prepared by the pharmacist-researcher will also be offered to patients to aid them. The pharmacist-researcher will be using a questionnaire (Appendix 4) to assess whether the carers found the session useful.

(e) Which of the following data categories are collected? Please tick where appropriate.

Data that reveals:

Race and ethnic origin	☐
Political opinions	☐
Religious and philosophical beliefs	☐
Trade union memberships	☐
Health	☒
Sex life	☐
Genetic information	☐

3. How do you explain the research to subjects and obtain their informed consent to participate? *(If in writing, append a copy of consent form.)* If subjects are minors, mentally infirm, or otherwise not legally competent to consent to participation, how is their assent obtained and from whom is proxy consent obtained? How is it made clear to subjects that they can quit the study at any time?
As explained in section 2, a study information sheet (Appendix 1) is distributed by the pharmacist-researcher to the carers. The pharmacist-researcher will be available to answer any queries. Carers accepting to participate will be asked to sign a consent form (Appendix 2). Carers are informed that they can withdraw from the research at any point in time . Inclusion criteria: Carers of children with type 1 diabetes mellitus; Are under the care of participating clinician; Able to understand English or Maltese; Not suffering from mental illnesses or impaired cognition

4. Do subjects risk *any* harm – physical/ psychological/ legal/ social – by participating in the research? Are the risks necessary? What safeguards do you take to minimize the risks?
No.

5. Are subjects deliberately deceived in *any* way? If so, what is the nature of the deception? Is it likely to be significant to subjects? Is there any other way to conduct the research what would not involve deception, and, if so, why have you not chosen that alternative? What explanation for the deception do you give to subjects following their participation?
No.

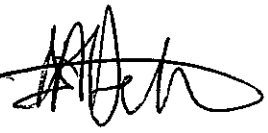
6. How will participation in this research benefit subjects? If subjects will be 'debriefed' or receive information about the research project following its conclusion, how do you ensure the educational value of the process? (*Include copies of any debriefing or educational materials)*
Better comprehension of hypoglyceamia and how to use glucagon in a safe and timely manner to reverse the effects of hypoglyceamia which can be life-threatening. Throughout these educational sessions the study aims to increase the awareness on the safe use of glucagon which improve the quality of life and safety of the peadiatric patients. Educational material intended for use to support sessions has been complied by the pharmacist-researcher (Appendix 6)

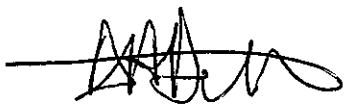
TERMS AND CONDITIONS FOR APPROVAL IN TERMS OF THE DATA PROTECTION ACT

- Personal data shall only be collected and processed for the specific research purpose.
- The data shall be adequate, relevant and not excessive in relation to the processing purpose.
- All reasonable measures shall be taken to ensure the correctness of personal data
- Personal data shall not be disclosed to third parties and may only be required by the University or the Supervisor for verification purposes. All necessary measures shall be implemented to ensure confidentiality and where possible, data shall be anonymized.
- Unless otherwise authorized by the University Research Ethics Committee, the researcher shall obtain the consent from the data subject (respondent) and provide him with the following information: The researcher's identity and habitual residence, the purpose of processing and the recipients to whom personal data may be disclosed. The data subject shall also be informed about his rights to access, rectify, and where applicable erase the data concerning him.

I, the undersigned hereby undertake to abide by the terms and conditions for approval as attached to this application.

I, the undersigned, also give my consent to the University of Malta's Research Ethics Committee to process my personal data for the purpose of evaluating my request and other matters related to this application. I also understand that, I can request in writing a copy of my personal information. I shall also request rectification, blocking or erasure of such personal data that has not been processed in accordance with the Act.

Signature: 

APPLICANT'S SIGNATURE: ***I UNDERSTAND THAT I WILL NOT INITIATE MY RESEARCH PRIOR TO RECEIVING APPROVAL FROM THE UREC.***  DATE 1-3-2016	FACULTY SUPERVISOR'S SIGNATURE *I have reviewed this completed application and I am satisfied with the adequacy of the proposed research design and the measures proposed for the protection of human subjects.*  DATE 1-3-2016

To be completed by Faculty Research Ethics Committee

We have examined the above proposal and advise

Acceptance **Refusal** **Conditional Acceptance**

For the following reason/s:

Signature: Date:

To be completed by University Research Ethics Committee

We have examined the above proposal and advise

Acceptance **Refusal** **Conditional Acceptance**

For the following reason/s:

Signature: Date:

APPENDIX 1B

APPROVAL BY UREC

L-UNIVERSITÀ TA' MALTA

Msida – Malta
Skola Medika
Sptar Mater Dei

UNIVERSITY OF MALTA

Msida – Malta
Medical School
Mater Dei Hospital

Ref No: **28/2016**

Tuesday 1st November 2016

Ms. Danika Agius Decelis
Joselove
Triq il-Merill
Mosta
MST4611

Dear Ms. Danika Agius Decelis

Please refer to your application submitted to the Research Ethics Committee in connection with your research entitled:

Glucagon use in Paediatric Type 1 diabetic Patients: An innovative approach to Improve outcomes

The University Research Ethics Committee granted ethical approval for the above mentioned protocol.

Yours sincerely,

Dr. Mario Vassallo
Chairman
Research Ethics Committee

APPENDIX 1C

APPROVAL BY DATA PROTECTION

APPENDIX 1D

CONSENT FORM

CONSENT FORM

I am a Maltese citizen and am over eighteen (18) years of age. I have been asked to participate in a research study entitled:

'Glucagon use in Paediatric Type 1 diabetic Patients: An Innovative Approach to improve outcomes.'

The purpose and details of the study have been explained to me by:

Danika Agius Decelis (Pharmacist)

and any difficulties which I raised have been adequately clarified.

I give my consent to the Principal Investigator and her delegate to make the appropriate observations. I am aware of the inconveniences which this will cause.

I understand that the results of this study may be used for medical or scientific purposes and that the results achieved from the study in which I am participating may be reported or published: however, I, or child under my care, shall not be personally identified in any way, either individually or collectively, without my express written permission.

I am under no obligation to participate in this study and am doing so voluntarily.

I may withdraw from the study at any time, without giving any reason. This will not influence in any way the care and attention and treatment normally given to me (applicable only in case of patients receiving treatment).

I understand that any complications and/or adverse effects which may arise during or as a consequence of the study will be recorded and any treatment which this may entail will be given within the Government Health Services.

I am not receiving any remuneration for participating in this study. In case of queries during the study I may contact Danika Agius Decelis (79415960)

Signature of participant_____

Name of participant _____

ID of participant _____

Signature of Chief Investigator _____

Name of Chief Investigator _____

ID of Chief Investigator _____

Date _____

PROPOSTA GĦALL-FORMULA TAL-KUNSENS

Jien/a ċittadin/a Malti/ja u għalaqt tmintax (18)-il sena.

Talbuni biex nieħu sehem fi studju riċerka bl-isem ta':

Glucagon use in Peadiatric Type 1 diabetic Patients: An innovative Approach to improve outcomes.

Il-għan u d-dettalji ta' l-istudju spejgathomli:

Danika Agius Decelis (Spizjara)

li wkoll iċċaratli xi mistoqsijiet li għamilt.

Nagħti l-kunsens tiegħi lill-persuna responsabbli għal-din ir-riċerka u l-assistenti tagħha biex jagħmlu l- osservazjonijiet li hemm bżonn u nifhem li dan jista' jkun ta' skomdu għalija.

Jiena nifhem li r-riżultati ta' dan l-istudju jistgħu jintużaw għal skopijiet xjentifiċi u jista' jiġi ppubblikat rapport bil-miktub: jekk isir hekk b'ebda mod ma nista' nkun identifikat/a, individwalment jew bħala parti minn grupp, mingħajr il-kunsens tiehħi bil-miktub.

Jiena ma għandi l-ebda dmir li niehu sehem f'dan l-istudju u dan qed nagħmlu minn rajja. Jiena nista', meta rrid, ma nkomplix niehu sehem fl-istudju, u mingħajr ma' nagħti raġuni. Jekk nagħmel hekk xorta nibqa' nieħu l-kura li ssoltu tingħatali (tapplika biss għal pazjenti li qed jieħdu kura).
Jiena nifhem li jekk ikun hemm xi kumplikazzjoniji jew effetti mhux mistennija waqt l-istudju, dawn jiġu mniżżla bil-miktub u jekk ikun hemm bżonn xi kura, tiġi mgħotija fis-Servizz Nazjonali tas-Saħħa.

