Pulmonary rehabilitation: insight into current trends

Anabel Sciriha, Stephen Montefort

Abstract

Pulmonary rehabilitation is a widely accepted therapeutic tool used to improve the quality of life and functional capacity of individuals with chronic lung disease. It is a multidisciplinary, comprehensive program designed to optimise autonomy and physical performance in patients with chronic respiratory impairment. There is sufficient evidence to support the use of pulmonary rehabilitation for a subset of patients and to indicate that it can improve exercise tolerance and symptoms of dyspnoea, as well as enhance health-related quality of life of patients with COPD and other respiratory conditions. According to projections in the Global Burden of Disease Study, COPD will be the fifth leading cause of disability-adjusted-life-year loss worldwide in 2020.

The goal of pulmonary rehabilitation is to help the individual achieve the highest level of independent functioning by improving pulmonary function, increasing exercise endurance and exercise work capacity, reducing dyspnoea and normalising blood gases.

Locally, no pulmonary rehabilitation service as described by respiratory societies is offered. Therefore, this paper will look into the current research focusing on future recommendations for this service in the international setting with an aim of implementing this into the local health care system.

Introduction

Rehabilitation is the restoration of individuals to the fullest medical, mental, emotional, social and vocational potential the individual is capable of. The basic premise of all rehabilitation is that it is possible to effect positive change under the poorest circumstances imaginable and that no effect of illness save for death is absolute.1

Pulmonary rehabilitation is defined as a program for people who have chronic lung disease.2 Its primary goal is to enable people to achieve and maintain their maximum level of independence and functioning. Although most pulmonary rehabilitation programs focus on people who have chronic obstructive pulmonary disease,2 people with other types of lung disease may benefit as well. The most successful rehabilitation programs are those in which services are provided by a physiotherapist, nurse, doctor, psychologist or social worker, and a dietitian working as the pulmonary rehabilitation team to coordinate complex medical services.3

Optimal length of the rehabilitation phase

Despite the increasing propagation of the efficacy of pulmonary rehabilitation, there is no definitive proposal for the best training strategy2-4 with variances in the duration and frequency.5,6 Significant gains in exercise tolerance, dyspnoea, and quality of life have been observed following rehabilitation programs as short as 10 days7 and others as long as 18 months8 with gains in exercise tolerance reported to be greater in the latter.9 Two randomised trials compared 3 months and 18 months of low-intensity exercise training. The longer intervention led to 6% increase in the 6 minute walk distance, 12% reduction in self-reported disability and faster completion of stair climbing and overhead tasks.10 No differences though were seen in pulmonary function studies between groups, after training. The investigators concluded that the benefits achieved after short-term pulmonary rehabilitation began to decay once the intervention was terminated, despite encouragement to continue participation in a home-based or community-based programme. On the other hand, Foy et al11 showed that only male patients achieved greater gains in Chronic Respiratory Disease Questionnaire scores following the 18-month program (compared to 3 months). In fact, more favourable scores than those in the short-term group were reported for dyspnoea, fatigue, emotional function and task mastery.

In a 2005 published prospective trial12 involving seven outpatient programmes, patients achieved significant gains in exercise tolerance (6 minute walk distance), dyspnoea and...
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Tuscany
acrylics on canvas, 23.5 x 18.0cm, July 2010

Dr Mark Muscat currently works as EUVAC.NET scientific co-ordinator at the Statens Serum Institut, Department of Epidemiology in Copenhagen, Denmark.
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PRESENTATION: Zolendronic acid. 100 mL solution bottle contains 5 mg zolendronic acid (anhydrous), corresponding to 5.330 mg zolendronic acid monohydrate.

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DOSE AND ADMINISTRATION: Osteoporosis: A single intravenous infusion of 5 mg Aclasta administered once a year, in patients with a recent low-trauma hip fracture, is recommended to give the osteoporosis treatment. It is recommended to give Aclasta within two or three weeks after hip fracture repair. Paget’s disease: A single intravenous infusion of 5 mg Aclasta. Specific re-treatment data are not available for Paget’s disease. Aclasta is administered via a venous infusion that lasts at least 15 minutes. A single dose of Aclasta should not exceed 5 mg. A single dose of Aclasta should not exceed 5 mg and the duration of infusion should be at least 15 minutes. Pre-existing hypercalcaemia and other disturbances of mineral metabolism must be treated appropriately before Aclasta infusion.

CONTRAINDICATIONS: Hypersensitivity to zolendronic acid or any of the excipients or to any bisphosphonate, hypocalcaemia, pregnancy, lactation.

PRECAUTIONS AND WARNINGS: Serum creatinine should be measured before each Aclasta dose. Aclasta should not be used in patients with creatinine clearance <30 ml/min. Transient increase in serum creatinine may be greater in patients with underlying impaired renal function. Monitoring of serum creatinine should be considered in all patients. Patients must be appropriately hydrated prior to administration of Aclasta, especially important for the elderly and for patients receiving diabetic therapy. Use with caution in conjunction with medications that can impact renal function. A single dose of Aclasta should not exceed 5 mg and the duration of infusion should be at least 15 minutes. Pre-existing hypercalcaemia and other disturbances of mineral metabolism must be treated appropriately before Aclasta infusion. It is strongly advised that patients with Paget’s disease receive supplemental calcium and vitamin D. Measurement of serum calcium before infusion is recommended for patients with Paget’s disease. Severe and occasionally incapacitating bone, joint and/or muscle pain has been infrequently reported with bisphosphonate therapy. Any patient being treated with zoledronate should not be treated with Aclasta. As a precaution against osteonecrosis of the jaw (ONJ), a dental examination with appropriate preventive measures should be considered prior to treatment in patients with concurrent risk factors (e.g., cancer, chemotherapy, corticosteroids, poor oral hygiene). While on treatment, these patients should avoid invasive dental procedures if possible. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw. Aclasta is not recommended in women of childbearing potential.

INTERACTIONS: Specific drug-drug interaction studies have not been conducted with zolendronic acid. Caution is recommended when Aclasta is used concomitantly with drugs that can significantly impact renal function, such as amino- glycosides and diuretics that can cause dehydration. In patients with renal impairment, the systemic exposure to concomitant medicinal products that are primarily excreted via the kidney may increase.

ADVERSE REACTIONS: The incidence of adverse reactions (e.g., fever, myalgia, flu-like symptoms, arthralgia and headache) are greater with the first infusion and decrease markedly with subsequent infusions. The majority of these reactions occur within the first three and seven days and resolve spontaneously within three days of the event onset. The incidence of these adverse reactions can be reduced with the administration of paracetamol or ibuprofen shortly after Aclasta administration. Very common: Fever, Common: Flu-like symptoms, chills, fatigue, pain, arthralgia, myalgia, bone pain, back pain, pain in extremity, nausea, headache, dizziness, atypical lymphocytosis, osteoporosis, increased transaminase, increased alkaline phosphatase. Very rare: Hypersensitivity, flushing, palpitations and others. Not known: Sepsis, orbital inflammation, hypersensitivity, impaired renal function, osteonecrosis of the jaw, hypercalcaemia secondary to post dose symptoms, hypocalcaemia.

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This issue of the Malta Medical Journal contains a historical perspective on medical publications in Malta over the years and it is a tribute to the medical community that over the last one hundred and seventy years, dedicated members of that profession have published articles of relevance to the practice of medicine in the Maltese Islands. The aim has been to highlight problems particular to the epidemiology, pathophysiology and management of disease endemic in Malta.

In a country with a population of just over 400,000, the survival of such publications has depended on a number of different factors – infrastructural, financial, and by the very nature of their content, relatively limited circulation with the resultant implications for indexing and the acquisition of an impact factor. Ultimately until recently the limited resources available to local researchers wishing to address specific hypotheses with the aim of improving patient centred medical care also impacted on the volume of scientific activity going on.

In this issue, there are articles related to chronic non-communicable disease which are having a significant impact on patient morbidity and mortality and the healthcare budget namely chronic respiratory problems and dementia. The provision of cost effective healthcare with rehabilitation and devolvement of patient care to the community represent major public health challenges at present and the identification of lacunae in service provision is the initial step in the development of national health strategies in chronic non-communicable diseases such as these two. The implementation of such strategies mandates the use of auditing and of analysis re local concordance with international established standards of health care. Genetic, cultural and health service structures differ in individual countries and in specific regions in individual countries. Hence the need to ensure that proposed measures and treatments are appropriate to the specific population in this case the Maltese population.

Subsequent to the establishment of postgraduate training programs, young trainees are now keen to research and publish and the Faculty of Medicine now has seen a significant increase in the number of students undertaking Masters and Doctoral studies. It is now possible to apply for research funds and a number of courses are available that focus on grantsmanship, research, statistics and scientific writing. The Malta Medical Journal which is published online and also in hard copy, provides such young researchers with a forum to publish their observations, under the supervision and with the help of their more senior colleagues.

This increase in research activity and publication will hopefully continue to increase over the coming years reflecting the local medical community’s healthy constructive critical attitude to work published in the international medical community and its relevance to the practice of medicine in Malta.

Josanne Vassallo
Editor
Pharmacotherapeutic aspects of dementia care in Malta

Charles Scerri, Stephen Abela, Anthea Innes

Abstract
Dementia is the most common neurodegenerative disorder of old age affecting one percent of the local general population. It is a major predictor of morbidity and mortality in the elderly, adding a significant burden on health and social care systems across Europe. The financial impact of caring for individuals with dementia is considerable and progressive loss of cognitive function does not only pose challenges to the patients but also adds significant strain on the well-being of caregivers and family members. Although no cure is available, disease progression can be delayed by early intervention and by the use of pharmacotherapeutic agents that interfere with central neurotransmitter systems involved in cognitive processes. This review presents current trends in pharmacotherapeutic intervention in dementia care together with caregiver perceptions on treatment expectations in Malta.

Keywords
Dementia, Malta, caregivers, pharmacotherapy

Introduction
Dementia is a complex clinical syndrome associated with behavioural, cognitive and personality changes. It usually presents itself as impairment in memory, abstract thinking, impaired judgment and other disturbances that are of such severity that they interfere with work and social activities. Several diseases are known to cause dementia. Alzheimer’s disease (AD) accounts for 50–70% of cases followed by Vascular dementia, Lewy Body Disease, fronto-temporal dementia and dementia secondary to disease. According to an estimate from World Health Organization (WHO), dementia is responsible for more years lived with disability in people older than 60 years (11.2%) than stroke (9.5%), cardiovascular disease (5%) or all forms of cancer (2.4%). Currently, there are more than 7.3 million people with dementia in Europe, a figure that is expected to double by the next 30 years. This will result in a growing burden on health care resources and family members who, in the majority of cases, provide informal care at home. A recent study estimated that approximately one percent of the general population in Malta has dementia, a figure that is expected to increase significantly by the year 2050 (Table 1).

Over the last two decades, a number of therapeutic strategies have been developed for the symptomatic management of the most common forms of dementia, particularly AD. The latter is characterised by the presence of amyloid plaques and neurofibrillary tangles coupled with significant degeneration of the central cholinergic system resulting in cognitive decline. Indeed, the first pharmacological agents to be approved for symptomatic treatment of AD were the acetylcholinesterase inhibitors which mainly block the enzyme acetylcholinesterase thus increasing the concentrations of the neurotransmitter acetylcholine in the synaptic area (Table 3). Studies showed that the use of these drugs (namely donepezil, galantamine and rivastigmine) significantly improved cognition and activities of daily living. Another drug that is also available in the therapeutic management of AD is the glutamatergic-system modifier memantine which partially blocks glutamate-induced overstimulation of the N-methyl-D-aspartate (NMDA) receptor thus reducing calcium-induced cytotoxicity (Table 3). In randomised clinical trials, this drug demonstrated the ability to delay cognitive and functional decline without any significant incidence of side effects. According to the latest guidelines issued by the UK National Institute for Clinical Excellence (NICE), acetylcholinesterase inhibitors should be recommended for use in moderate AD whereas memantine should...
only be considered for clinical trials. Apart from Malta and Latvia, all EU-member states offer some form of financial reimbursement to any of these classes of anti-dementia drugs. In recent years, strategies on dementia care have also been developed in parallel with pharmacotherapeutic research since caregivers suffer from high rates of physical and mental disorders including anxiety and depression. Caregivers are also generally excluded in providing their views on the effectiveness of anti-dementia pharmacotherapy in ameliorating the symptoms as most research is focused on the disease model. A recent review study found that not one of the 63 papers (listed in medical databases) reporting on the effectiveness of drug treatments included the carer perspective. Indeed, the carer perspective becomes important in assessing the effectiveness of a particular anti-dementia pharmacotherapeutic regimen in enhancing the quality of life and assessing caregiver burden. The input of carers would also be instrumental in providing qualitative information that should aid medical professionals to adjust therapy ensuring better pharmacotherapeutic outcomes.