Mhux qed nitħallas biex nieħu sehem f'dan l-istudju.

Jekk ikolli xi diffikulta' waqt l-istudju, nista' nistaqsi għal:

Firma tal-parteċipant _____

Isem tal-parteċipant _____

Numru ta' l-identita _____

Firma tal-persuna responsabbli għal din ir-riċerka _____

Isem tal-persuna responsabbli għal din ir-riċerka _____

Numru ta' l-identita _____

Data _____

APPENDIX 2: GLUCAGON TOOL KIT AND OTHER INFORMATION CREATED (MALTESE AND ENGLISH)

APPENDIX 2A

STUDY INFORMATION SHEET

Study Information Sheet

Who is doing this study?

The study is being carried out by Danika Agius Decelis, a pharmacist reading for a doctorate in Pharmacy. Thesis entitled *"Glucagon use in Paediatric Type 1 diabetic patients: An innovative Approach to Improve outcomes".* The study is being undertaken under the supervision of the Pharmacy Department at the University of Malta.

What are the aims of the study?

This study aim is to develop and evaluate the impact of educating carers of peadiatric patients with type one diabetes mellitus on the emergency use of glucagon in hypoglycemia, in a safe way.

Who can participate in the study?

Carers of children who have type 1 diabetes Mellitus at Mater Dei Hospital and who are under the care of the participating consultants.

What will happen if I decide to participate in the study?

As a routine you will be asked about glucagon use and you will be given information about how and why it is used.

Will I have to take part in questionnaires?

You will be asked to take part in 1 questionnaire namely:

i. Glucagon Assessment Questionnaire

The questionnaire will be repeated at a few months' interval. The questionnaires take about 10-15 minutes to be filled in and the researcher will help you to fill them in.

Will the study affect my treatment?

The study will not affect your treatment. You will not undergo additional procedures to current routine. You will continue your regular visits to the clinic and will continue being under the care of your current consultant paediatric endocrinologist.

Who will view the information?

The information will only be accessed by the researcher. Addresses and contact numbers will only be used to contact you.

You are free to withdraw from the study at any point in time.

If you require further information, please do not hesitate to contact me on 79415960.

Thank you

Danika Agius Decelis

Department of Pharmacy
University of Malta

Informazzjoni dwar l-istudju

Min qed jagħmel dan l-istudju?

Dan l-istudju qed issir min Danika Agius Decelis, spiżjara li qed tagħmel id-dottorat fil-farmaċija. L-istudju bl-isem ta': "Glucagon use in Paediatric Type 1 diabetic patients: An innovative Approach to Improve outcomes". Dan l-istudju qed issir taħt is-superviżjoni tal- fakulta tal-farmaċija fl-universita ta' Malta.

L-għan ta' l-istudju?

l-għan ta' l-istudju hu biex jiġu żvilupati u evalwati l- impatt ta'l-edukazzjoni li toffri l-ispiżjara għal minn jieħu ħsieb lit-tfal li għandhom id-dijabete ('type 1') b'mod speċjali, iffukat fuq l-użu tal-'glucagon' f emerġenza meta wieħed jitbaxxilu ħafna l-livell taz-zokkor.

Minn jista jipparteċipa f'dan l-istudju?

Persuni li jieħdu ħsieb tfal li għandhom id-dijabete ('Type 1') li jigu Mater Dei u dawk li qedin taħt il kura ta xi konsulent li qed jipparteċipa f'dan l-istudju.

X'jiġri jekk niddeċidi li irrid nipparteċipa f'dan l-istudju?

Tkun mistoqsi fuq l-użu tal- 'injection' tal-'glucagon' u tkun mogħti informazzjoni u tagħrif fuq kif, meta u għala għandek tużha.

Inkun irrid nieħu sehem f'xi kwestjonarju?

Inti tkun mitlub tieħu sehem fil- kwestjonarju:

i. Għarfien fuq il-'glucagon'.

Dan il-kwestjonarju jiġi irrepetut wara ftit xhur. Il-kwestjonarju jieħu madwar 10-15 –il minuta biex jintela' b'l-għajnuna ta l-ispiżjara-riċerkatur.

L-istudju għandu xi impatt fuq it-trattament li qed nieħu?

Le, l-istudju ma jaffetwax it-trattament li qed tieħu. Ma għandekx għalfejn tagħmel proċedura iktar min dik li normalment tagħmel u tkompli tattendi b'mod regolari għal- visti normali taħt il- kura tal- konsulent tiegħek.

Minn ha jara' l-informazzjoni li nagħti?

L-informazzjoni tkun aċċessibli biss għar-riċerkatur u informazzjoni personali biex tigi ikkuntatjat jiġu użati biss għall-skop ta din ir-riċerka.

Bħala parteċipant f'dan l-istudju iżomm id-dritt li tieqaf mill-kontribuzzjoni tiegħek, meta trid.

Jekk trid iktar informazzjoni ikkuntatjani fuq 79415960.

Grazzi

Danika Agius Decelis

APPENDIX 2B

DEMOGRAPHICS DATA SHEET

Demographics Data Sheet.

Code: _____

Contact number: _____

Main Carer

1) Male __ Female __

2) Age group: 18-25 years __
26-35 years __
36-45 years __
46- 55years __
56-65 years __
66-75 years __
76 years + ___

3) Nationality? _____

4) Level of education:

__ Primary
__ Secondary
__ Post secondary
__ Tertiary

5) Do you have Type 1 Diabetes and take insulin yourself?

Yes I am diabetic and take insulin treatment ___
Yes I am diabetic and take oral treatment___
Not diabetic _

6) Is this your first time dealing with diabetes and insulin therapy? _ Yes _ No

Child with diabetes

7) Male _ Female _

8) Age of child ____

9) Year of onset?

10) How was it discovered?

Symptomatic Hyperglycaemia__ Other_____

11) From the scale of 1-10 how well informed about the disease do you think you are, with regards to

	1	2	3	4	5	6	7	8	9	10
A) Meal planning										
B) Medication taken										
C) Hyperglyceamia										
D) Hypoglyceamia										
E) Did find the necessary support for diabetes Type 1										

12)Insulin Regimen: Standard Insulin (twice a day) _____
Insulin Analogue (4 times a day) _____

13)How long has the child been on this most recent treatment? __

14)Are you satisfied about the child's glycemic control? Yes _ No__

15)Does the child have any other condition? _____

16)Does the child take any other medications besides those for diabetes?

Yes _ No __

17) Do you have glucagon injection at home? Yes _ No __

18) How often is blood glucose tested?

19)What is the average HBA1C level over the last year _____

APPENDIX 2C

GLUCAGON ASSESSMENT QUESTIONNAIRE BEFORE INTERVENTION

Glucagon Assessment Questionnaire

Introduction

Code ____

1A) Did your child ever experience an incident of hypoglycaemia before?

□ Yes □ No

1B) If yes, how was your child affected?

□ unconscious
□ delusional/confused
□ other

2A) Has your child ever been hospitalised due to very low blood sugar levels? □ Yes □ No

2B) If yes, how many times?

Hospitalised twice in the last 6 months □
More than 4 times in the last year □
Once in the past year □
Never □
Other □

3A) In the event of a hypoglycaemic attack, have you ever used glucagon?

□Yes □ No

3B) How many times have you used glucagon before?

_____

3C) If so, on whom did you use it?

□ Your child □ Other

Assessing carer's knowledge

4) Hypoglycaemia is best described as a blood sugar level below 4mmol/L

□ True □ False □ Do not know

5) Glucagon works by unlocking glucose in the liver so it will increase blood glucose

□True □ False □ Do not Know

6) Glucagon is used when blood sugar levels are low that child loses consciousness

□True □ False □ Do not Know

Symptoms of Hypoglycaemia

Kindly reply to the statements below by ticking a value from 1 to 5 (1 is the least, 5 is the most)

7) In the event of a hypoglycaemic attack, the child will:

	1 Least →	2	3	4	5 Most
a) Start shaking					
b) Have a fast heart beat					
c) Start sweating					
d) Feel dizzy					
e) Feel anxious					
f) Be hungry					
g) Have an Impaired Vision					
h) Be Weak					
i) Suffer from a Headache					
j) Be Irritable					
k) Become hyper					

Glucagon Use

8) Do you have glucagon at home?

□ Yes □ No □ Do not Know

9A) Do you have it at any other location?