**Hospital-based pharmacotherapeutic management**

In Malta, no research has yet been carried out on the use of pharmacotherapeutic agents in treating the various symptoms observed in dementia. In order to have an indication on the use of anti-dementia drugs in a local hospital-based clinic, a small scale exercise involving ten persons with dementia was conducted in October 2008. Also involved were seventeen caregivers, the latter comprising five spouse carers (two husbands and three wives), nine children (eight daughters and one son) and three daughter-in-laws. The sample of potential caregivers was selected from the Zammit Clapp Hospital Memory Clinic and was subsequently interviewed by a member of the research team. All participants had to be caring for a relative who had a formal diagnosis of dementia, who was attending the Memory Clinic, who continued to live in the community and who was over 65 years of age. The medical history of individuals with dementia was analysed for parameters including Mini Mental Scale Examination (MMSE) scores (which classify dementia into mild, moderate and severe), date of first attendance to the Memory Clinic, date of diagnosis, medical conditions besides dementia and pharmacotherapy. Ethical approval was obtained from three sources prior to conducting the interviews with caregivers. These included the University of Stirling (UK) Ethics Committee, the University of Malta Research Ethics Committee and the Malta Health Department. All relatives participating in the study received a written information sheet prior to consenting to participate and this was also discussed verbally prior to obtaining written consent.

The results showed that more than half of the persons with dementia participating in the exercise had the moderate form of dementia in which there is clear impairment of cognitive function that may require continuous supervision (Figure 1). The rest of the patients had mild or questionably significant deficits in the person with dementia continues to function normally with support and assistance. No patient had a Mini Mental State Examination score of less than 10 denoting the severe form of the condition which requires continuous supervision and assistance in their Activities of Daily Living (ADL). Table 2 shows the time intervals from when the person with dementia visited the Memory Clinic for the first time until diagnosis of dementia and initiation of treatment was performed. The mean number of days elapsed from first visit to diagnosis was that of 41.3±19.3 (mean±SEM) days. The majority of patients had their diagnosis of dementia during their first visit to the clinic. The mean number of days elapsed from diagnosis till the initiation of treatment was that of 69.4±42.3 (mean±SEM) days with most patients prescribed anti-dementia medication on the day of diagnosis. The mean total number of elapsed days from the patient first visit to the clinic till the initiation of treatment was of 108.3±34.9 (mean±SEM) days. Figure 2 shows the percentage of other pathological disorders in conjunction with dementia (taken as 100% to signify that all patients participating in this exercise had dementia). Most of the patients had depression and a significant number had diabetes, hypertension and hypercholesterolaemia. Other less common comorbidities included gout, anxiety, hearing loss and previous surgical interventions prior to dementia diagnosis. Figure 3a shows the amount of drugs prescribed for every person with dementia. The total number of drugs prescribed was 59 giving an average of 5.9 drugs per patient. The majority of patients were prescribed four or more drugs. All persons with dementia, except one,

<table>
<thead>
<tr>
<th>Year</th>
<th>30-59</th>
<th>60-64</th>
<th>65-69</th>
<th>70-74</th>
<th>75+</th>
<th>Total cases</th>
<th>% of total population</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>203</td>
<td>293</td>
<td>316</td>
<td>629</td>
<td>2947</td>
<td>4388</td>
<td>1.12</td>
</tr>
<tr>
<td>2015</td>
<td>204</td>
<td>268</td>
<td>444</td>
<td>749</td>
<td>3227</td>
<td>4892</td>
<td>1.25</td>
</tr>
<tr>
<td>2020</td>
<td>201</td>
<td>285</td>
<td>404</td>
<td>1035</td>
<td>3660</td>
<td>5585</td>
<td>1.44</td>
</tr>
<tr>
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<td>201</td>
<td>253</td>
<td>422</td>
<td>931</td>
<td>4538</td>
<td>6345</td>
<td>1.66</td>
</tr>
<tr>
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<td>190</td>
<td>257</td>
<td>332</td>
<td>881</td>
<td>5161</td>
<td>6821</td>
<td>1.91</td>
</tr>
<tr>
<td>2050</td>
<td>150</td>
<td>268</td>
<td>414</td>
<td>970</td>
<td>4567</td>
<td>6369</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 1: Current and projected number of total dementia cases in the Maltese islands (adapted from Abela et al).
were prescribed anti-dementia pharmacotherapy which mainly consisted of the acetylcholinesterase inhibitor galantamine and the partial NMDA receptor antagonist memantine. A total of fifty drugs were used to control other coexisting medical conditions with the majority being cardiovascular agents followed by antidiabetics, antidepressants and lipid lowering agents. Supplements and vitamins were prescribed in a number of cases whereas antipsychotics were used in one of the patients (Figure 3b).

The qualitative interviews with seventeen caregivers showed a lack of perceived support by carers when caring for a person with dementia. The majority of participants mentioned the lack of professional healthcare services specifically aimed for patients with cognitive difficulties. Most importantly, caregivers reported the significant financial costs involved in the purchase of anti-dementia medication since dementia is not included among the conditions listed in the Fifth Schedule of the Malta Social Security Act. It was also observed that relatives are ambivalent as to the effectiveness of these drugs but they were unwilling to discontinue treatment in case it made caregiving more difficult or that the symptoms will worsen. This is reported in detail elsewhere.

**Discussion**

Dementia is an ever-growing condition that is associated with significant social, physical, psychological and psychiatric disability not only in individuals diagnosed with the illness but also in caregivers and family members. Up until recently, there was no effective pharmacotherapeutic intervention to manage the cognitive symptoms associated with dementia. Although the benefits of current treatments are deemed to be modest in that they do not halt the disease progression, they represent a major step forward in the clinical management of these patients. Although the presented small scale exercise

**Table 2:** Time intervals from first visit to initial diagnosis and treatment for each person with dementia (PWD) participating in the exercise (* signifies diagnosis of dementia during the first visit at the Memory Clinic, ** signifies initiation of treatment on the same day of dementia diagnosis).

<table>
<thead>
<tr>
<th>PWD</th>
<th>Days elapsed from first visit to diagnosis</th>
<th>Days elapsed from diagnosis to initiation of treatment</th>
<th>Total number of days from first visit to initiation of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>111</td>
<td>0**</td>
<td>111</td>
</tr>
<tr>
<td>2</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>3</td>
<td>0*</td>
<td>306</td>
<td>306</td>
</tr>
<tr>
<td>4</td>
<td>90</td>
<td>0**</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>26</td>
<td>0**</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>0*</td>
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<td>77</td>
</tr>
<tr>
<td>7</td>
<td>0*</td>
<td>103</td>
<td>103</td>
</tr>
<tr>
<td>8</td>
<td>0*</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>9</td>
<td>145</td>
<td>0**</td>
<td>145</td>
</tr>
<tr>
<td>10</td>
<td>0*</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>
A generation of girls and young women is depending on you to vaccinate with SILGARD™

<table>
<thead>
<tr>
<th>Cervical cancer</th>
<th>Genital warts</th>
<th>Vulvar lesions</th>
<th>Vaginal lesions</th>
</tr>
</thead>
</table>

*SILGARD*—the cervical cancer vaccine that helps prevent HPV®-related:

**USES:**
- Cervical cancer
- Genital warts
- Vulvar lesions
- Vaginal lesions

*HPV=Human Papillomavirus.

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The indication is based on the demonstration of efficacy of SILGARD in adult females 16 to 26 years of age and on the demonstration of immunogenicity in older age groups. Since no vaccine is 100% effective and SILGARD will not provide protection against every HPV type, or against existing HPV infections, routine cervical screening remains critically important and should follow local recommendations. For any age class of use of SILGARD it is recommended that the vaccine be administered to prepubertal girls before sexual debut.

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Common adverse reactions that were observed include fever and injection-site erythema, pain, swelling, and pruritus. Syncope, sometimes associated with falling, has occurred after vaccination with SILGARD (See section 4.8). Therefore, vaccinees should be carefully observed for approximately 15 minutes after administration of SILGARD. The vaccine should be given with caution to individuals with thrombocytopaenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these patients. The vaccine should be administered to individuals with impaired immune responsiveness, whether due to the use of potent immunosuppressive therapy, a genetic defect, Human Immunodeficiency Virus (HIV) infection, or other causes, may not respond to the vaccine. Routine cervical screening remains critically important and should follow local recommendations. For any age class of use of SILGARD it is recommended that the vaccine be administered to prepubertal girls before sexual debut.

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- Hypersensitivity to the active substances or to any of the excipients. Individuals who have previously been vaccinated with SILGARD (see section 4.4).
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has its limitations in terms of the number of subjects involved, the general trend observed indicate that at the Zammit Clapp Hospital Memory Clinic, patients are mostly diagnosed early upon their first clinical appointment, are mostly managed with acetylcholinesterase inhibitors and usually suffer from other comorbidities which may or may not be related to dementia. Furthermore, the overall feeling of caregivers and family members is that they are being left out from decisions on pharmacotherapy prescribed for patients with dementia under their care.

Various studies suggest that pharmacotherapeutic intervention with anti-dementia medication early in the disease process may slow down the disease progression and thus improve the quality of life for both patient and caregivers. Although this exercise did not examine the time lapse prior to seeking clinical advice following the emergence of the first symptoms, it is clear that most of the patients did not seek medical intervention early and thus the majority were in the moderate stages of the disease. Reasons for such delay may include caregiver’s lack of knowledge or reluctance to seek help, and patient, family, and physician-related factors. In participating patients, pharmacotherapeutic dementia-related intervention consisted of the use of both acetylcholinesterase inhibitors and glutamatergic-system modifiers. Whether the use of these agents had any significant effect on delaying the disease progression or controlling the behavioural symptoms of our patients is unclear and was beyond the scope of this exercise.

Acetylcholinesterase inhibitors were the first pharmacological treatment approved for symptomatic treatment of AD. These drugs have been found to stabilise the cognitive decline for up to 3-6 months. Memantine, the only glutamatergic system modifier approved for the treatment of AD, was also reported to improve dementia symptoms by reducing the rate of clinical deterioration among patients with moderate to severe AD. Currently there is a strong debate on the cost effectiveness of the

<table>
<thead>
<tr>
<th>Medication</th>
<th>Pharmacological class</th>
<th>Mode of action</th>
<th>Recommended use</th>
<th>Potential adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donepezil hydrochloride (Aricept®)</td>
<td>AChEI</td>
<td>Block acetylcholinesterase enzyme</td>
<td>Mild-to-moderate AD</td>
<td>Anorexia, diarrhoea, dreams, fatigue, insomnia, muscle cramps, nausea, vomiting, weight loss</td>
</tr>
<tr>
<td>Rivastigmine tartrate (Exelon®)</td>
<td>AChEI</td>
<td>Block both acetyl- and butyryl-</td>
<td>Mild-to-moderate AD</td>
<td>Anorexia, diarrhoea, nausea, vomiting, weight loss</td>
</tr>
<tr>
<td>Galantamine hydrobromide (Reminyl®)</td>
<td>AChEI</td>
<td>Block acetylcholinesterase enzyme. Allosterically stimulates nAChRs</td>
<td>Mild-to-moderate AD</td>
<td>Anorexia, nausea, vomiting, weight loss</td>
</tr>
<tr>
<td>Memantine hydrochloride (Axura®, Ebixa®)</td>
<td>Glutamatergic system modifier</td>
<td>Partial NMDA receptor antagonist</td>
<td>Moderate-to-severe AD</td>
<td>Agitation, constipation, dizziness, hallucinations, headache, insomnia</td>
</tr>
</tbody>
</table>

Table 3. Characteristics of pharmacotherapeutic agents used in the management of Alzheimer’s disease (AChEI: acetylcholinesterase inhibitor, AD: Alzheimer’s disease, nAChRs: nicotinic acetylcholine receptors, NMDA: N-methyl-D-aspartate).
This prescribing behaviour is in concordance with current recommendations denoting that early initiation of therapy is associated with greater long-term benefits.

A significant number of participating patients were diagnosed with depressive illness possibly indicating a high prevalence rate of depression in patients with dementia. This was also reflected by the significant use of antidepressants as part of the overall prescribed treatment regimen. Epidemiological studies show a possible pathological association between the two conditions, with depression possibly acting as a prodromal sign or early symptom of AD. Due to the limited number of patients participating in this exercise, it was not possible to investigate any link between depression and dementia although this would be an interesting research area for future consideration. The same is also valid with the other main pathologies observed. Although cardiovascular disease, diabetes and hypercholesterolaemia are risk factors in vascular dementia, these conditions are also prevalent in old age.