□ Yes □ No □ Not Sure

9B) If so, where else do you have it: _____

9C) Do you carry it around with you? □ Yes □ No □ Not Sure

If yes, how often and when do you take it out with you? _____

If No, why? _____
If No, what would you do if you do not take it out with you and a hypogylceamic attack occurs?

10)Where is it stored? □ Fridge □ Freezer □ Room temperature □ Do not Know

11) If you store glucagon at room temperature, what will happen to its expiry date?

□ Stays the same
□ is shorter- by how much_____
□ Injection is no longer good
□ Do not know

12) Were you ever advised on how to prepare glucagon prior to administration?

□ Yes □ No □ Do not know

13) How well informed are you about the use and preparation of glucagon?

□ very informed □ informed □ not so informed □ not informed

14) Briefly explain how you (would) prepare glucagon prior to administration?

_____
_____
_____

15)When mixing glucagon, kindly indicate how important the points below are:

Kindly reply to the below statements by ticking a value from 1 to 5 (1 is the least, 5 is the most)

	1 Least →	2	3	4	5 Most
a) ALL the white powder must dissolve					
b) When mixing, the needle must be kept in the bottle					
c) Air should be removed from the syringe before injecting					

16) What dose would you give your child?

_____

17) Are other carers of your child knowledgeable of the glucagon administration process in case you are not available?

□ Yes □ No □ Do not know

If no, why?

_____

_____

Kindly reply to the below statements by ticking a value from 1 to 5 (1 is the least, 5 is the most)

	1 Least →	2	3	4	5 Most
18) How confident do you rate your ability to use glucagon?					
Assessing fear					
19) How concerned are you, from a scale of 1 to5, that your child will have a severe hypoglycaemic episode?					

20)What action do you take to avoid hypoglyceamia?

A. Give sugars to child often
B. Give child a lot of sugar before bedtime
C. Give child a lot of sugar to take to school
D. Do not give more sugar than required (keep glucose level within limits) but keep sweets and glucagon constantly with you to be prepared if an attack occurs.

21A) How confident are you to leave your child under the supervision of others?

□very confident □ confident □ not so confident □ not confident at all

21B) When you leave your child with someone else, do you advise on the use of glucagon and hypoglycaemia?

□ Yes, only initially

□ From time to time

□ When I remember

□ Rarely

□ Never

22A) Has it ever happened that the child needed glucagon when you were away?

□ Yes □ No □ Never

22B) If yes, is the child afraid that it will happen again when you are not there?

□ Yes □ No □ Do not know

23) Have you ever told the child's school administrator or teacher about hypoglycaemia?

□ Yes □ No

If No- why?

_____

If no- what would you do if the child develops an attack at school?

_____

Kwestjonarju dwar l-gharfien fuq il-'Glucagon'.

Introduzzjoni

Kodici _____

1. A Qatt xi darba t-tifel/tifla tbaxxielhom hafna z-zokkor?

   □ Iva □ Le

1B Jekk iva kemm kienu gravi:

□ Intilfu minn sensihom
□ konfuzi
□

2. A Qatt xi darba dahhalt lit-tifel/tifla l-isptar minhabba li waqalhom hafna l-livell taz-zokkor fid-demm?

   □ Iva □ Le □ Ma Nafx

2.B Jekk Iva kemm il-darba?

□ Dahal/dahlet l-isptar darbtejn f l-ahhar sitt xhur
□ Aktar min 4 darbiet f l –ahhar sena
□ Darba f l-ahhar sena
□ Qatt
□

3.A F kas ta'zokkor baxx fid dehem, qatt uzajt l 'injection' tal-'Glucagon' ?

□Iva □ Le □ Ma nafx

3B) Kemm -il darba uzajtha?

_____

3C) Fuq min intuzat?

□ Fuq it-tifel/tifla tieghek □ Xi hadd iehor

Evaluazjoni ta l-gharfien tal-'carer'

4. L ahjar definizjoni ta meta jitbaxxa z-zokkor fid-demm hija li l-livel taz-zokkor ikun baxx iktar min 4mmol/l:

□Vera □ Falz □ Ma nafx

5. Il-medicina 'glucagon' tahdem billi bhal cavetta, tiftah iz-zokkor li jkun hemm fil-fwied ghal god-demm (izzid iz-zokkor fid –demm)

□ Vera □ Falz □ Ma nafx

6. Din il-medicina 'glucagon' tuza' meta jkollok iz-zokkor baxx hafna tant li tifel/tifla jintilfu min sensijhom:

□ Vera □ Falz □ Ma nafx

Sintomi ta' meta jaqalek iz-zokkor
Wiegeb billi timarka numru mill-1 sa 5 (1: l-inqas, 5: l-iktar)

7. Meta t-tifel/a jkollhom iz-zokkor baxx, it-tifel tifla:

	1 L-Inqas	2	3	4 →	5 L-iktar
a) Jibda jirtod					
b) Qalb tghaggel					
c) Jeghreq hafna					
d) Jhossu/ha stordut/a					
e) Jhossu/ha anzjuz/a					
f) Jkun/tkun bil-guh hafna					
g) Ma jibqax/tibax jara/tara sew					
h) Jkollu/a ghejja Kbira					
i) Ugieh ta'ras					
j) Jkun/tkun irritat/a					
k) Isir/issir fuq ruhu/a hafna					

Uzu tal – 'Glucagon'

8. Ghandek 'injection' tal-'glucagon' id-dar?

□ Iva □ Le □ Ma Nafx

9. A. Ghandek ohra xi post iehor?

□Iva □Le □ Mhux certa

9B) Jekk Iva Fejn: _____

9C) Igorrha miak?

□ Iva □ Le □ Ma Nafx

Jekk Iva, kemm il darba igorrha u meta igorrha miak? _____

Jekk le, ghala le? _____

X taghmel jekk ma igorriex u jigri xi episodju li jaqa z zokkor? _____

10. Fejn izzommha? □ Fil-Fridge □ Fil-Freezer □ Barra f'xi karma □ Ma nafx

11. Jekk l 'injection' tal-glucagon qeghdha barra x'jigrilha d-data ta' l-iskadenza?

□ Tibqa l-istess
□ tiqsar – jekk tiqsar b kemm? ____
□ ma tibqax tajba
□ ma nafx

12. Qatt kont marraf fuq kif ghandek tiprepara l-glucagon qabel ma tigi amministrat?

□ Iva □ Le □ Ma nafx

13. Kemm inti infurmat fuq l-uzu u l preparazjoni tal-glucagon?

□ infurmat hafna □ infurmat □ mhux daqsek infurmat □ mhux infurmat

14. Spjega, fil qossor kif tiprepara l- glucagon qabel ma din tigi amministrata(qabel tuzaha):

_____

_____

_____

_____

15. Meta tkun qed thallat il-'Glucagon', indika, l-importanza taghhom:

Wiegeb billi timarka numru mill-1 sa 5 (1: l-inqas, 5: l-iktar)

	1 L-inqas →	2	3	4	5 L-iktar
a) It- trab l-abjad kollu irid jithallat					
b) Meta thallat, trid izzomm s-siringa fil-flixkun					
c) Nehhi l-arja minn gos-siringa qabel ittaqqab lit-tifel/a					

16. X doza taghti lit-tifel/a tieghek?

---

17. Meta inti ma tkunx mat-tifel/a, min ikun qed jiehu hsieb it-tifel/a jaf kif juza l-'injection'?

□ Iva □ Le □ Ma nafx

<u>Wiegeb billi timarka numru mill-1 sa 5 (1: l-inqas, 5: l-iktar)</u>

	1 L-inqas →	2	3	4	5 L-iktar
18) Kemm thossok kunfidenti tuza l-'glucagon'					
<u>Mistoqsijiet fuq il-Biza'</u>					
19) Kemm (mill-1 – 5), tibza' li t-tifel/a jkollhom episodju ta' 'hypoglycaemia' severa					

20. X'azzjoni tiehu biex ma jigrix dan?

A. Naghti lit-tifel/a zokkor kontinwu
B. Naghti lit-tifel/a hafna zokkor qabel jorqdu
C. Naghti lit-tifel/a hafna zokkor biex jiehdu l-iskola
D. Naghti zokkor biss kemm ikun hem bzonn (biex izzomm il-livell taz-zokkor fid-demm tajjeb) imma zzomm helu u il-'glucagon' fuqek biex jekk jigri xi haga tkun preparat.