The use of multiple medication (polypharmacy) in the elderly has always been regarded as a complex issue in pharmaco-geriatric management. Although polypharmacy may be the only choice in some individuals, multiple medication use may increase the risk of non-compliance, medication error and potentially adverse drug interactions. Prescribing for elderly patients with dementia proves to be even more challenging due to the changing needs that accompany cognitive decline and related behavioural symptoms. Furthermore, more medications may be indicated in patients with dementia due to the presence of other pathologies which are common in old age. Our data indicated that, on average, each person with dementia was prescribed with more than five different medications for the management of dementia and other comorbidities. This finding raises important clinical concerns, especially for individuals who still live in the community, in some cases on their own. Furthermore, because the use of polypharmacy increases the risk of falls, prescribing unnecessary medication may further enhance institutionalisation. Polypharmacy is also associated with increased risk of adverse drug-drug interactions which can have potential life-threatening consequences in older adults. This is especially critical in patients with dementia who are cognitively impaired and therefore not be able to explain or self report the symptoms. Interestingly, only one drug (lorazepam) was found to be part of the Beers Criteria, a list of medications that are generally considered to be inappropriate when given to the elderly. No potentially serious drug-drug interactions were observed. In line with guidelines issued by NICE, prescription of antipsychotic drugs was only present in one participating patient attending the Memory Clinic. Recent data shows that the use of these drugs in persons with dementia is associated with an increase in the risk of fatality.

Studies including the views and experiences of caregivers on the effectiveness of anti-dementia drugs are lacking with a major focus directed towards conventional scientific evidence which is mostly relevant to clinicians and research scientists.

Figure 3: Number of PWD on polypharmacy (a) and total number of drugs prescribed to all patients as per drug mode of action or therapeutic class (b).
This lack of caregiver perspective was apparent in our qualitative assessment of the participating subjects. Caregivers were mostly concerned with the lack of support from the central health authorities in caring for their relatives. The greatest concern is the lack of financial assistance in purchasing anti-dementia medication which, in some cases, can take up a third of the person with dementia pension. Together with Latvia, Malta is the only country where the health authorities do not offer any form of financial support in accessing these drugs. Even though some caregivers interviewed were unsure of the efficacy of anti-dementia medication in slowing the disease progression, they were unwilling to stop treatment.

Conclusion

Although more research is needed, using a larger sample number, the trends observed highlight the need for a nationwide strategy that includes the various aspects involved in pharmacological and non-pharmacological management of dementia. Such strategy should include the views of policy makers, healthcare professionals as well as patients and their caregivers with the aim of designing and implementing a series of recommendations that should enhance high-quality dementia care in Malta.

Acknowledgements

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References

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Pulmonary rehabilitation: insight into current trends

Anabel Sciriha, Stephen Montefort

Abstract
Pulmonary rehabilitation is a widely accepted therapeutic tool used to improve the quality of life and functional capacity of individuals with chronic lung disease. It is a multidisciplinary, comprehensive program designed to optimise autonomy and physical performance in patients with chronic respiratory impairment. There is sufficient evidence to support the use of pulmonary rehabilitation for a subset of patients and to indicate that it can improve exercise tolerance and symptoms of dyspnoea, as well as enhance health-related quality of life of patients with COPD and other respiratory conditions. According to projections in the Global Burden of Disease Study, COPD will be the fifth leading cause of disability-adjusted-life-year loss worldwide in 2020.

The goal of pulmonary rehabilitation is to help the individual achieve the highest level of independent functioning by improving pulmonary function, increasing exercise endurance and exercise work capacity, reducing dyspnoea and normalising blood gases.

Locally, no pulmonary rehabilitation service as described by respiratory societies is offered. Therefore, this paper will look into the current research focusing on future recommendations for this service in the international setting with an aim of implementing this into the local health care system.

Keywords
Asthma, COPD, Pulmonary rehabilitation, chronic, acute

Introduction
Rehabilitation is the restoration of individuals to the fullest medical, mental, emotional, social and vocational potential the individual is capable of. The basic premise of all rehabilitation is that it is possible to effect positive change under the poorest circumstances imaginable and that no effect of illness save for death is absolute.

Pulmonary rehabilitation is defined as a program for people who have chronic lung disease. Its primary goal is to enable people to achieve and maintain their maximum level of independence and functioning. Although most pulmonary rehabilitation programs focus on people who have chronic obstructive pulmonary disease, people with other types of lung disease may benefit as well. The most successful rehabilitation programs are those in which services are provided by a physiotherapist, nurse, doctor, psychologist or social worker, and a dietitian working as the pulmonary rehabilitation team to coordinate complex medical services.

Optimal length of the rehabilitation phase
Despite the increasing propagation of the efficacy of pulmonary rehabilitation, there is no definitive proposal for the best training strategy with variances in the duration and frequency. Significant gains in exercise tolerance, dyspnoea, and quality of life have been observed following rehabilitation programs as short as 10 days and others as long as 18 months with gains in exercise tolerance reported to be greater in the latter. Two randomised trials compared 3 months and 18 months of low-intensity exercise training. The longer intervention led to 6% increase in the 6 minute walk distance, 12% reduction in self-reported disability and faster completion of stair climbing and overhead tasks. No differences though were seen in pulmonary function studies between groups, after training. The investigators concluded that the benefits achieved after short-term pulmonary rehabilitation began to decay once the intervention was terminated, despite encouragement to continue participation in a home-based or community-based programme. On the other hand, Foy et al showed that only male patients achieved greater gains in Chronic Respiratory Disease Questionnaire scores following the 18-month program (compared to 3 months). In fact, more favourable scores than those in the short-term group were reported for dyspnoea, fatigue, emotional function and task mastery.

In a 2005 published prospective trial involving seven outpatient programmes, patients achieved significant gains in exercise tolerance (6 minute walk distance), dyspnoea and...
health status (Medical Outcomes Study 36-item Short Form and quality-of-life index) after 12 weeks of pulmonary rehabilitation. Following an additional 12 weeks of rehabilitation, exercise tolerance, but not health status or dyspnoea, outcomes improved further, suggesting that programme duration may not impact all outcomes equally. Also, in support of longer term exercise training, 6-month outpatient pulmonary rehabilitation programmes composed of moderate-to-high-intensity aerobic and strength exercise training led to significant improvements in exercise performance and quality of life. Although this study did not compare the 6-month programme with a shorter one, the benefits gained following the 6-month training program persisted 18 months after the completion of rehabilitation.

Severe COPD patients were also found to achieve greater improvements in treadmill endurance, incremental shuttle walk distance, and quality of life following a 7-week outpatient pulmonary rehabilitation programme compared with an identical program of only 4 weeks duration. However, patients who underwent the 4-week programme were not reassessed at the 7-week time point to enable the direct comparison of outcomes.

Overall, although some studies suggest that the duration of the pulmonary rehabilitation programme impacts exercise tolerance improvement, it is less clear that other outcomes such as health status or dyspnoea are similarly affected by programme duration. Randomised controlled trials have shown that short-term pulmonary rehabilitation (4 to 12 weeks) can reduce the number of hospitalisations, improve quality of life, reduce respiratory symptoms, improve exercise tolerance, increase self-efficacy, and improve the ability to perform activities of daily living. However, only a few studies have looked at the benefits of long-term (12 weeks or more) supervised pulmonary rehabilitation (Table 1).

It has not been established to what degree the benefits of short-term pulmonary rehabilitation diminish over time, how long these benefits persist with continued supervised intervention, or the optimal nature of long-term pulmonary rehabilitation intervention. The confounding effects of multiple study designs including varying durations of exercise, education, breathing retraining, and home exercise interventions have hindered solid conclusions about these issues.

Rehabilitation in the acute and chronic phase

Acute exacerbations of COPD represent a major burden for patients and health care systems. They are a common reason for hospital admissions and severely affect health-related quality of life and prognosis. Mortality rates during hospitalisations are around 10% and during the following year hospitalisation may be as high as 40%. From the health care provider’s perspective, COPD is resource consuming and about 10% of COPD patients suffering from acute exacerbations account for over 70 percent of costs caused by COPD, primarily due to emergency visits and hospitalisations.

Position papers of the American College of Physicians and American College of Chest Physicians provide recommendations on the management of acute exacerbations. However, no recommendations on how future exacerbations and hospitalisations could be prevented are indicated, despite this being one of the main goals of COPD management. One solution that has been adopted in clinical practice is to provide rehabilitative care after treatment of acute exacerbation including physical exercise, patient education focusing on self-management strategies and psychosocial support.

The rationale to offer rehabilitation in patients recently treated for acute exacerbation is to enhance quality of life, as in stable COPD patients and modify factors associated with increased risk for post-exacerbation morbidity and mortality. Patients with frequent exacerbations have more pronounced skeletal muscle weakness and a more limited six minute walking distance, which is in turn a risk factor for exacerbations and mortality. Thus, respiratory rehabilitation may have the potential to reduce hospital admissions by improving exercise capacity. It is surprising that research on the effects of respiratory rehabilitation in patients after acute exacerbations, is very scant.

Randomised controlled trials evaluating the effects of pulmonary rehabilitation after hospitalisation for acute exacerbations of COPD report improvements in outcome measures at three months after hospital discharge with significant improvements in walking distance ($p=0.0002$), health status scores ($p=0.002$), all four domains of the Chronic Respiratory Questionnaire (dyspnoea, $p=0.003$; fatigue, $p=0.004$; emotion, $p=0.008$; mastery of tasks, $p<0.001$). Therefore, this trend showed that early intervention with pulmonary rehabilitation after a hospital admission for acute exacerbations of COPD is safe and leads to statistically and clinically significant short-term improvements in exercise capacity and health status.

Compared to rehabilitation during stable periods, the effects of rehabilitation tend to be larger after acute exacerbations. Studies looking at the acute phase are relatively small in sample size, therefore there is the tendency to overestimate the effect of an intervention compared to large trials. Also, methodological limitations were found and one cannot exclude that the estimates provided by the meta-analyses represent overestimations of the effect of respiratory rehabilitation after acute exacerbation. Therefore, larger trials seem justified to challenge the data available.

When conducting studies post acute exacerbations, recruitment of patients may be difficult because not all of them may want to be randomly allocated to respiratory rehabilitation or conventional care, in a situation of poor health status. It must also be taken into consideration that exercise capacity is particularly low after acute exacerbations, and therefore the exercise programme should be designed carefully. Strength exercise and tolerable whole body exercise modalities such as interval exercise may be particularly suitable for these patients. Rehabilitation may not only reduce the number of acute exacerbations, but also their severity. Patients may learn to notice imminent exacerbations and seek medical attention earlier leading to a shift from inpatient to the less costly outpatient treatment of acute exacerbations. The significant reduction in hospital readmissions is suggestive of a beneficial cost-benefit balance.
Pulmonary rehabilitation in respiratory conditions other than COPD

Although there are some studies stretching the beneficial role of pulmonary rehabilitation to other respiratory diseases, the reported evidence is highest for COPD.19

It is believed that pulmonary rehabilitation has positive effects in a large range of chronic pulmonary conditions including asthma.20,21 The scientific rationale for providing pulmonary rehabilitation to patients with non-COPD diagnoses is the same as for COPD. As in COPD, persons with other forms of chronic respiratory disease commonly experience deconditioning and exercise intolerance, disabling symptoms of dyspnoea and fatigue, impaired health status and quality of life, systemic inflammation, nutritional impairments, and/or muscle dysfunction (related to deconditioning, loss of fat-free mass, and/or corticosteroid use) that collectively impair functional status along with abnormalities of pulmonary function.20

Modification of the relative emphasis on the core programme components and overall programme content may be required to maintain patient safety and to meet individual patient needs and goals which may differ from the standard goals for COPD.7 Disease-appropriate and age-appropriate tools for the assessment of exercise capacity, health status, and quality of life should be utilised, and efforts must be made to integrate topics relating to non-COPD diagnoses in situations in which the patient group is composed predominantly of COPD patients.

Although most of the studies published to date, which investigate the outcomes of pulmonary rehabilitation for disorders other than COPD are uncontrolled trials or case series, randomized clinical trials are beginning to emerge22,23 with the strength of existing evidence supporting pulmonary rehabilitation varying across the different diseases.