21. A) Kemm thossok kunfidenti li thalli t-tifel/a ma xi hadd iehor?

□ kunfidenti hafna □kunfidenti □ma tantx inkun kunfidenti □ ma inkun kunfidenti xejn

21B) Meta thalli it-tifel/tifla ma' xi hadd, tispjegalhom kif tuza l 'injection' u fuq meta jitbaxxa z-zokkor fid-demm?

□Iva, ghal- bidu li joqod/toqod ma dik il persuna
□ Kultant – min zmien ghal zmien
□ Meta niftakar
□ Rari
□ Qatt

22. A) Qatt gratlek li hrigt u t-tifel/tifla kellhom bzonn juzaw l- injection?

□ Iva □ Le □ Qatt

22B) Jekk iva, it-tifel/tifla jibzaw li din terga tigri u ma tkunx hem inti?

□Iva □Le □ Ma nafx

23. A) Lill-ghalliema jew lill-assistenti ta' l-iskola qatt spjegajtilhom fuq x'jigri jekk jitbaxxa il-livell taz-zokkor tat-tifel/tifla?

□Iva □Le

23B) Jekk Le –ghala?_____

23C) Jekk le- x taghmel jekk ikollu/jkollha xi attack l-iskola u ma jkollomx l injection?

_____

_____

APPENDIX 2D

GLUCAGON ASSESSMENT QUESTIONNAIRE AFTER INTERVENTION

Glucagon Assessment Questionnaire

Introduction

Code ____

1A) Did your child ever experience an incident of hypoglycaemia since we last spoke?

□ Yes □ No

1B) If yes, how was your child affected?

□ unconscious
□ delusional/confused
□ other

2A) Has your child been hospitalised due to very low blood sugar levels? □ Yes □ No

3A) In the event of a hypoglycaemic attack, have you used glucagon?

□Yes □ No

3B) How many times have you used glucagon before?

_____

3C) If so, on whom did you use it?

□ Your child □ Other

Assessing carer's knowledge

4) Hypoglycaemia is best described as a blood sugar level below 4mmol/L

□ True □ False □ Do not know

5) Glucagon works by unlocking glucose in the liver so it will increase blood glucose

□True □ False □ Do not Know

6) Glucagon is used when blood sugar levels are low that child loses consciousness

□True □ False □ Do not Know

Glucagon Use

7) Do you have glucagon at home?

□ Yes □ No □ Do not Know

8A) Do you have it at any other location?

□ Yes □ No □ Not Sure

8B) If so, where else do you have it: _____

8C) Do you carry it around with you? □ Yes □ No □ Not Sure

If yes, how often and when do you take it out with you? _____

If No, why? _____
If No, what would you do if you do not take it out with you and a hypogylceamic attack occurs?

---

9)Where is it stored? □ Fridge □ Freezer □ Room temperature □ Do not Know

10) If you store glucagon at room temperature, what will happen to its expiry date?

□ Stays the same
□ is shorter- by how much_____
□ Injection is no longer good
□ Do not know

11) How well informed are you about the use and preparation of glucagon?

□ very informed □ informed □ not so informed □ not informed

12) Briefly explain how you (would) prepare glucagon prior to administration?

_____
_____
_____

13)When mixing glucagon, kindly indicate how important the points below are:

Kindly reply to the below statements by ticking a value from 1 to 5 (1 is the least, 5 is the most)

	1 Least →	2	3	4	5 Most
a) ALL the white powder must dissolve					
b) When mixing, the needle must be kept in the bottle					
c) Air should be removed from the syringe before injecting					

14) What dose would you give your child?

_____

15) Are other carers of your child knowledgeable of the glucagon administration process in case you are not available?

□ Yes □ No □ Do not know

If no, why?

_____

_____

Kindly reply to the below statements by ticking a value from 1 to 5 (1 is the least, 5 is the most)

	1 Least →	2	3	4	5 Most
16)How confident do you rate your ability to use glucagon?					
Assessing fear					
17) How concerned are you, from a scale of 1 to5, that your child will have a severe hypoglycaemic episode?					

18) When you leave your child with someone else, do you advise on the use of glucagon and hypoglycaemia?

□ Yes, only initially

□ From time to time

□ When I remember

□ Rarely

□ Never

19) Has it ever happened that the child needed glucagon when you were away IN THE LAST 4 WEEKS?

□ Yes □ No □ Never

To ask After intervention questions

20) Did you find the intervention given by the pharmacist useful? (1 not at all, 5 very useful)

1_2_3_4_5

21) Did you use the educational material provided (video, chart and information sheet)?
□ Yes □ No

22) Where did you put the chart? _____

23) Has your level of confidence about the use of glucagon increased after the intervention?

□ Yes □ No □ Do not know

24) Is there any other information/training that you would like to receive?

□ Yes □ No □ Do not know

25) If yes – kindly indicate what information you would like to receive:
_____

Kwestjonarju dwar l-gharfien fuq il-'Glucagon'.-WARA

Introduzzjoni

Kodici _____

1. A Qatt xi darba t-tifel/tifla tbaxxielhom hafna z-zokkor minn lahhar li iltqajna?

   □ Iva □ Le

1B Jekk iva kemm kienu gravi:

□ Intilfu minn sensihom
□ konfuzi
□

2. A Dahhalt lit-tifel/tifla l-isptar minhabba li waqalhom hafna l-livell taz-zokkor fid-demm?

   □ Iva □ Le □ Ma Nafx

2.B Jekk Iva kemm il-darba?

□ Dahal/dahlet l-isptar darbtejn f l-ahhar sitt xhur
□ Aktar min 4 darbiet f l –ahhar sena
□ Darba f l-ahhar sena
□ Qatt
□

3.A F kas ta'zokkor baxx fid dehem, uzajt l 'injection' tal-'Glucagon' ?

□Iva □ Le □ Ma nafx

3B) Kemm -il darba uzajtha?

_____

3C) Fuq min intuzat?

□ Fuq it-tifel/tifla tieghek □ Xi hadd iehor

Evaluazjoni ta l-gharfien tal-'carer'

4. L ahjar definizjoni ta meta jitbaxxa z-zokkor fid-demm hija li l-livel taz-zokkor ikun baxx iktar min 4mmol/l:

□Vera □ Falz □ Ma nafx

5. Il-medicina 'glucagon' tahdem billi bhal cavetta, tiftah iz-zokkor li jkun hemm fil-fwied ghal god-demm (izzid iz-zokkor fid –demm)

□ Vera □ Falz □ Ma nafx

6. Din il-medicina 'glucagon' tuza' meta jkollok iz-zokkor baxx hafna tant li tifel/tifla jintilfu min sensijhom:

□ Vera □ Falz □ Ma nafx

<u>Uzu tal – 'Glucagon'</u>

7. Ghandek 'injection' tal-'glucagon' id-dar?

□ Iva □ Le □ Ma Nafx

8. A. Ghandek ohra xi post iehor?

□Iva □Le □ Mhux certa

8B) Jekk Iva Fejn: _____

8C) Igorrha miak?

□ Iva □ Le □ Ma Nafx

Jekk Iva, kemm il darba igorrha u meta igorrha miak? _____

Jekk le, ghala le? _____

X taghmel jekk ma igorriex u jigri xi episodju li jaqa z zokkor? _____

9. Fejn izzommha? □ Fil-Fridge □ Fil-Freezer □ Barra f'xi karma □ Ma nafx

10. Jekk l 'injection' tal-glucagon qeghdha barra x'jigrilha d-data ta' l-iskadenza?

□ Tibqa l-istess
□ tiqsar – jekk tiqsar b kemm? ____
□ ma tibqax tajba
□ ma nafx

11. Kemm inti infurmat fuq l-uzu u l preparazjoni tal-glucagon?

□ infurmat hafna □ infurmat □ mhux daqsek infurmat □ mhux infurmat

12. Spjega, fil qossor kif tiprepara l- glucagon qabel ma din tigi amministrata(qabel tuzaha):

13. Meta tkun qed thallat il-'Glucagon', indika, l-importanza taghhom:

Wiegeb billi timarka numru mill-1 sa 5 (1: l-inqas, 5: l-iktar)

	1 L-inqas	2	3	4	5 L-iktar
a) It- trab l-abjad kollu irid jithallat					
b) Meta thallat, trid izzomm s-siringa fil-flixkun					
c) Nehhi l-arja minn gos-siringa qabel ittaqqab lit-tifel/a					

14. X doza taghti lit-tifel/a tieghek?

15. Meta inti ma tkunx mat-tifel/a, min ikun qed jiehu hsieb it-tifel/a jaf kif juza l-'injection'?

□ Iva □ Le □ Ma nafx

Wiegeb billi timarka numru mill-1 sa 5 (1: l-inqas, 5: l-iktar)

	1 L-inqas	2	3	4	5 L-iktar
16) Kemm thossok kunfidenti tuza l-'glucagon'					

Mistoqsijiet fuq il-Biza'					
17) Kemm (mill-1 – 5), tibza' li t-tifel/a jkollhom episodju ta' 'hypoglycaemia' severa					

18. B) Meta thalli it-tifel/tifla ma' xi hadd, tispjegalhom kif tuza l 'injection' u fuq meta jitbaxxa z-zokkor fid-demm?

□Iva, ghal- bidu li joqod/toqod ma dik il persuna
□ Kultant – min zmien ghal zmien
□ Meta niftakar
□ Rari
□ Qatt

19. Qatt gratlek li hrigt u t-tifel/tifla kellhom bzonn juzaw l- injection f dawn l ahhar 4 gimghat?

□ Iva □ Le □ Qatt

_____

Wara l- intervent ta' l- ispizjar staqsi dawn il-mistoqsijiet:

20. Kemm sibtha utli din l-informazzjoni?

1_2_3_4_5

21. Uzajt l materjal li kont moghti (chart, vidjo, infromazjoni l ohra) li kont moghti?

□ Iva □ Le

22. Fejn poggejtha t tabella li kont moghti? _____

23. Il livell ta kunfidenza biex tuza l-'injection' tal-'glucagon' zdiedet issa wara l-informazzjoni moghtija?

□Iva □ Le □ Ma nafx

24. tahseb li hemm xi informazjoni/training ohra li tixtieq tircievi?

□iva □ le □ ma nafx

25. jekk iva indika x informazjoni tixtieq li tircievi: _____

APPENDIX 2E

INFORMATION SHEET ON GLUCAGON USE

TOOL KIT ON GLUCAGON USE

Information leaflet

Danika Agius Decelis- 2016

This work is part of a dissertation undertaken in partial fulfilment towards the Doctorate of Pharmacy degree by the University of Malta in collaboration with the University of Illinois at Chicago.

- **What is hypoglycaemia?**

This is generally when blood glucose levels drop to a level of less or equal to 3.9 mmol/l.

- **What to do when it happens**

A **source of glucose** must always be available to all children suffering from diabetes, for immediate use in case of a hypoglycaemic episode [1].

Mild Hypoglycaemia Management: This is associated with mild symptoms and signs - mild sweating, pallor, tremor, and occasionally headaches and behaviour changes. This is generally treated with 15g of an easily absorbed carbohydrate followed by a protein containing snack [2].

Moderate Hypoglycaemia Management: This is when oral treatment is used however it is administered by someone other than the patient. Symptoms such as aggressiveness, drowsiness and confusion are evident. Management usually requires 15g of glucose to restore the blood glucose levels.

Retesting of blood glucose levels are necessary after 10-15 minutes to determine if the response is adequate or not. If no response or inadequate, oral intake is repeated. Carbohydrates, such as fruit, bread, cereal or milk, can be consumed to prevent further episodes of hypoglycaemia [3].

Severe Hypoglycaemia management: This requires treatment with intramuscular glucagon or intravenous glucose. it is associated with the patient becoming unconscious and unable to swallow or take oral treatment due to disorientation [4].

- **Glucagon-administration**

Place child in the recovery position before administering the medication and follow the below steps[5]:

1) Open the hard container and remove caps from the vial and needle
2) Insert the needle through the rubber stopper within the marked circle of the small vial
3) All liquid must be injected and the needle must be kept in the vial
4) While holding both the syringe and the vial together, the vial is shaken gently until all the white particles are dissolved
5) One has to ensure that the plunger is completely down
6) Once all solution is clear, the plunger is slowly withdrawn so that all the solution is back in the syringe
7) Care should be taken so the plunger does not come off from the syringe
8) Remove the small vial is removed
9) With the needle pointing upwards the syringe is tapped softly with your fingers so any air bubbles collect to the top of the syringe
10) Very gently, the plunger is pushed until all air is removed- this is noted since a small amount of liquid is pushed out
11) Once this is done the syringe in injected into a muscle, such as the thigh

You should always carry the injection with you if you are going out of the house for at least half an hour or more.

- **The dose to be administered is dependent on the weight of the child[6,7]:**

Children above 25kg: The entire syringe [1ml dose] is injected.
Children below 25kg: Half the syringe [0.5ml dose] is injected.

Side effect: vomiting

Once the patient has regained consciousness a snack high in sugar should be administered to prevent another episode from occurring. If patient has not regained consciousness within 10 minutes, then medical assistance is sought.

- **Glucagon storage and expiry** [8,9,10]

The glucagon container is to be stored at a temperature of +2 to +8 degrees
It can be stored at room temperature(25degrees) for up to 18 months within its shelf life. **In other words, you should reduce 6 months from the expiry date written on the box. Example: if the expiry date states 5.2018, reduce this to 11.2017**

Freezing is not an option and if the reconstituted solution produces signs of insoluble particles this is discarded immediately.

CLICK HERE TO WATCH VIDEO:

http://vimeo.com/glucagon/1 FOR ENGLISH VERSION

http://vimeo.com/glucagon/2 FOR MALTESE VERSION

References:

1,3- Ly TT, Maahs DM, Rewers A, Dunger D,Oduwole A, Jones TW. ISPAD Clinical Practice Consensus Guidelines- Hypoglycaemia: Assessment and management of hypoglycaemia in children and adolescence with diabetes. *Paediatric Diabetes*. 2014; 15(20): 180-192

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4 - ADA[American Diabetes Association Workgroup on Hypoglyceamia] Defining and reporting Hypoglycaemia in Diabetes. *Diabetes Care.* 2005; 28(5): 1245-1249

5,6,9-Summary of Product Characteristics: GlucaGen, Novo Nordisk A/S 2015. Accessed via internet https://www.medicines.org.uk/EMC/medicine/4258/SPC/GlucaGen+Hypokit+1+mg/ on 18.12.15

7,8-Patient Information Leaflet, GlucaGen, Novo Nordisk A/S 2015. Accessed via internet https://www.medicines.org.uk/emc/medicine/4257 on 18.12.15

10- NICE Guidelines. Diabetes (Type 1 and Type 2) in Children and Young people: diagnosis and Management, 2015.

TOOL KIT FUQ L- UżU TAL- GLUCAGON

Informazzjoni

Informazzjoni miġbura minn Danika Agius Decelis-2016

Din l-informazzjoni hija parti minn riċerka li qed issir bħala parti mid-dottorat fil-farmaċija mill-universita ta Malta, b' kollaborazzjoni ma' L-universita ta' Illinois f' Chicago

- **Xi tfisser 'Hypoglyceamia'?**

Meta il-livell taz-zokkor fid-demm ikun inqass min 3.9 mmol/l

- **X'għandek tagħmel meta tiġri:**

Dejjem għandek iġġorr fuqek sors ta zokkor (glucose) għal li jista jinqala[1].

Meta jitbaxxilek ftit il livell taz-zokkor: Dan ikun assoċjat ma rodda ħafifa, tibdil fil-burdata tat-tfal, jorqu xi ftit u ftit uġiħ ta'ras. Dan ġeneralment jista jiġi trattat billi tieħu 15- il gramma ta'starch u proteina[2].

Meta il livell taz-zokkor fid-demm jitbaxxa b'mod moderat: Da jiġri meta t-trattament ikun forma ta ħelwa ukoll iżda it-tifel jew tifla ma jkunux kapaċi jeħduwa huma imma ħaddieħor irid jejnhom. Is-sintomi f' dan il kass ikunu ta tfal isiru aggressive, għajjina ħafna u konfusi b' tali mod li ma jibqawx jagħmlu sens. 15g ta zokkor huwa meħtieġ biex iz-zokkor fid-demm jerġa jiġi għan-normal.

Importanti li il- livell taz zokkor jerġa jiġi eżeminat wara 15-il minuta biex tkun ċerta li t-tifel/tifla qedin jirkupraw. Jekk tara li ma hemmx effett, jew ma kienx biżżejjed, erġa' għati x jikol/tikol iktar zokkor [3].