Importance of nutritional and psychological care

The need of a multidisciplinary programme also includes nutritional and psychological assessment. Nutritional depletion is commonly found in COPD patients and this affects both the respiratory and skeletal muscle function, contributing to an increased morbidity and mortality.24 Schols and colleagues

<table>
<thead>
<tr>
<th>Study/ year</th>
<th>Study type</th>
<th>Country/Setting</th>
<th>No of Patients</th>
<th>Outcomes/results</th>
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<tr>
<td>Troosters et al. 2000</td>
<td>RCT: 6 vs 18 months vs usual care</td>
<td>Belgium/OP</td>
<td>100</td>
<td>Pulmonary function; exercise capacity; muscle strength; QOL</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Walking distance (p&lt;0.05); exercise capacity (p&lt;0.02); no significant effects of training programme on PF measures vs usual care; improved quadriceps strength (p&lt;0.05) and QOL (p&lt;0.001)</td>
</tr>
<tr>
<td>Foy et al. 2001</td>
<td>RCT: short- vs long-term PRP</td>
<td>United States/OP</td>
<td>140</td>
<td>Four domains of CRQ. Significant changes in short vs long term in all domains</td>
</tr>
<tr>
<td>Green et al. 2001</td>
<td>RCT: single-blind; short vs long-term PRP</td>
<td>UK/OP</td>
<td>44</td>
<td>Endurance; HRQL CRDQ (p&lt;0.011); dyspnoea (p&lt;0.021), emotion (p&lt;0.003), mastery (p&lt;0.027)</td>
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<tr>
<td>Berry et al. 2003</td>
<td>RCT: single-blind; short vs long-term PRP</td>
<td>United States/OP</td>
<td>140</td>
<td>Physical function and disability; pulmonary function</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Disability: p&lt;0.016 long- vs short-term</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Physical function: increased walk distance (p&lt;0.03 long term); stair climb time (p&lt;0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pulmonary function: NS</td>
</tr>
<tr>
<td>Sewell et al. 2006</td>
<td>RCT conventional seven-week supervised program (n=50) or to a four-week supervised programme (n=50).</td>
<td></td>
<td>100</td>
<td>At seven-week follow-up, patients in the four-week program attained higher submaximal exercise performance times for a mean difference 124 seconds (p=0.024).</td>
</tr>
</tbody>
</table>

Table 1: Reported durations and outcomes of pulmonary rehabilitation programmes. (RCT: randomized clinical trial; OP: outpatient, PRP: pulmonary rehabilitation programme, QOL: quality of life; PF: pulmonary function; NS: not significant)
found that patients who increased their weight by more than 2 kg had a significantly better survival, independently of their initial body mass index.\textsuperscript{25} Because of the morbidity and mortality associated with underweight COPD patients, it is therefore being recommended that interventions should be extended to prevention and early treatment of weight loss, before patients become extremely wasted, and therefore put more emphasis on dietary change than on medically prescribed supplementation.\textsuperscript{26,27}

The psychological input is also required as patients with chronic respiratory diseases have an increased risk for anxiety, depression, and other mental health disorders\textsuperscript{26-27} leading to frustration with poor health and an inability to participate in activities which can present as irritability, and a hostile attitude toward others. In the later stages of respiratory disease, progressive feelings of hopelessness and inability to cope often occur. When psychologic support is provided within the rehabilitation setting, one will be able to help facilitate the adjustment process by encouraging adaptive thoughts and behaviours as well as helping patients to reduce any negative emotions present.

As is documented in a review of randomized studies, Griffiths and colleagues reported reduced symptoms of anxiety and depression following a 6-week pulmonary rehabilitation program, with symptoms of depression remaining significantly reduced at the 12-month follow-up.\textsuperscript{28} Also, Emery and colleagues\textsuperscript{28} found reduced anxiety and improved cognitive function following a 10-week pulmonary rehabilitation intervention.

**Recommendations and conclusion**

With a constant increase in COPD patients, and this disease ranking 4\textsuperscript{th} for mortality and morbidity rates, more research in this field is required to further look into the above discussed issues in order to help the local development of the best pulmonary rehabilitation service for the treatment of respiratory patients. Coordination of services is very important, especially during episodes of exacerbation, which are characterized with high morbidity and a marked increase in use of health care resources.

**References**

Management of inflammatory dentigerous cysts in children: report of two cases

Erica Scerri, Alexander Azzopardi

Abstract

Inflammatory dentigerous cysts are usually associated with a carious or non-vital primary tooth. Consequently they are found in children with a mixed dentition. This report describes two cases of inflammatory dentigerous cysts associated with the lower second premolars. Both cases were treated by marsupialisation of the cysts that eventually led to the spontaneous eruption of the premolars.

Introduction

Odontogenic cysts in children are rare with only 1% of the radicular cysts and 9% of the dentigerous cysts occurring in the first decade of life. Dentigerous cysts are developmental in origin and are usually associated with impacted teeth or teeth that erupt late. Inflammatory dentigerous cysts are associated with the roots of carious or non-vital primary teeth and the crowns of unerupted permanent successors. Consequently, they can only be found in the mixed dentition. A possible pathogenesis of these cysts is periapical inflammation from a non-vital deciduous tooth spreading to involve the follicle of the unerupted permanent successor tooth. The inflammatory exudate causes the reduced enamel epithelium to separate from the enamel leading to the formation of a dentigerous cyst. Several authors have reported cases of dentigerous cysts associated with an infected predecessor tooth. The following two case reports show the successful management of two such cases referred from general dental practice.

Keywords

Dentigerous cysts, Children, Inflammatory, Treatment

Case report 1

A healthy 7-year old boy was referred to the Dental Department of St Luke’s Hospital, Malta in May 2005 following extraction of a carious lower right second deciduous molar (85) in General Dental Practice. A hard swelling in the lower right buccal sulcus in the premolar region did not subside even following antibiotics and was still present one week after the extraction. A panoramic radiograph (Figure 1) showed a large unicocular radiolucency surrounding the crown of the lower right second premolar with displacement of the lower right premolar crowns towards the lower border of the mandible. Marsupialisation of the cyst was carried out under local anaesthesia, and a specimen was sent for histological examination. The patient was provided with an acrylic plate with a plug and was instructed to irrigate the cyst cavity with a chlorhexidine mouthwash. The histology report was that of a radicular cyst. The patient was reviewed every month to reduce the depth of the acrylic plug. Radiologic examination showed the cyst to be reducing in size and by August 2005, a panoramic radiograph showed the lower right premolars to be migrating occlusally. In October 2005, the cyst opening had closed completely and it was decided to re-open the cyst cavity. This was carried out under local anaesthesia and cold curing acrylic was used to build-up the plug on the lower plate. Two months later, radiologic examination showed that the cyst cavity was decompressing and the lower right premolars were erupting into position (Figure 2). By January 2007 the lower right premolars were clinically visible and by July 2007 they were fully erupted. The patient is still being reviewed at the orthodontic clinic of Mater Dei Hospital, waiting for the permanent dentition to be established.

Figure 1: Inflammatory dentigerous cyst involving the mandibular right second premolar.

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Case report 2

In November 2006, a healthy 10-year old boy presented at the Dental Department with a firm swelling associated with a grossly decayed lower left second deciduous molar. The lower left first deciduous molar and the lower right deciduous molars had been previously extracted. A panoramic radiograph (Figure 3) revealed a well defined unilocular radiolucency embedding the crown of the lower left second premolar which was displaced apically. The carious lower left second deciduous molar was extracted and cyst marsupialisation was carried out under general anaesthesia. The cavity was packed with Bipp gauze during the first two weeks post-operation. The patient was then provided with a removable lower space maintainer with an acrylic plug in the cyst region to maintain the opening of the cyst patent. The patient was instructed to rinse with a chlorhexidine mouthwash and was reviewed every two weeks to reduce the height of the plug. The lower left premolars erupted spontaneously as the cyst decompressed. By May 2007 the lower left first premolar had started to erupt and the lower left second premolar was clinically visible by July 2007. The acrylic plug was removed completely but the patient was instructed to keep on wearing the lower space maintainer to prevent mesial tilting of the lower first molars. In April 2008, a panoramic radiograph (Figure 4) showed that the radiolucent lesion in the lower left premolar region had resolved completely. The lower left second premolar was however impacted beneath the contact point of the lower left first molar. The patient also had a developing Class III malocclusion and impacted upper second premolars and was therefore referred for orthodontic treatment. He is still being followed up at the orthodontic clinic of Mater Dei Hospital.

Discussion

There have been 20 reported cases of dentigerous cysts in Maltese children in approximately the first decade of life from 1961 till 2006. They are more common in boys and more likely to occur in the lower jaw (unpublished data compiled by Prof. G. E. Camilleri). Both cases described here were associated with the lower second premolar teeth and both patients were males. The radiographic appearance of the cystic lesion in both cases was that of a unilocular, well defined radiolucency enclosing the crown of the second premolar tooth suggesting the diagnosis of a dentigerous cyst. However, since dentigerous cysts are usually associated with impacted teeth or teeth that erupt late, the radiographic signs, in both cases, did not support the diagnosis of a developmental dentigerous cyst. In the first case presented here, there was still no root formation of the second premolar and therefore it was unlikely that tooth eruption had started. In the second case, although root formation had started, there was nothing to suggest that the second premolar might have been impacted. Therefore it was unlikely that the pathogenesis of both cystic lesions was that of a dentigerous cyst which is developmental in origin. On the other hand, there appeared to be a definite correlation between the cystic lesion and periapical pathology from the overlying carious predecessor tooth especially in the second case were the roots of the carious deciduous second molar could be seen touching the cyst wall. This suggested that the cystic lesions were inflammatory dentigerous cysts. A specimen was sent for histological examination in the first case only and although the histopathological report came back as a radicular cyst it is histologically very difficult to distinguish between inflammatory dentigerous cysts and radicular cysts and radicular cysts associated with deciduous teeth are very rare. Unfortunately a specimen was not sent for histology in the second case. Therefore, a diagnosis of the cystic lesion in this case was not possible. However it is worth noting that a biopsy should always be taken to exclude odontogenic tumours and other cystic lesions such as the odontogenic keratoctyst. These lesions may present in a similar way but would necessitate more aggressive treatment.
Dentigerous cysts in adults are usually treated by surgical enucleation and extraction of the associated tooth affected by the cyst. In the case of small cysts, enucleation and preservation of the involved tooth is sometimes advocated in younger patients. Larger cysts are initially reduced in size by marsupialization followed by surgical enucleation at a later stage. A more conservative approach has been used in our two cases of inflammatory dentigerous cysts because of the young age of the patients. Following the removal of the carious deciduous teeth, decompression of the cysts was carried out and the opening was then kept patent with the use of an acrylic plug to allow the cyst to shrink and at the same time allow bone regeneration to occur. This eventually resulted in the spontaneous eruption of the premolars in both cases and has prevented the loss of any permanent teeth or damage to any of the adjacent structures.

The above two cases highlight the importance of preventive measures and proper management of carious deciduous teeth to avoid these complications. Regular follow-up of the deciduous dentition is of the utmost importance because an inflammatory dentigerous cyst can attain a considerable size before the patient becomes aware of it, this usually being asymptomatic. Simple management of inflammatory dentigerous cysts usually results in a satisfactory outcome without loss of teeth. The prognosis is much better in children because of the greater eruptive potential of teeth with open apices and the greater regenerative potential of young bone.

Acknowledgements
We would like to thank Professor George Edward Camilleri for providing us with the data of dentigerous cysts in Maltese children.

References
A rare cause of hypoglycaemia

Robert Sciberras

Abstract
This paper describes a case study concerning a young man on treatment for psychiatric illness who developed severe episodes of hypoglycaemia. After several investigations, lithium therapy was implicated. Stopping this treatment resulted in the patient being relieved of these episodes.

A rare cause of hypoglycaemia
F.A. is a 36 year old male health care worker with a long-standing history of psychiatric illnesses and repeated admissions to the Psychiatric Short-Stay Ward. The depressive illness was precipitated by an accident in a previous work-place. Other past history included hypertension of 4 years duration and spinal surgery for a prolapsed disc in 2006.

The patient is married to a diabetic lady, who is on gliclazide and metformin. She monitors her own blood glucose at home using a glucose meter.

F.A. was referred in October 2008 complaining of recurrent hypoglycaemic attacks occurring approximately every 2 days for the past 4 weeks. The low glucose levels ranging between 2.2mmol/L and 2.7mmol/L were documented by his wife using her glucose meter. The hypoglycaemic attacks were typical and included excessive sweating, tremors, nausea and at times, episodes of confusion. The episodes were relieved by the patient ingesting a large bar of chocolate followed by sugary drinks.

The patient was on clozapine 25mg, ½ tablet three times a day, lithium 400mg tabs, 600mg at night, mianserin 10mg, two tablets three times a day and paroxetine 20mg two tablets in the morning and one tablet in the evening. His blood pressure was well controlled with amlodipine 5mg once daily.

There were no other systemic complaints, and no relevant family history. There was no recent change in appetite or weight. Examination was unremarkable. Given his work-place and also his home situation, surreptitious ingestion of oral hypoglycaemic agents was suspected but subsequently eliminated as the cause for his attacks. At his place of work he did not have access to any hypoglycaemic agents. At home, his wife kept her medications under lock and key particularly because the couple had two small children. She could also account for all her tablets. Psychiatric consultation concerning whether any of the psychiatric medications could be causing hypoglycaemia proved negative. All investigations including thyroid function tests were normal. Serum lithium level was 0.45mmol/L (normal range 0.6-1.2mmol/L). The patients did not present a history of lithium toxicity.

The patient was admitted to Gozo General Hospital for monitoring at the end of October 2008. During admission two hypoglycaemic episodes occurred and were witnessed by the author. The glucose levels were 2.6mmol/L and 2.7mmol/L respectively. The hypoglycaemic attacks had to be aborted rapidly by dextrose infusion as the patient became very symptomatic, confused and on the point of becoming aggressive. Blood tests were taken during the hypoglycaemia: C-Peptide level was 5.85ng/ml (normal range is 0.80-4.00ng/ml), insulin level was 31.0microU/ml (normal range 2.0-25.0microU/ml), and proinsulin level was 88pmol/L (normal range is 6.4-9.4pmol/L). These levels were inappropriately high for a patient with hypoglycaemia.

An insulinoma was suspected and an urgent computerised axial tomography of the abdomen was carried out, including 1.5mm slices at the pancreatic level. This was reported as normal.

Meanwhile hypoglycaemic episodes were still occurring in spite of continuous dextrose infusion and so the patient was started on prednisolone 10mg three times a day. This medication put an end to the hypoglycaemic episodes and the patient was discharged home pending further investigations.

An Indium-111 octreotide scintigraphy was performed on the 17th of December 2008, 4 hours and 24 hours following intravenous administration of 160MBq of Octreoscan. Both whole body and
SPECT images were acquired. There was no abnormal focus of tracer accumulated in the abdomen. Physiological activity was seen in liver, spleen and kidneys with intestinal activity evident at 24 hours. It was therefore concluded that there was no definite evidence of insulinoma. However sensitivity of octreotide scintigraphy is in the range of only 50% (see discussion below). Surgical consultation resulted in the patient being scheduled for exploratory laparotomy which might have included total pancreatectomy. At the eleventh hour the surgery was postponed due to repeated hypoglycaemic episodes. During one of these episodes, blood investigations showed an insulin level of 22 microU/ml (reference range 2.0-25.0 microU/ml), C-peptide level of 3.64 ng/ml (reference range 0.80-4.00 ng/ml), and proinsulin level of 30.4 pmol/L (reference range 6.4-9.4 pmol/L). The patient was started on diazoxide 50mg, four tablets three times a day and discharged home on the 10th of March 2009.

Two days later the patient was admitted urgently to hospital complaining of fever of 102 degrees Fahrenheit, severe muscle aches and pains, shortness of breath and inability to walk due to generalized weakness and stiffness. There was no wheezing or rash. His eosinophil count was normal. The symptoms had started on initiating diazoxide therapy. A reaction to the medication was suspected, the drug withdrawn and all symptoms resolved. At this point, lithium therapy started to be suspected to be causing the hypoglycaemic episodes in this patient. The dose of lithium was reduced to 400mg at night and the patient discharged. The rest of the medication was kept at the same dose throughout the investigative period. Further visits at out-patients revealed that no further episodes of hypoglycaemia were occurring since reduction of lithium therapy, in spite of the steroids being tailed down. Lithium was eventually reduced to 200mg at night and steroids completely stopped on the 27th of April 2009.

On the 15th of May 2009, the patient was admitted to hospital for a prolonged fasting test. He was advised not to eat anything between 4.00 pm and 8.00 am the following morning. He was allowed to drink water only. Blood glucose was monitored every hour. There were no low blood glucose readings. At 8.00 am, a 75g glucose oral drink was administered. Three hours later the patient suffered a symptomatic hypoglycaemic attack with blood glucose falling to 2.5mmol/L. The insulin level checked at this time was 11.0 microU/ml (normal range 2.0-25.0 microU/ml), C-peptide level was 3.73 ng/ml (normal range 0.8-4.00 ng/ml) and proinsulin level was 61.7 pmol/L (normal range 6.4-9.4 pmol/L). At this point, therefore, the patient was not having spontaneous hypoglycaemic episodes but had a late one precipitated by a glucose load. The lithium therapy was eventually tailed off by the end of June 2009.

The prolonged fasting test was repeated on the 23rd of July 2009. Serum lithium level was <0.10 mmol/L (normal range 0.6-1.5 mmol/L), and this confirmed that the patient had indeed stopped lithium therapy as instructed. During the fast, the patient did not have hypoglycaemic episodes. At 8.00 am, a 75g glucose load was administered and the patient was observed for six hours later and was allowed to drink water only. Contrary to the first prolonged fasting test, the blood glucose estimations every 30 minutes were stable and there were no hypoglycaemic episodes after the glucose load.

The patient is still being seen regularly at the hospital outpatients department. He is well and has had no further problems since. A letter to the Medicine Authority has been sent reporting the adverse effects caused by lithium and diazoxide.

Discussion

Lithium salts are used in the prophylaxis and treatment of mania, in the prophylaxis of bipolar disorders (manic-depressive disorder) and in the prophylaxis of recurrent depression (unipolar illness or unipolar depression). A literature search for the association of lithium therapy with hypoglycaemia did not reveal significant results. Pinelli et al reported neonatal hypoglycaemia with maternal lithium therapy, apart from Ebstein’s anomaly, cyanosis, rhythm disturbances and thyroid dysfunction.1 Shah et al performed five-hour oral glucose tests (OGTT) in nine patients receiving lithium therapy and in seven control patients.2 During GTT mean nadir serum glucose was significantly lower in the lithium-treated patients as compared to controls. The study suggested that chronic lithium treatment may be associated with symptomatic and biochemical hypoglycaemia during OGTT due to a rise in serum cortisol but lack of appropriate rise in plasma glucagon concentrations. Other hormonal effects were studied by Grof et al.3 In this study, lithium treatment resulted in a dramatic reduction in prolactin and growth hormone response to insulin hypoglycaemia. The reduced prolactin response to hypoglycaemia was also confirmed by Grof et al.4 However, other studies tend to contradict these findings. In the intact rat, lithium was found to inhibit glucose- and tolbutamide-induced insulin release, which in turn, causes glucose intolerance and prevents tolbutamide-induced hypoglycaemia. The literature describes one report of a patient with lithium toxicity who presented with hypoglycaemia, aceneform lesions, hypothyroidism and nephrogenic diabetes insipidus.6 However the case study presented above was not a case of lithium toxicity as was proved by repeated blood tests.

The first oral glucose tolerance test also suggested a rebound type of hypoglycaemia. This could explain the fact that when the patient presented originally, his eating chocolate bars to alleviate a hypoglycaemic attack was in fact triggering the next one. The levels of pro-insulin were very high (up to 9 times the upper laboratory reference range). Pro-insulin has weak insulin-like biological activity of its own right, but a much longer half-life than insulin. It might therefore have contributed to a reactive-type of hypoglycaemic reactions. A diagnostic problem which was encountered was the fact that the octreotide scan is not always helpful, since the false negative rate could reach up to 50% due to different types of somatostatin receptors present in this tumour type.7,8,9

The duration of the prolonged fasting tests might not be the recommended one, however in this case it served its purpose since the difference between the 2 tests occurred after the glucose challenge; when the patient was on lithium there was...
severe hypoglycaemia and while off lithium the patient did not suffer any adverse events. So the two scenarios were directly comparable. Furthermore, stopping lithium therapy has resulted in the total absence of further hypoglycaemic episodes to date, virtually ruling out insulinomas since no definite treatment for these tumours was undertaken. Furthermore the patient has not developed other conditions e.g. diabetes mellitus.

It is clear that further studies need to be carried out in order to investigate the role of lithium in causing hypoglycaemia. However any patient on lithium suffering from recurrent episodes of hypoglycaemia may need a review of psychiatric treatment.

Acknowledgements

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References

Implementation of a graft surveillance programme for infrainguinal vascular bypass surgery

Noel Cassar, Branko Dunjic, Kevin Cassar

Abstract

Aim: Patients undergoing bypass graft placement in the lower limb are often entered into a graft surveillance programme using duplex scanning. The aim of this programme is to identify stenoses in vein grafts before they become symptomatic and treat these by angioplasty or surgery, thus prolonging the patency of the graft. This paper aims at reporting on the progress and viability of this programme at Mater Dei Hospital, Malta.

Method: Infrainguinal bypass grafts carried out between July 2007 and May 2009 were enrolled. Scanning starts during the patient’s in-hospital stay at one week post-operation. It is then scheduled at 6 weeks, 3 months, 12 months, 18 months, 24 months, and yearly afterwards. When a significant stenosis is encountered, the patient is referred for angioplasty. Surgery would be considered in cases when angioplasty is not an option.

Results: During this period 56 patients were recruited. At one week post-op the patency rate was 100%. At 6 months the primary unassisted patency was 77.5% while the primary assisted patency was 87.5%. At 12 months the primary unassisted patency was 50% while the primary assisted patency was 77%. Secondary patency rates at 6 and 12 months were 95% and 82% respectively.

Conclusion: The graft surveillance programme ensures that any problem detected in the post-operative period is dealt with as soon as possible. The study shows that this programme is being effective in that assisted rates (i.e. after angioplasty or surgery) are better than unassisted rates.

Keywords

peripheral vascular disease, ischaemia, angioplasty, duplex Doppler ultrasonography

Introduction

For patients with severe peripheral vascular disease, especially those with long occlusions of the superficial femoral and popliteal arteries, infringuinal vascular bypass surgery may be the only option for revascularization of the limb. There are three main types of infringuinal bypass surgery – femoro to above knee popliteal bypass, femoro to below knee popliteal bypass and femoro to distal bypass. The latter can be femoro to anterior tibial, femoro to posterior tibial or femoro to peroneal bypass. Once patients have been scheduled for a bypass procedure they are assessed medically to check whether they are fit for the operation and they are scanned by the vascular surgeon in charge to look for any suitable vein graft which can be used as a new conduit. Vein grafts are preferred over PTFE grafts as they have longer patency than the latter. Patients who undergo such operations are not simply discharged once they have recovered from their operation, but are followed up on a regular basis to check the progress of their graft and therefore of their clinical condition.

This is in accordance with the recommendations of The Trans-Atlantic Inter-Society Consensus on the Management of Peripheral Arterial Disease (TASC), which states that patients “who undergo bypass graft placement in the lower extremity for the treatment of claudication or limb-threatening ischaemia should be entered into a clinical surveillance program.” This consists of asking the patients how they are doing in regards to their previous symptoms and whether any new symptoms have developed since the operation. Vascular examination of the lower limb should take place as well with palpation of inflow, graft and outflow vessel pulses. Resting and post-exercise Ankle brachial pressure indices (ABPI) should be measured as well.

Although strictly not a TASC recommendation, as ongoing trials are still needed to determine its efficacy, many surgeons also enter their patients into a graft surveillance programme whereby the graft is scanned by duplex ultrasound at regular intervals. The aim of this scanning is to check that the graft is working and to detect and treat any stenosis in the graft. This article reports on the setting up of such a graft surveillance programme in Malta.

Methods

Once a patient undergoes a vascular bypass operation he or she spends a day in an ITU/HDU setting and is then transferred to a normal surgical ward. The patient is seen daily to monitor his or her progress and at one week post-op the first graft scanning takes place. The scanning needs to answer two main questions:

• Is the graft working?
• Is there any stenosis?
Duplex ultrasound Doppler is used to answer these questions, by means of waveform analysis and peak systolic velocities measurement. Colour Doppler is used to detect blood flow (Figures 1 and 2).5,6

In terms of waveform analysis, triphasic waveforms represent better blood flow than biphasic which are in turn better than monophasic waveforms.

Blood flow is assessed in the artery proximal to the graft, the graft itself and the outflow artery. An increase in Peak Systolic Velocity of more than 3 times along the vessel is considered significant and is suggestive of a stenosis (Figure 3).5,6 Peak systolic velocities of less than 20cm/sec indicate that the flow through that segment of graft is poor and may require intervention.7

Stenosis may occur at any site along the graft including the proximal and distal anastomosis.

If during this process any stenosis is identified the patient can then be sent for angioplasty of the stenosis. This ideally should happen before such a stenosis becomes clinically significant. Sometimes graft scanning will reveal long occlusions which are not amenable to angioplasties. In such cases, if possible, the patient will be offered redo bypass surgery.