Karboidrati bħal frott, ħobż u ċereal jistaw jiġu ikkunsmati wara li jaddi dan l-episodju biex jiġi evitat li t-tifel/tifla jerġa jiġrilhom hekk.

Meta il livell taz-zokkor fid-demm jitbaxxa ħafna: F'dan il kas it tifel/tifla ma jkunux jistghu jibilgħu u jkun mitluf/a min sensih/a għalura importanti li tuża l 'injection' tal-glucagon[4].

- **Kif tuża l-Glucagon**

Poġġi t-tifel/tifla f 'recovery position' u imxi ma dawn il-passi [5]:

1) Iftaħ il-kaxxa u neħħi it-tappijiet min fuq il-labra u flixkun żajr (vjal)
2) Daħħal il-labra ġor-'rubber' tal-flixkun (vjala) ġoċ-ċirku li għandek immarkat
3) Battal ll-likuidu kollu ta ġos-siringa u żommha fil-vjala
4) żommhom it-tnejn flimkien u ħawwad sew, sakemm it-trab l-abjad kollu jdub.
5) Trid tkun żgura li waqt li qed tagħmel dan is-siringa tkun kollha mafusa u ma jkollha xejn ġo fija
6) Malli tara li t-trab abjad dab kollhu ibda iġbed ftit ftit il-planġer sakemm il-likwidu kollhu qed fis-siringa
7) Oqod attent li il-planġer ma jinqalax min mas-siringa
8) Neħħi il-vjala (flixkun żajr)
9) Bil-labra tas-siringa tipponta l-fuq teptep ftit fuq is-siringa ħalli l-arja tas-siringa jitla l' fuq
10) Bil mod għafas il-planġer u neħħi il ftit arja li jkollok- tinduna li ħarġet l-arja kollha għax joħroġ ftit likwidu
11) Issa tista tuża s-siringa biex ittaqqab it-tifel/tifla fil-koxxa ta saqajh/a

<u>Din l-'injection' għandek dejjem iġorrha miak jekk tkun se toħroġ għall-iktar minn nof sija mid-dar.</u>

- **Id-dosa li għandek tuża tidependi fuq kemm jiżen it-tifel/tifla [6,7]:**

Tfal li jiżnu iktar minn 25kg: Għati 1ml jew aħjar id-dosa li jkollok kollha

Tfal li jiżnu inqas minn 25kg: Għati nofs id-dosa li jkollok

Xi effetti li jkollhom tal-mediċina stess hija li jirremettu

La darba it-tifel/tifla jiġi/tiġi f'sensih għati 'snack' b' ħafna zokkor biex tipreveni li jerġa jiġri xi episodju ieħor bħal dan. Jekk sa 10 minuti t-tifel/tifla għadhom ma ġewx f'sensijhom ċempel l-abbulanza ħalli tasal assistenza medika.

- **Kif għandek terfa' l-Glucagon u d-data ta'l- iskadenza [8,9,10]**

Għandek iżommha f'temperature ta +2 sa +8 gradi, għalkemm tista iżommha ukoll f'temperatura ta 25-il grad. F'dan il kas trid tuża' sa 18-il xagħar fi ħdan id-data ta l-iskadenza, li jkollu immarkat fuq il-kaxxa. **Fi kliem ieħor, naqqas 6 xhur mid- data ta l-iskadenza li għandek fuq il-kaxxa. Eżempju, jekk id- data tal-kaxxa hija 5.2018 din trid tonqos għall- 11.2017**

Qatt ma għandek tifriża u jekk meta titħallat, tara xi biċċiet li ma jkunux jistaw idubu ġo fija, din għandha tintrema.

ARA L-VIDEO HAWN:

http://vimeo.com/glucagon/1 għall-verżjoni b l- ingliż

http://vimeo.com/glucagon/2 għall-verżjoni bil-malti

Referenzi:

1,3- Ly TT, Maahs DM, Rewers A, Dunger D,Oduwole A, Jones TW. ISPAD Clinical Practice Consensus Guidelines-Hypoglycaemia: Assessment and management of hypoglycaemia in children and adolescence with diabetes. *Paediatric Diabetes*. 2014; 15(20): 180-192

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10- NICE Guidelines. Diabetes (Type 1 and Type 2) in Children and Young people: diagnosis and Management, 2015

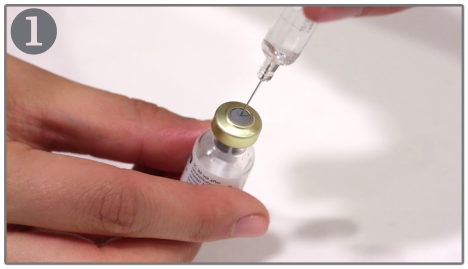
APPENDIX 2F

VIDEO

APPENDIX 2G

CHART

Glucagon



Insert the needle through the rubber stopper.

Inject all the liquid and keep the needle in the vial.

Shake vial (still attached to syringe) until all white particles are dissolved.

Withdraw the clear mixture back into the syringe.

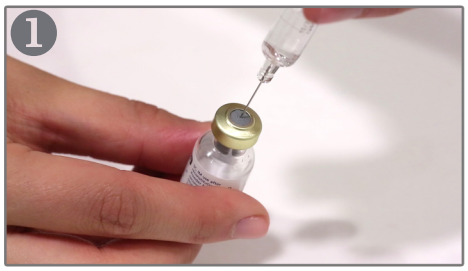
Tap syringe with fingers to collect all air bubbles to the top of syringe.

Push plunger to remove all air from syringe.

See video here: http://vimeo.com/glucagon/1

Danika Agius deCelis (2016)

Glucagon



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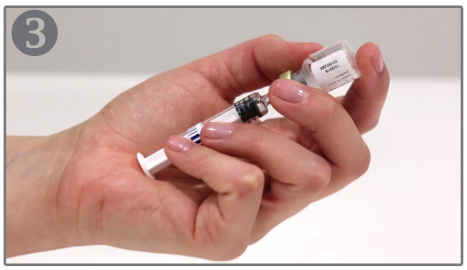

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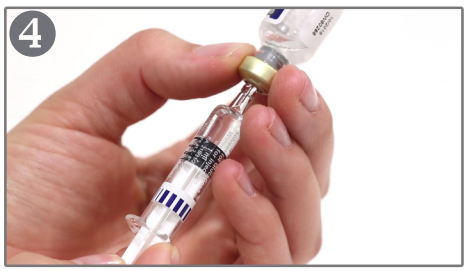

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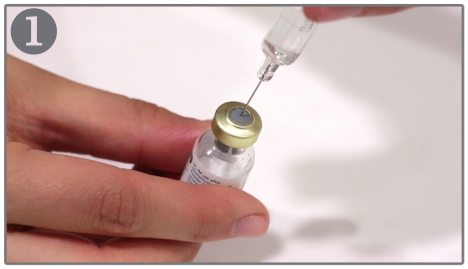
Danika Agius deCelis (2016)

Glucagon



Daħħal il-labra fil-vjala fiċ-ċirku mmarkat.

Battal il-likwidu kollhu fis-siringa ġol-vjala.

Żommhom it-tnejn flimkien u ħawwad sew sakemm it-trab l-abjad idub kollhu.

Iġbed il-likwidu kollhu fis-siringa.

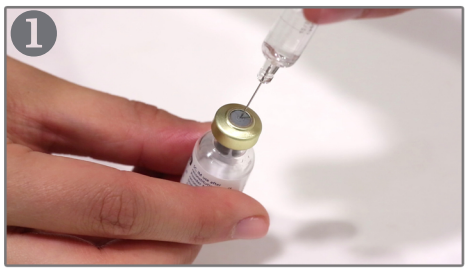
Teptep fuq is-siringa ħalli l-arja titla l-fuq.

Agħfas is-siringa ħalli tneħħi l-arja kollha.

Ara l-vidjow hawn: http://vimeo.com/glucagon/2

Danika Agius deCelis (2016)

Glucagon



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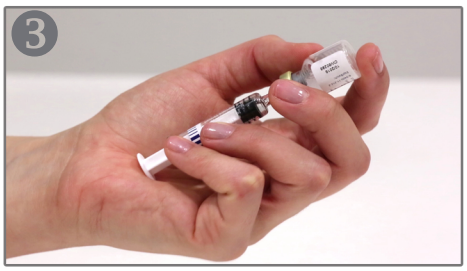

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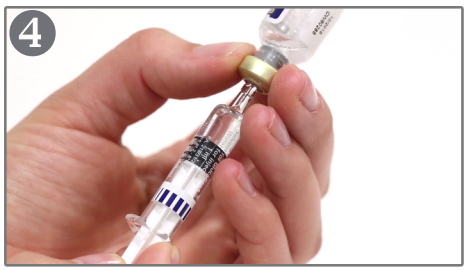

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Ara l-vidjow hawn: http://vimeo.com/glucagon/2

Danika Agius deCelis (2016)

APPENDIX 2H

PHARMACIST GLUCAGON ASSESSMENT

QUESTIONNAIRE

Glucagon Use in Paediatric T1DM patients: An Innovative Approach to Improve Outcomes

Dear Pharmacist,

I am a pharmacist who is currently reading for a Doctorate in Pharmacy (Pharm D) at the University of Malta in collaboration with University of Illinois, Chicago.

The aim of this study is to develop material and evaluate the impact of educating carers of paediatric type one diabetes mellitus patients, on the emergency use of glucagon in hypoglycaemia, in a safe way.

This educational material is also extended to pharmacists.

Kindly fill in the below questions which will help me immensely in my analysis. It will only take around 5 minutes to fill it in.

While thanking you in advance I do hope that the material provided will be useful and will facilitate advice given when dispensing and using glucagon.

Please feel free to share the video clip (approx.1.5minutes long) on use and preparation of glucagon by visiting:

http://vimeo.com/glucagon/1

http://vimeo.com/glucagon/2

Kindest regards

Danika Agius Decelis

BSc.PharmSci (Hons) M.Pharm (Melit.)

* Required

General Information

1. **Area of practice** *
   Mark only one oval.

   - ◯ Hospital
   - ◯ Community
   - ◯ Regulatory Affairs
   - ◯ Industry
   - ◯ Academia
   - ◯ Medical Representative
   - ◯ Procurement Section
   - ◯ Other: _____

2. **Gender** *

Mark only one oval.

- ◯ Male
- ◯ Female

3. **Age Group** *

Mark only one oval.

- ◯ 18-25 years
- ◯ 26-35 years
- ◯ 36-45 years
- ◯ 46-55 years
- ◯ 56 years +

4. *

Mark only one oval per row.

	Yes	No	Do not know/ Do not remember
Are you insulin dependent diabetic?	◯	◯	◯
Any member of your close family is insulin dependent diabetic?	◯	◯	◯
Have you ever used Glucagon Injection	◯	◯	◯
Did you ever provide advice on the use of glucagon	◯	◯	◯
Have you ever had requests for information about use of glucagon	◯	◯	◯

5. **If advice was given, how often:**

Mark only one oval.

- ◯ With every dispensed injection
- ◯ Monthly
- ◯ Yearly
- ◯ Rarely
- ◯ Other: _____

6. **Before referring to the information provided, kindly indicate what will happen if glucagon is stored at room temperature(not exceeding 25°C) :** *

Mark only one oval.

- ◯ It has to be used immediately
- ◯ It has to be discarded
- ◯ Expire date has to be decreased
- ◯ Do not know

Tool Kit on Glucagon use

Kindly read below information together with video clip on how to prepare glucagon before answering the questions in this section. The 1 and a half minute long video clip can be accessed

on : http://vimeo.com/glucagon/1 or http://vimeo.com/glucagon/2

TOOL KIT ON GLUCAGON USE

Information leaflet

Danika Agius Decelis- 2016

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- **What to do when it happens**

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6) Once all solution is clear, the plunger is slowly withdrawn so that all the solution is back in the syringe
7) Care should be taken so the plunger does not come off from the syringe
8) Remove the small vial is removed
9) With the needle pointing upwards the syringe is tapped softly with your fingers so any air bubbles collect to the top of the syringe
10) Very gently, the plunger is pushed until all air is removed- this is noted since a small amount of liquid is pushed out
11) Once this is done the syringe in injected into a muscle, such as the thigh

You should always carry the injection with you if you are going out of the house for at least half an hour or more.

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Freezing is not an option and if the reconstituted solution produces signs of insoluble particles this is discarded immediately.

CLICK HERE TO WATCH VIDEO:

http://vimeo.com/glucagon/1 FOR ENGLISH VERSION

http://vimeo.com/glucagon/2 FOR MALTESE VERSION

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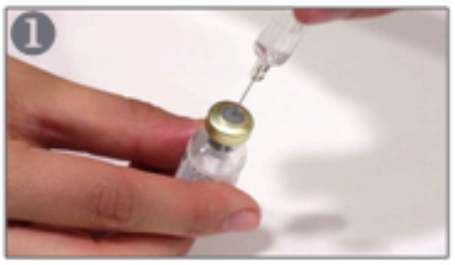
10- NICE Guidelines. Diabetes (Type 1 and Type 2) in Children and Young people: diagnosis and Management, 2015.

Glucagon



Insert the needle through the rubber stopper.

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Shake vial (still attached to syringe) until all white particles are dissolved.

Withdraw the clear mixture back into the syringe.

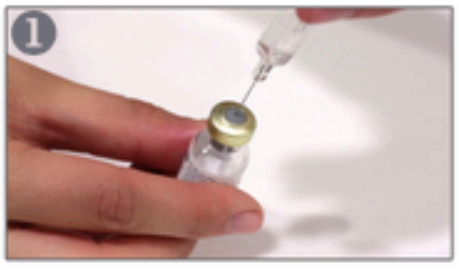
Tap syringe with fingers to collect all air bubbles to the top of syringe.

Push plunger to remove all air from syringe.

See video here: http://vimeo.com/glucagon/1

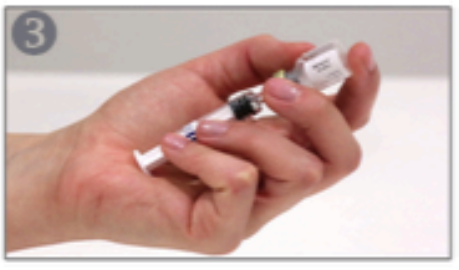
Danika Agius deCelis (2016)

Glucagon



Daħħal il-labra fil-vjala fiċ-ċirku mmarkat.

Battal il-likwidu kollhu fis-siringa ġol-vjala.



Żommhom it-tnejn flimkien u ħawwad sew sakemm it-trab l-abjad idub kollhu.

Iġbed il-likwidu kollhu fis-siringa.

Teptep fuq is-siringa ħalli l-arja titla l-fuq.

Agħfas is-siringa ħalli tneħħi l-arja kollha.

Ara l-vidjow hawn: http://vimeo.com/glucagon/2

Danika Agius deCelis (2016)

7. **From the Scale of 1 (minimum) to 5 (Maximum)** *

Mark only one oval per row.

	1	2	3	4	5
Do you think there is adequate awareness about the reconstitution and use of glucagon amongst carers of paediatric Type 1 Diabetes patients?					
Rate your knowledge on glucagon reconstitution and use PRIOR to viewing the Tool kit provided					
Rate your knowledge on glucagon reconstitution and use AFTER viewing the Tool Kit provided					
Rate your confidence on use and administration of Glucagon PRIOR to this session					
Rate your level of confidence on use and administration of glucagon AFTER this session					

8. **From the Scale of 1 (minimum) to 5 (Maximum)** *

Mark only one oval per row.

	1	2	3	4	5
How informative is the Tool Kit provided?					
How concise is the video in the Tool Kit provided?					
Rate the usefulness of the Tool Kit					

APPENDIX 3: LIST OF PUBLICATIONS

APPENDIX 3A

ABSTRACT FOR EAHP CONFERENCE 2017

DEVELOPMENT AND VALIDATION OF A PHARMACIST TOOL KIT ON GLUCAGON USE

Danika Agius Decelis[1], Louise Grech[1,2], John Torpiano[3], Lilian M. Azzopardi[1]

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Email : danika.agius-decelis.08@um.edu.mt **(Abstract number:** DI-048 **ATC code :** A10 - Drugs used in diabetes)

Department of Pharmacy

University of Malta

INTRODUCTION

Lack of education and confidence on the appropriate use and administration of glucagon by non-trained carers can lead to medication errors and untreated hypoglycaemic episodes.

AIMS

To validate the usefulness of a specifically developed educational tool kit intended for education of pharmacists on timely and appropriate use of glucagon.

METHOD

A Glucagon Tool Kit was created and validated by a panel of experts prior to distribution to all pharmacists.