Scanning takes place at one week post-op, then continues at 6 weeks, 3 months, 6 months, 12 months, 18 months, 24 months and yearly afterwards. Only patients who underwent bypasses using vein grafts are scanned. PTFE grafts are not routinely scanned as they cannot be angioplastied should the need arise.

This report covers graft scanning done for those infrainguinal bypasses carried out between August 2007 and May 2009 at St Luke’s Hospital and Mater Dei Hospital by the firm of one of the authors (KC).

Records for primary unassisted patency, primary assisted patency, and secondary patency were kept. Primary unassisted patency refers to patency of the graft without any intervention. Primary assisted patency refers to patency of the graft with the help of angioplasties when stenosis occurs, whilst secondary patency refers to those cases where the graft is occluded and needs surgical intervention (redo bypass) to revascularise the limb.

Results
Our study period was over 22 months (from August 2007 to May 2009). During this period sixty infrainguinal vascular bypasses were done. These patients entered the study at different times; therefore not all of them had the same number of scans post-op. Those patients who were operated near the end of the study period, had only a few number of scans.

Post-operatively at 1 week all the grafts were patent. Out of the 60 patients, 56 made it to the first scan at one week post op and these were all patent.

At 6 weeks, 49 patients were scanned and 46 grafts were patent (94%). One of the other patients had successful redo vascular bypass surgery bringing the secondary patency rate to 96%.

At 3 months, 44 patients had their grafts scanned and 40 patients had patent grafts (90%). Another patient needed redo surgery and this brings the secondary patency rate up to 95%.

At 6 months 31 out of the 40 patients scanned had their grafts patent (77.5%). Another patient needed redo surgery and this brings the secondary patency rate up to 95%.

At 12 months 22 patients were scanned. At this point primary unassisted patency was 50%, i.e. only 11 patients had their graft patent. Primary assisted patency was much better at 77%, with another 6 patients having angioplasties. Secondary patency was slightly better at 82% (18 patients out of 22).

At 18 months only nine patients were scanned. Four of these grafts were patent – 44% primary unassisted patency, while another patient had an angioplasty, thus putting the primary assisted patency at 56%. Another patient had redo-surgery with the secondary patency rate thus being 67%.

The above information is shown in Table 1 and in the Kaplan-Meier curves (Figure 4) for the various patencies described above. The primary end-point is sonographically detected graft stenosis.

Discussion
As we can see from the figures in the table below, primary assisted patency and secondary patency were significantly better
than primary unassisted patency from the sixth month onwards. This indicates that the graft surveillance programme, which aims at treating significant stenoses or occlusions as soon as possible by sending them to angioplasty or surgery if necessary, is being efficient at detecting those patients who need further treatment. Were it not for the surveillance programme these patient might present at a later stage where treatment would be more complex, if at all possible. This is in keeping with several other studies which also mentioned the importance of graft surveillance by duplex ultrasound.8-10

Conclusion

This study shows that a graft surveillance programme makes a lot of sense in the setting of infrainguinal bypass surgery and we look forward to official recommendations by TASC on this matter.

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Historical Perspective

The nurse of the Mediterranean

Saviour Pisani

During the First World War Malta did not take an active part in the fighting. Britain was joined in an ‘entente’ a friendship agreement with France since 1904 and later with Russia in 1907. On the other hand Germany was allied to the Austrian-Hungarian Empire, hence when the Great War started in July 1914 there were France, Britain and Russia on one side and Germany and Austria-Hungary on the other. The British fleet “ruled the waves”, hence with France and Britain as allies, to be joined later by Italy, the Mediterranean was more or less an allied lake, with Malta in the centre.

During the nineteenth century the Ottoman Empire was falling apart, and one of the big problems that faced the foreign office of Britain in the nineteenth century was the Ottoman Empire known as the sick man of Europe. Russia was looking at it from the part of the chief inhibitor of its demise, while Britain was taking the role of a doctor. Russia is a vast country, stretching from the Baltic to the Pacific and from the Arctic to the Black Sea. Its biggest problem was that it could not use its ports throughout the whole year. Its arctic port, the Archangel, was blocked by ice; its Baltic ports had a similar problem in winter. Furthermore the Baltic Sea was dominated by the German navy in XXXII. The latter was secondary to that of Britain. Russia’s far eastern ports – Vladivostok – was also frozen and far too distant. The Black Sea ports were closed by the Ottoman Empire during hostilities. The Russian ships had to pass through the Dardanelles to reach the Mediterranean and if the Dardanelles were under a hostile power no merchant ship could pass – i.e. the Russian navy was bottled up in the Black Sea.

The British were always suspicious of the Russian intentions towards the Ottoman Empire, and the Crimean War of 1854 was fought by Britain, France and the Ottoman Empire against Russia to destroy its main base of Sevastapol and its fleet. By the treaty of San Stefano and the convention of Berlin blocked by Bismarck, the small Balkan states of Bulgaria, Serbia, Rumania and Montenegro appeared and these showed that they were very jealous of their independence and were far more efficient than the decadent Ottoman Empire to thwart Russian ambitions to enter the Mediterranean Sea. Still the Balkans was not so stable and in 1911-1912 the Balkan Wars erupted. In 1914 after the Archduke Ferdinand was assassinated in Sarajevo, Austria-Hungary declared war on Serbia and the First World War started. The Ottoman Empire had a friendly relationship with Germany, its military was trained by Prussian officers and when the battle cruisers – Goeben and Breslan – were caught in the Mediterranean in July 1914 and sailed on to Constantinople where they were given as a present to the Sultan, the Ottoman Empire found itself on the German side together, incidentally with Bulgaria which felt short-changed by Serbia.

The First World War started in high spirits by both sides. However, it soon degenerated in trench warfare. The British old professional army, known as the old contemptible was soon decimated and new regiments came from Britain and its empire to replace the heavy losses. The French also lost many soldiers when they moved on Alsace and Lorraine, lost in 1870. The Russians lost thousands and thousands of soldiers in the battle of Tannenberg. Their equipment was found most wanting and it was clear to all military chiefs that Russia could not sustain a war of attrition. The soldiers went into battle without rifles, they had to pick rifles from dead or wounded colleagues as they advanced along the front. The Russian army needed munitions, heavy guns, transport, rifles and all that a modern war entails. The French knew that if the Russian front were to collapse – as it did later in the war, the full fury of the German army would be let loose on them. The only way available to supply them was by sea. The Baltic Sea was dominated by the German fleet, while the Archangel was hardly practical. Hence Winston Churchill, who was lord of the Admiralty at that time, thought of supplying the Russian army from its Black Sea ports. To do this he had to open the Dardanelles to allied shipping, which really meant he had to knock the Ottoman empire out of the war. This he deemed a not so difficult task - after all the Ottoman Empire had been falling apart for more than a century, and it was kept in one piece thanks to the efforts of the British Government, the

Keywords
nurse, Mediterranean, first world war, Rupert Brooke

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Possibilities were very good. With Constantinople in British and French hands, the Russian army could be supplied. The Czar government secure from its internal enemies - the Bolshevists – could initiate a new Russian offensive in the East, thus relieving the Western Front from pressure.

Churchill thought that the Dardanelles could be forced by the navy alone. In conjunction with the French, the British sent the pre-dreadnaughts. This led to a major disaster, the Turkish waters were infested with mines and the approaches with heavy fortified forts. The allies lost a number of battleships through enemy activity and German submarines were reputed to be in the area. Hence it was thought that the Gallipoli Peninsula should be cleared of the hostile troops by landing troops on it – the Anzacs, Australinian and New Zeland troops who were in Egypt at that time. However, the element of surprise had been lost and when the troops finally landed they found the Turkish troops ready for them. No real progress was done and after a few months, in which thousands of Allied troops were either killed or wounded, they were evacuated from the Gallipoli beaches,

Malta was warned to get itself prepared to receive the wounded of the Gallipoli campaign. The Governor at that time was Lord Methuen who was a very good organiser. Plans were immediately started to turn Malta into a giant hospital. At that time there were four hospitals in Malta, the Central Hospital for civilians, the Blue Sisters’ hospital for merchant seamen, Bighi hospital for the navy and Mtarfa Hospital for the army. Their total capacity was about three hundred beds, if all the rooms and available space were utilized there would be five hundred beds – far short of what was necessary. The Holy Infirmary at Valletta was roped into service. Some new schools were turned into hospitals and barracks which had been vacated by the troops turned into hospitals. Originally Allied command in Egypt asked for 3000 beds. However, with mounting injuries it was soon found that that estimate was not nearly enough and more bed space was created. A hospital is totally useless without adequate staff, doctors, nurses, attendants, labourers, technicians, cooks, laundry people, etc., etc.

The soldiers invaded the Gallipoli Peninsula on the 25th April 1915. Many soldiers were wounded or killed. Up to the end of May 1915, 38,000 soldiers were either killed or wounded. These figures will make us understand the extent of the problem facing the authorities over here. The first wounded reached Malta on the 4th May 1915. They were carried on hospital ships, painted white with a big red cross painted on their sides. When the people realized that the wounded of Gallipoli were entering the bastions, the mood was very sombre. The harbour had the aspect of a sick ward in a general hospital, silence all around.

One thousand two hundred soldiers, wounded from the front were brought on that day. Barges went against the hospital ships and the injured soldiers were brought down very gently by the cranes on stretchers and from the barges onto the shore. From the quay they were taken to the Holy Infirmary at Valletta where they were examined by top British and Maltese doctors, from there they were sent to other centres according to their injuries. A Maltese doctor appointed by the Governor himself for such duties was Dr Robert Randon who was placed in charge of Fort Tigne, now turned into a hospital of about 1,000 beds.

The processes of wounded soldiers on stretchers drawn by mules and horses passed through Kingsway, now Republic street, in Valletta on its way to the Holy Infirmary. It was described as that of Good Friday, silence reigned and people on each side on the pavements welcomed the soldiers with cigarettes, sweets, flowers and chocolate. The wounded soldiers most of them very young showed their appreciation by waving to the people and from that day the close bond between Malta and Australia was born. Indeed a lot of these soldiers died in Malta and they were buried at Braxia Cemetery at Pietà near where the football club now stands.

May I be permitted here to read Rupert Brooke poem The Soldier written in that period of time.

If I should die, think only this of me
That there in a corner of a foreign field
That is forever England. There shall be
In that rich earth a richer dust concealed.
A dust whom England bore, shaped, made aware
Gave, once, her flowers to love, her ways to name,
A body of England’s, breathing English air,  
Washed by the XX, blast by suns of home.

Perhaps if we were to substitute Australia for England here, we can better understand the atmosphere, the sorrow and anguish that reigned in Malta that summer of 1915.

Up till the end of May, 4,000 wounded had arrived and they were being treated in 8 hospitals. By September, 10,000 wounded had arrived. By March 1916, there were 20,000 hospital beds, in all 80,000 soldiers were treated in Malta. A percentage of them found their grave in Malta. Military funerals were the order of the day, sometimes with eight or more dead soldiers buried on the same day. Since these funerals were having a depressing effect on the general population, it was decided to conduct them from outside the limits of Floriana, from Portes des Bombes to Braxia cemetery.

The Gardens of Argotti, the Mall, and the streets of Valletta were all full of wounded soldiers. Some of them had an amputated arm pushing at colleague in a wheelchair with amputated legs. Some had bandaged heads, others were blind. However, they were cheerful and made friends with the Maltese people who opened the doors of their homes and hearts to them. Ladies organised tea parties and concerts for them. They started to sponsor children by giving them cards found in cigarette boxes. In general the soldiers who survived the Gallipoli experience were quite happy for things could have been far worse for them. In all they were treated in 27 military hospitals, one of them being the newly built school of Sliema. Archbishop Caruana was asked to tell the parish priests not to
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Contraindications:
- Known hypersensitivity to the components of this product or to sulfonamides
- History of angioedema with aliskiren
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- Severe renal impairment (creatinine clearance < 30 mL/min)
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Warnings/Precautions:
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- Caution in patients with heart failure
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- Caution is advised when administering Rasilez HCT to patients with aortic and mitral valve stenosis.
- Caution with moderate P-gp inhibitors such as clarithromycin.
- Caution with patients with history of allergy and asthma.
- Not recommended in patients below 18 years of age.
- Excipients: Contains lactose and wheat starch.

Interactions:
- Monitoring when used concomitantly with furosemide, lithium, products affected by serum potassium disturbances (eg digitalis glycosides, antiarrhythmics, calcium supplements or calcium sparing medicinal products)
- Possible interaction with digoxin, irbesartan, St. John’s wort, and rifampicin.
- Meals with high fat content substantially reduce absorption.
- Alcohol.