Informative Chart

Snap Shots from video to aid use of glucagon kit

Tool Kit

Information Sheet

Briefly highlights issues related to glucagon, such as storage, steps to reconstitute and dosage regimen

Online Video

- In Maltese and English; 1.5 minutes long
- Explains how to reconstitute and administer Glucagon
- http://vimeo.com/glucagon/1 for English version
- http://vimeo.com.glucagon/2 for Maltese version

A questionnaire was compiled to assess the knowledge and confidence of glucagon use by pharmacists. The questionnaire was run twice, prior to distribution of the Glucagon Tool Kit and again immediately after the distribution of the Glucagon Tool Kit.

RESULTS

A total of 139 pharmacists completed the questionnaire out of whom 44% were community pharmacists.

The knowledge of pharmacists on the use of glucagon increased when a Likert Scale was used to measure knowledge (1 least, 5 most knowledgeable). Mean knowledge before was 2.165 which increased to 4.327 (Wilcoxon Sign Test $p<0.001$) following the distribution of the educational Glucagon Tool Kit. (Figure 1)

The pharmacists' confidence on the use of glucagon increased when a Likert Scale was used to measure confidence (1 least, 5 most confident). Mean confidence before was 1.99 which increased to 3.98 (Wilcoxon Sign test $p<0.001$) following the use of the educational Glucagon Tool Kit. (Figure 2)

The majority of respondents (95%) found the video is sufficiently concise, 91% thought that the Tool kit was very useful and 95% rated it as informative.

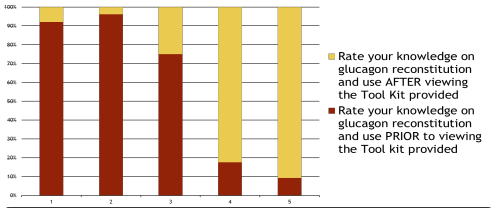

Figure 1: Pharmacist Knowledge on glucagon reconstitution and use before (red) and after (yellow) Tool kit Provision (n=139) ($p>0.001$)

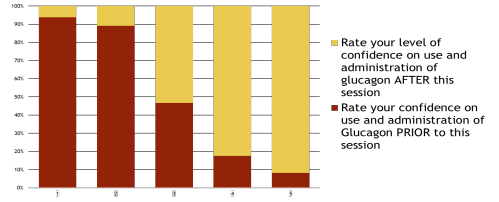

Figure 2: Pharmacist confidence on glucagon reconstitution and use before (red) and after (yellow) Tool kit Provision (n=139) ($p>0.001$)

CONCLUSION

The educational material developed had a significant impact on the knowledge and confidence the pharmacist has on the use and reconstitution of glucagon. Improving the knowledge and confidence of pharmacists on the appropriate use of glucagon will empower them to support patients and carers in the use of glucagon in emergencies.

DI-047 IMPACT OF PILL BURDEN ON DURATION OF FIRSTLINE ANTIRETROVIRAL THERAPY IN REAL LIFE SETTING

[1]N Valcarce*, [2]H Alvarez, [3]L Vilariño, [1]I Rodríguez, [2]A Mariño. [1]Complexo Hospitalario Universitario de Ferrol CHUF, Hospital Pharmacy, Ferrol, Spain; [2]Complexo Hospitalario Universitario de Ferrol CHUF, Infectious Diseases, Ferrol, Spain; [3]Complexo Hospitalario Universitario de Ferrol CHUF, Internal Medicine, Ferrol, Spain

10.1136/ejhpharm-2017-000640.294

Background The firstline antiretroviral treatment (ART) is often considered a long term therapy at treatment initiation. The complexity of ART could influence persistence, making it shorter.
Purpose To investigate the duration of firstline ART, the main reasons for switching the firstline ART and the association between daily antiretroviral pill burden and switching.
Material and methods This was a retrospective observational study. We included all naive adult HIV infected patients who started their firstline ART in a second level hospital from January 2012 to April 2015. Duration was the time from the start of the first ART until treatment modification for any reason or last follow-up visit. Demographics and pharmacotherapeutic data were collected from electronic medical and antiretroviral dispensing records and a specific database for HIV patients.
Results 42 patients started their first ART in this period, 86% men. Median age was 43 years (IQR 33–51). 14 patients (33%) started a once daily single tablet regimen (STR): Atripla in 9 patients (64%), Eviplera in 4 patients (29%) and Stribild in 1 patient. 28 patients started a triple tablet regimen (TTR): 22 (79%) had a protease inhibitor combined with two nucleoside reverse transcriptase inhibitors and 6 (21%) had raltegravir plus a tenofovir including backbone. 71% were maintained on STR, median duration 29 months (IQR 19–40), and 39% on TTR, median duration 32 months (IQR 20–43). Firstline ART was modified in 18 patients (43%). At the time of change all patients maintained virologic suppression. In the STR group, 3 patients (21%) switched to secondline ART. Changes were for safety reasons (2 patients) and due to difficulty in swallowing (1 patient). There were 15 patients (54%) who changed in the TTR group: 11 simplifications (73%), 3 toxicity preventions (20%) and 1 drug interaction. At the end of the follow-up period, 2 patients with TTR (1 transfer to another centre and 1 death) and 1 patient with STR (transfer to another centre) discontinued ART.
Conclusion TTR was preferred as firstline ART. Median duration of the different regimens was similar and independent of pill burden. More than half of the patients on TTR switched their first ART and the main reason for change was simplification.

No conflict of interest

DI-048 DEVELOPMENT AND VALIDATION OF A PHARMACIST TOOL KIT ON GLUCAGON USE

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10.1136/ejhpharm-2017-000640.295

Background Lack of education and confidence on the appropriate use and administration of glucagon by non-trained carers can lead to medication errors and untreated hypoglycaemic episodes.
Purpose To validate the usefulness of a specifically developed educational tool kit intended for education of pharmacists on timely and appropriate use of glucagon.
Material and methods A Glucagon Tool Kit was created as part of continuous professional training intended for pharmacists. The Glucagon Tool Kit consisted of an online video, information sheet and informative chart. The video was available in both Maltese and English, lasted 1.5 min and explained how to reconstitute and administrate glucagon. The information sheet provided concise information on hypoglycaemia and briefly highlighted issues related to glucagon, such as storage, steps to reconstitute and dosage regimen. The informative chart depicted the reconstitution procedure with the help of images and short phrases. The Glucagon Tool Kit was validated by an expert panel and distributed to all pharmacists. A questionnaire was compiled to assess the knowledge and confidence of glucagon use by pharmacists. The questionnaire was run twice—namely prior to distribution of the Glucagon Tool Kit and again immediately after distribution of the kit.
Results 135 pharmacists completed the questionnaire of whom 44% were community pharmacists. The knowledge of pharmacists on the use of glucagon increased from 12.6% to 89.6% (paired sample t-test $p<0.001$) following the distribution of the educational Glucagon Tool Kit. The pharmacists' confidence on the use of glucagon increased from 11.1% to 76.3% (paired sample t-test $p<0.001$) following the use of the educational Glucagon Tool Kit. The majority of respondents (95%) found the video sufficiently concise, 91% thought that the Tool kit was very useful and 95% rated it as informative.
Conclusion The educational material had a significant impact on the knowledge and confidence the pharmacist had on the use and reconstitution of glucagon. Improving the knowledge and confidence of pharmacists on the appropriate use of glucagon will empower them to support patients and carers in the use of glucagon in emergencies.

No conflict of interest

DI-049 GOOD PRACTICE ON ANTIBIOTIC USE: TIGECYCLINE IN A MEDICAL INTENSIVE CARE UNIT

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10.1136/ejhpharm-2017-000640.296

Background Tigecycline is an interesting therapeutic alternative in case of infections due to multidrug resistant bacteria and/or complex clinical situations. The Marketing Authorisation (MA) allows the use of tigecycline for skin and soft tissue infections and for complicated intra-abdominal infections. Its prescription must be rationalised in order to slow down the emergence of resistance. Therefore, our hospital has implemented an 'Antimicrobial Stewardship' (AS) programme since January 2015. It aims to organise the prescription of some precious antibiotics.
Purpose Our study aimed to judge the degree of conformity of tigecycline prescriptions with the MA criteria and to

Agius Decelis D., Grech L., Torpiano J., Azzopardi LM., Development and Validation of a Pharmacist Tool Kit on Glucagon Use. Eur J Hosp Pharm 2017;24(Suppl. 1): A134