Adverse reactions:
- Common: Diarrhoea
- For the aliskiren component, other reported adverse reactions include: Uncommon: Rash. Rare: Angioedema.
- Laboratory values: Decrease in haemoglobin and haematocrit, increase in serum potassium.

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ring the bells to let the patients rest. The Archbishop obliged and the bells stopped ringing.

Ghajn Tuffieha was turned into a giant camp for convalescent soldiers. In all there were 4,000 beds under tents. Three hundred civilian and military doctors were employed. Some top British surgeons came to Malta, like Balance and Garrod, and 1000 British nurses came from the UK.

Gradually things started to calm down. It was obvious that the Allies were making no headway in Gallipoli and they were pushed back. However, on the 25th December 1915 the British and the French landed in Salonika to help the Serbians. The First World War started from Serbia. In the Balkan wars of 1911 and 1912, Bulgaria was offered Macedonia but its share went to Greece and Serbia. Hence Serbia was attacked by Bulgaria, and the British and French went to help. This time the Maltese makeshift hospitals were filled with malaria and typhoid. It is interesting to note that the first cardiac operation was done in Malta on a soldier who had been shot by a Bulgarian sniper.

As the Gallipoli and Salonika campaigns subsided so did the Maltese hospitals empty, to fill again by the Spanish Influenza victims. Employment during the war and when the war finished there was massive unemployment in Malta. A lot of ships had been sunk, food was scarce and hard to get, there was massive inflation and the safety valve of emigration non-existent since Australia had problems of its own. With political aspirations on the increase, the unemployed workers looked at the political leaders like Sir Filippo Sciberras and the next scene was the Sette Gungio rites of 1919.

When the First World War was nearly over the so-called Spanish Flu appeared. The pandemic killed more people than the war itself, although one can attribute it to the war itself. When there is mass movement of troops and civilians with the most basic requisites of hygiene ignored and non-existent, one can expect epidemics. In WW1 Spain was neutral and the first reported cases came from Spain since the censorship of the media was free. It appeared in the US where young people were being called for service in Europe by Widrow Wilson, thousands died in their training camps. It infected the allied army in Northern France where a depot was located and then spread to the German army. In all there were three waves of this pandemic and it was characterized by fever, breathing problems, haemoptysis and cyanosis. Hence our hospitals started to fill again on the 4th October 1918. The Government issued regulations to prevent the spread of the disease – avoiding overcrowding and general cleanliness. Between the 1st September 1918 and 1st March 1919 there were 651 deaths. March was the high point of the third wave. The Influenza continued onto 1920. In February and March 656 cases were reported with a mortality of over 30%. The total mortality of the 1918 – 1919 pandemic in Malta was 3 per 1000 of the population.

On the 10th December 1917 His Excellency the Governor declared at the beginning of the session of the Council of Government. “I also desire to record my grateful recognition of the sympathetic hospitality which the people of Malta and Gozo have extend to the sick and wounded that have been brought during the war, of the support that they have given to the British Red Cross and the Order of St John of Jerusalem and the other charitable institutions that have been formed.” This was not the first time that Malta took the role of a Nurse in Wartime and it is said that Malta had added a bright chapter to human history and the severance to its hospitals ever be named; for their sacrifice has once more been enthroned, and unselfishness, garbed in nurses’ cape or surgeons’ uniform, proclaimed the triumph of love.
Abstract

After the establishment of freedom of the press in 1839, the Maltese medical community initiated the publication of a medical journal in their efforts to maintain professional standards through continuing medical education. The first initiatives unfortunately were often relatively short-lived due to a number of factors. These initiatives were often undertaken by individuals and were often dependant on paid subscription for their maintenance. Longer lasting publications required a change in management policies. The second half of the twentieth century saw the first long-lasting initiative being undertaken by the medical student association; this journal’s financial support being dependant on income from advertisements. Twenty years later, the Faculty of Medicine and Surgery initiated a professional journal. These two journals have since changed their name and editorial policies but are still extant in the current publications Murmur and the Malta Medical Journal.

The governments occupying the Maltese Islands had always been on their guard against any form of sedition that could ferment dissent against their governance. This policy required a strict control of locally published material of any form. The French occupation and the subsequent insurrection had however deeply instilled the concept of freedom, including freedom of speech. In the early decades of the 19th century, the Maltese political movement Comitato Generale Maltese under the leadership of George Mitrovich and Camillo Sciberras started pressuring the British Government for a more liberal governance constitution. This political pressure saw the setting up of the 1836 Austin-Lewis Commission that, among other things, was favourable to the introduction of freedom of the press provided that the public interest and loyalty to the British Crown was preserved. By 1838, even before the formal legal withdrawal of press censorship through Ordinance IV published 22nd March 1839, two newspapers - Lo Spettatore Imparziale and Il Portafoglio Maltese - initiated publication. The eventual publication of the ordinance saw a sudden proliferation of newspapers such as The Harlequin, and Il Mediterraneo - Gazzetta di Malta.

The withdrawal of press censorship was quickly availed of by the medical community in Malta. In the last quarter of 1838, before the formal withdrawal of press censorship, Dr. C.G. Schinas issued L’Ape Melitensis - Giornale di Medicina with the aim of compiling a journal that appealed to both new graduates and the more experienced professional. The journal served to review contemporary medical literature with material being written in the Italian language by the editor himself. L’Ape Melitensis ran for only four issues through September to December 1838, the whole volume amounting to 288 pages. Besides the reviews, the journal also include seven original articles that dealt with the 1837 cholera epidemic, Werlhoff’s purpura, smallpox vaccination, the pharmacology of Segala Cornuta, the use of calomel in intestinal disorders, animal magnetism, phrenology and a description of an improved urinary catheter designed by Dr. Giuseppe Stilon.

The initiative for establishing a medical journal was again taken up on the 1st January 1841 by Dr. C. G. Schinas together with the assistance of the doctors on the staff of the Civil, Ta’ Sawra and Santo Spirito Hospitals. This editorial board undertook the publication of a new journal entitled Il Filocano - Giornale Medico Scientifico e di Educazione circulated to subscribers against payment [annual subscription: 2½]. Initially published monthly, it soon increased its publication frequency to fortnightly. This journal had a wider remit than the previous medical publication, and served as a medium for local and foreign practitioners to publish their views and observations including case descriptions. Its articles included discussions on smallpox and its prophylaxis, and the management of conditions such as tetanus, puerperal sepsis, and mental disease. Il Filocano was first issued in January 1841 and was eventually published fortnightly. It ceased publication in December 1842 after
Help Protect Your Patients From Osteoporotic Fractures

NEW With 5,600 IU of Vitamin D!

FOSAVANCE™ (alendronate/colecalciferol)

The Only Osteoporosis Therapy That Provides

- Demonstrated Fracture Prevention at the Hip and Spine Plus 5,600 IU of Vitamin D
- In a Single, Once-Weekly Tablet

FOSAVANCE™ is indicated for treatment of postmenopausal osteoporosis in patients who are not receiving vitamin D supplementation and are at risk of vitamin D insufficiency. FOSAVANCE reduces the risk of vertebral and hip fractures.1

FOSAMAX™ and FOSAVANCE are contraindicated in patients with esophageal abnormalities which delay esophageal emptying (eg, stricture or achalasia) and in patients unable to stand or sit upright for at least 30 minutes. FOSAMAX and FOSAVANCE are contraindicated in patients with hypocalcemia (see WARNINGS AND PRECAUTIONS) and in patients with hypersensitivity to any component of these products. Hypersensitivity reactions including urticaria and angioedema have been reported. FOSAMAX and FOSAVANCE, like other bisphosphonates, may cause local irritation of the upper gastrointestinal mucosa.1

In postmarketing experience, severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates that are approved for the prevention and treatment of osteoporosis. The time to onset of symptoms varied from one day to several months after starting the drug. Discontinue use if severe symptoms develop. Most patients had relief of symptoms after stopping treatment.1

Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection, often with delayed healing, has been reported in patients taking bisphosphonates.1

NOF = National Osteoporosis Foundation.

References

Before prescribing, please read the full Prescribing Information on the adjacent page.

FOSAVANCE™ (alendronate/colecalciferol) and FOSAMAX™ (alendronate) are trademarks of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc. Whitehouse Station, NJ, U.S.A.

FOSAVANCE 5600 retail price (Pack of 4) € 37,55

Updated NOF guidelines recommend 800–1,000 IU of vitamin D per day for adults ≥50 years2
Mineral water) at least

FOSAVANCE must be taken with water only (not with food,

Patients should not be due to food and other that the food which they should not be following:

The following instructions should be followed exactly in order to minimize

FOSAVANCE is only intended for use in postmenopausal women and

Caution:

Vitamin D3 is produced in the skin by conversion of 7-dehydrocholesterol to

Vitamin D3 is rapidly metabolized by hydroxylation in the liver to

Vitamin D3 is bound to vitamin D-binding protein.

The principal action of 1,25 dihydroxyvitamin D3 is to increase intestinal

Conversion to the active calcium-mobilizing hormone

Vitamin D3 in FOSAVANCE is similar to 5600 IU vitamin D3 administered

acetildenafil (intravaginal, transdermal, or oral) while taking alendronate. No adverse

Results in secondary hyperparathyroidism, hypophosphataemia, proximal

Individual responses to FOSAVANCE may vary (see section 4.8).

Rare: oesophageal stricture*, oropharyngeal ulceration*, upper

These are usually small and asymptomatic. However, from time to time rare symptomatic oesophageal perforation, which has been reported by one patient 3 months after

The incidence of symptoms varied from one day to several months after starting

Most patients had relief of symptoms after stopping treatment. A

Bone, joint, and/or muscle pain has been reported in patients taking alendronate in clinical trials. These symptoms have been reported in patients taking

Rare: oesophageal stricture*, oropharyngeal ulceration*. The above reactions, such as upset stomach, heartburn, oesophagitis, gastritis, or

Causes of osteoporosis other than oestrogen deficiency and ageing

Osteoporosis should be considered in any patient with multiple fractures of the proximal femur (known as pathological fractures) or fracture of the spine (in patients who have sustained a vertebral fracture).

The incidence of symptoms was dose related. Higher doses (5 mg and 10 mg) resulted in an increased incidence of mild to moderate upper gastrointestinal symptoms. These symptoms included indigestion, heartburn, flatulence, abdominal pain, and nausea. The proportion of patients (least squares estimates) who reported indigestion, heartburn, flatulence, and abdominal pain was 41%, 24%, and 24%, respectively, at 5 mg and 39%, 23%, and 21%, respectively, at 10 mg.

The mean serum concentration of calcium, total calcium and phosphate was measured in 102 patients with hypercalcaemia, including four with hypercalcemic crisis. The mean serum calcium concentration during hypercalcemic crisis was 30.4 ± 1.2 mg/dL and the mean serum phosphate concentration was 5.5 ± 0.9 mg/dL.

Individuals who have a reduced efficiency in converting 7-dehydrocholesterol to vitamin D3 (hypocholesterolaemia, hypothyroidism, chronic renal failure, Crohn’s disease, or malabsorption syndromes) may be at risk of vitamin D deficiency. In such individuals, 1250 IU/day together with other sources of vitamin D may be insufficient to meet their requirements.

The effect of the lower class of FOSAVANCE tablets

The effect of the lower class of FOSAVANCE tablets

In studies in which calcium supplementation had been interrupted, the incidence of oesophageal irritation and erosive damage increased and the incidence of symptoms and erosions decreased. In clinical trials, calcium supplementation should always be continued when taking alendronate.

Individuals who have a reduced efficiency in converting 7-dehydrocholesterol to vitamin D3 (hypocholesterolaemia, hypothyroidism, chronic renal failure, Crohn’s disease, or malabsorption syndromes) may be at risk of vitamin D deficiency. In such individuals, 1250 IU/day together with other sources of vitamin D may be insufficient to meet their requirements.

No specific information is available on the treatment of overdose with

Since NSAID use is associated with gastrointestinal irritation, caution

The alendronate component in the FOSAVANCE (70 mg/5600 IU)

The mean alendronate concentrations in patients with normal renal impairment who had GFR of 60 mL/min - 90 mL/min, (6.6 µmol/L [0.3 mg/dL]) and

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of this journal was to primarily serve as a newsletter to the company and promote its products. It also carried occasional general articles related to specific pharmaceuticals and items of medical history. A similar commercial-biased journal that primarily serves as a newsletter and service promotion is the publication the St. Philip's Hospital Newsletter first published in August 1996 [six issues: 1996-1997] and the currently running Dear doctor! – The Healthcare newsletter from Saint James Hospital first published in February 1999,

In the latter part of the twentieth century, a move was made to sponsor medical journals through advertisements from commercial businesses, rather than rely solely on reader support. The first initiative of this type was taken by the Malta Branch of the British Medical Students Association [after 1956, the Malta Medical Students Association] who in 1948 published the medical student journal Chestpiece with Charles Xuereb as its first editor. The journal served to publish contributions from both medical students and qualified practitioners on various aspects of medical practice, generally of a review nature. The first volume 1948-56 saw the publication of 11 issues, often carrying articles written by university or hospital staff. A supplement to the first volume carried an address by the Minister of Health Dr. A. Schembri Adami who introduced the concept of the National Health Insurance scheme; while in 1949 the journal carried a reprint of Pope Pius XII’s pronouncement on artificial insemination and in 1950 carried an article on BCG inoculation by Dr. Andreas Widemann. The publication of the second volume was marked by a significant five year lapse in publication during 1959-63. The contribution in this volume similarly had a strong bias for medical staff contributions. The third volume starting in 1971, in a new format, had a lapse in publication during 1973-74 and 1977-78. The last issue of Chestpiece was published in 1979. The first issue of the third volume comments that the editors [J.V. Psaila and D. Vella Briffa] wished “further promoting contributions from students. This issue has had to rely, to some extent, on articles from our competent teachers, but we still feel that the bulk of the contents should come from the student.” This policy seems to have been maintained in the subsequent five issues, with the last issue carrying four articles authored by medical students and only one by a member of the medical faculty. The MMSA again embarked with a revived journal named Mediscope published during the period 1983-1991 with a total of fourteen issues. The first editor was Mark Bugia who continued in this role after his graduation. This journal was replaced in 1992 by the medical student journal Murmur which serves primarily as a medical student newsletter. The latter journal is still extant.

The publication of a more scientific-based medical publication was undertaken in 1966 by the consultant staff at St. Luke’s Hospital, together with the Faculties of Medicine & Surgery and Dentistry. Entitled the St. Luke’s Hospital Gazette, this biannual journal set out to publish scientific articles reflecting the research activities and interests of the Maltese medical profession. It also received contributions from foreign specialists, including an article on heart transplantation by Prof.
Christian Barnard. There was also a strong bias in contributions related to the humanities as these pertain to medicine. Articles related to the medical humanities, including history, literature, ethics and law, accounted for 17.6% of the contributions. The first appointed editor was Dr. Emmanuel Agius. He was replaced by Dr. Roger Ellul-Micallef in 1975. The publication of this journal was interrupted as a result of the Trade Unionist conflict of 1977. The 11 published volumes had included a total of 296 articles (Figure 1). The last volume published in 1976 is included in the PubMed database.

An attempt was made by the Faculty to re-establish publication of a medical journal in 1982 entitled *Journal of the Malta Medical School*, but these efforts were not successful. A specialist annual journal was published in this interim period by the Association of Anaesthesiologists in Malta - *Acta Anaesthesiological Melitensis* with the aim of serving as a forum for the publication of research and review articles. The first Editorial Board was made up of Drs. N. Boskovski, N. Azzopardi, D. Spiteri, AKMA Zaman and J. Sedlecek. The first issue was published in November 1983. The journal unfortunately ceased publication after six issues in 1989. Besides the anaesthetists and other medical practitioners working in Malta, the journal attracted contributions from other countries such as Denmark, Belgium, Egypt, Czechoslovakia, and Poland. Another professional medical publication issued by a medical association representing a medical speciality is the journal *It-Tabib tal-Familja – Journal of the Malta College of Family Doctors* first published by the Malta College of Family Doctors in 1991. This journal carries a broad selection of contributions generally of a review nature. The journal is still extant and is distributed to all Malta-registered medical practitioners.

The Faculty of Medicine and Surgery did eventually re-initiate the publication of a refereed medical journal in 1989 under the title *Maltese Medical Journal*, circulated to all the Malta-registered medical and dental practitioners. The first series initiated publication under the editorship of Dr. Joseph L. Pace and was published biannually, except in the last two volumes that were published annually. The first series saw the publication of 12 annual volumes with 23 issues. The articles ranged from research articles, review articles, historical articles, and case presentations (Figure 2). It also carried local news items occurring in the medical community.

The journal lapsed publication in 2001, but the Faculty soon re-established a new editorial board under the chairmanship of Prof. J. Cacciottolo and Prof. J. Vassallo as editor. The new board revised the editorial policies and format of the journal now under the title *Malta Medical Journal*. The first issue of the new series was published in November 2002. The frequency of publication was gradually increased to quarterly issues, with supplements that carry the abstracts of the Malta Medical School Conference in 2003, 2006 and 2009. The journal continues to publish articles ranging from research articles, review articles, historical articles, and case presentations (Figure 2). All submitted contributions are peer-reviewed. This journal established itself on the Internet in 2003. This has helped the journal to significantly widen its circulation, so that during 2008...
the web-version was accessed by a total of 72781 visitors with 230471 page hits annually. Of the visitors, 32298 visited the site only once while 5376 visited more than once. Visitors were the most active from the United States of America and Canada (59804 visitors), the European Union (8708 visitors including 3866 from Malta), other European countries (654 visitors), Australasia (2096 visitors), African continent (263 visitors), with the remainder 1256 visitors were from various countries in the Middle East and South American continent. This increased circulation has helped the journal to achieve recognition and be included in a number of web-based professional databases including Scopus, Index Academicus, and the Directory of Open Access Journals.

Another extant publication is The Synapse – The Medical Professionals’ Network first launched by Dr. Wilfred Galea in January 2001. This paper-based magazine supplements the web-based service offered by the Medical Professionals’ Network on the Internet launched in 1996. The paper-based publication carries short review medical and non-medical articles in an attempt to stimulate continuing professional development. It is distributed free of charge to all Malta-registered doctors, dentists and pharmacists.20

The Maltese professional have always strived to promote continuing professional education with efforts to keep updated through reference to foreign journals. The establishment of a regularly published journal further supported the CPE efforts while encouraging the local professionals to adopt a scientific outlook to their practice. These endeavours by the medical profession have been emulated by other paramedical professionals including the pharmacists and midwives who have also published dedicated professional journals.

References
NEW INDICATION

Now indicated for patients estimated to be at high risk of a first major CV event in conjunction with correction of other risk factors*

Based on data from a post hoc analysis of high risk patients (SCORE ≥ 5% or Framingham > 20%) from the JUPITER study*

WITH CRESTOR† if SHE’S AT HIGH RISK...

YOU CAN NOW HELP PREVENT HER FIRST MAJOR CV EVENT

IN CONJUNCTION WITH CORRECTION OF HER OTHER RISK FACTORS*

† NOTE: JUPITER used CRESTOR 20mg. The recommended start dose for hypercholesterolaemia is 5 or 10mg (refer to SPC)

* modifiable risk factors include smoking cessation, exercise, weight loss and diet

References:
**Release sustained strength against COPD with 24-hour Onbrez® Breezhaler®**

**Onbrez® Breezhaler®**  The only Ultra - LABA — offers patients:

- Superior improvements in FEV₁ vs other bronchodilators
- Clinically meaningful improvements in breathlessness
- Improvements in quality of life
- A good overall safety and tolerability profile

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Onbrez Breezhaler® (indacaterol) inhalation powder, hard capsules

**PRESENTATION:** Onbrez Breezhaler® 150mcg and 300mcg inhalation powder hard capsules containing indacaterol maleate, and separate Onbrez Breezhaler inhaler.

**INDICATIONS:** For maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD). Dose: Adjust dose in patients with severe COPD. Daily dose: 150mcg once daily.

**CONTRAINDICATIONS:** Hypersensitivity to the active substance, to any of the other excipients. Warnings and Precautions: Arterial hypotension is a medical emergency. Cardiovascular effects: Indacaterol may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms. In such cases, the dose should be reduced. Hyperkalaemia: Increases in plasma glucose. Upon initiation of treatment with Onbrez Breezhaler plasma glucose should be monitored more closely in diabetic patients. Pregnancy and Lactation: No data available from the use of indacaterol in pregnant women. Onbrez Breezhaler should only be used during pregnancy if the expected benefits outweigh the potential risks. Not known whether indacaterol is excreted in human milk. A decision must be made whether to discontinue breast-feeding or discontinue treatment with Onbrez Breezhaler therapy, taking into account the benefits of breast-feeding for the child and the benefit of therapy for the woman. INTERACTIONS: Concomitant administration of other sympathomimetic agents may potentiate the untoward effects of Onbrez Breezhaler. Onbrez Breezhaler should not be used in combination with other bronchodilators. **LEGAL CATEGORY:** POM (Prescription Only Medicine).
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Clopidogrel
75mg film-coated tablets
Antithrombotic Agent

For further information please refer to the Full Summary of Product Characteristics or to our website: www.actavis.com.mt
DIAMICRON® MR 60 mg
modified release tablets
Gliclazide

1 to 2 tablets
at breakfast

Evidence-based medicine including the ADVANCE study, the largest morbidity-mortality trial in diabetes

First scored modified release formulation allowing progressive titration

Efficient glycemic control with well proven tolerability and weight neutrality

Protective on the β-cell and the cardiovascular system

Composition: Each modified-release tablet contains 60 mg of gliclazide. Indication: Type 2 diabetes. Dosage: One half to 2 tablets per day, ie, 30 to 120 mg as a single daily intake at breakfast time, including in elderly patients and those with mild to moderate renal failure. One DIAMICRON 60 mg modified release tablet is equivalent to two DIAMICRON 30 mg modified release tablets. The breakability of the DIAMICRON 60 mg modified release tablet enables flexibility of dosing to be achieved. Properties: DIAMICRON MR 60 mg is a sulfonylurea lowering blood glucose levels by stimulating insulin secretion thereby restoring the first peak of insulin secretion and increasing the second phase of insulin secretion in response to a meal or intake of glucose. Independent hemovascular properties. No active circulating metabolite. Contraindications: Hypersensitivity to sulfonylureas or sulfonamides, type 1 diabetes, diabetic precoma and coma, diabetic ketoacidosis, severe renal or hepatic insufficiency, treatment with miconazole, breast-feeding. Interactions: Increased risk of hypoglycemia with miconazole, phenylbutazone, alcohol, other antidiabetics, β-blockers, fluconazole, ACE inhibitors, H2-receptor antagonists, MAOIs, sulfonamides, NSAIDs. Risk of hyperglycemia with danazol, chlorpromazine, glucocorticoids, β2 agonists, ritaline, salbutamol, terbutaline, anticoagulants. Adverse effects: Hypoglycemia, gastrointestinal disturbance; more rarely: skin and subcutaneous reactions, hematological disorders, hepato-biliary disorders, visual disorders. Overdosage: Possible severe hypoglycemia requiring urgent NG glucose and monitoring. Please refer to the complete summary of product characteristics for your country as variations may exist. LES LABORATOIRES SERVIER France, Correspondent: SERVIER INTERNATIONAL 35, rue de Verdun, 92284 Suresnes Cedex, France. www.servier.com
found that patients who increased their weight by more than 2 kg had a significantly better survival, independently of their initial body mass index.\textsuperscript{28} Because of the morbidity and mortality associated with underweight COPD patients, it is therefore being recommended that interventions should be extended to prevention and early treatment of weight loss, before patients become extremely wasted, and therefore put more emphasis on dietary change than on medically prescribed supplementation.\textsuperscript{25,27}

The psychological input is also required as patients with chronic respiratory diseases have an increased risk for anxiety, depression, and other mental health disorders\textsuperscript{26-27} leading to frustration with poor health and an inability to participate in activities which can present as irritability, and a hostile attitude toward others. In the later stages of respiratory disease, progressive feelings of hopelessness and inability to cope often occur. When psychologic support is provided within the rehabilitation setting, one will be able to help facilitate the adjustment process by encouraging adaptive thoughts and behaviours as well as helping patients to reduce any negative emotions present.

As is documented in a review of randomized studies, Griffiths and colleagues reported reduced symptoms of anxiety and depression following a 6-week pulmonary rehabilitation program, with symptoms of depression remaining significantly reduced at the 12-month follow-up.\textsuperscript{28} Also, Emery and colleagues\textsuperscript{29} found reduced anxiety and improved cognitive function following a 10-week pulmonary rehabilitation intervention.

**Recommendations and conclusion**

With a constant increase in COPD patients, and this disease ranking 4\textsuperscript{6} for mortality and morbidity rates, more research in this field is required to further look into the above discussed issues in order to help the local development of the best pulmonary rehabilitation service for the treatment of respiratory patients. Coordination of services is very important, especially during episodes of exacerbation, which are characterized with high morbidity and a marked increase in use of health care resources.

**References**