Journal Update

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MMJC
Malta Medical Journal Club

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Letter from the Editors

Welcome to the third issue of Journal Update! As we continue to evolve this publication we are adding a more diversified selection of article styles. In addition to another interesting "clinical pearls" we have also added a "Case based teaching" section which we hope you might find interesting and useful.

This issue is based on contributions from medical students and medical doctors and we would like to thank everyone contributions and help us in our mission to spread new and relevant medical knowledge. Special thanks also goes to Prof. Stephen Montfort for his encouraging words and help.

As some of you might be aware Alexander Moses Clayman a hard working MD4 student has been organising the Grand Rounds in Mater Dei. They are relatively new but after attending them both of us were very impressed by the quality and educational value of these sessions. Hence, we cannot recommend them enough and encourage you to go and see for yourself. They are planned on the 1st and 3rd Thursday of each month, however we recommend that one follows the Facebook page for precise updates.

Grand Rounds Mater Dei Facebook page: goo.gl/IVSE9p

If you wish to contribute to the next issue of Journal update please contact us on our email found below, one can also find a link to a set of guidelines to help you write a contribution.

Everyone is free to submit articles as long as it is relatively new and clinically relevant information, we are also accepting contributions for clinical pearls and a potential new segment in Journal Update related to local studies, so if you want your audit/study/case presentation to get some exposure contact us!

The Editors

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Foreword

It was with great pleasure and pride that I read the first issues of 'Journal Update'. This is indeed an admirable and much awaited initiative by some members of the student body to highlight peer reviewed scientific papers which they felt were important enough for them to analyse and report to their colleagues and teachers alike.

However what really pleased me was the fact that a good number of our medical students have realised that gone are the days where one opened a text-book and digested facts which might not be entirely agreed upon by various medical bodies and which might not possibly be up-to-date some time after the latest edition of the said book. The teaching they are receiving and the differing views they might have heard from the medics around them seems to have rightly instilled the natural curiosity in the intelligent and inquisitive minds of our medical students to seek recent medical research to check what novel advances are going on around us.

Such actions will lead to our students to learn how to judge medical scientific studies for protocol design, methodology, results, limitations and conclusions of the said study. They will also lead to compare other similar studies and see whether the original results were repeatable and if not whether the reasons brought forward for such differences were robust or not. This experience in such critical reading will not only increase scientific knowledge which can be used in under and postgraduate competitive exams but should also hopefully 'ignite the fire' of wanting to start carrying out research projects themselves.

In this day and age research is encouraged to start at an early stage in a doctor's career and it might become so exciting to some, that these doctors might decide to seek an academic rather than a clinical career, and in some cases, a job with a mix of both. Our medical school strongly supports such views and one can see that we are already reaping results with a record of more than 60 young academics reading for a PhD degree and more than 900 abstracts submitted for the coming Malta Medical school conference being held in December.

Thus I cannot encourage enough the editors of this journal club publication to continue in their endeavour and truly hope that they will have ever increasing numbers of medical students submitting interesting research papers which they would have analysed critically.

Prof. Stephen Montfort

Clinical Pearls in Anaesthesia: Peripheral intravenous cannulation

Hanging around the neck of the busy on-call junior doctor one finds not only a stethoscope and a pager, but also their trusty tourniquet neatly clipped away and ready for use in the search for veins.

Amongst the first clinical procedures carried out by foundation doctors is peripheral intravenous cannulation, and most doctors, unless entering certain specialities such as anaesthesia, will probably insert more cannulas during their two years of housemanship than throughout the rest of their careers.

However despite, or perhaps because, it is such a commonly performed procedure the technique of cannula insertion is not often taught in a structured way. In patients who have difficult veins this may lead to unnecessary struggling by the doctor and suffering for the patient.

"Tabib ghandek venflon!"

While nothing can substitute the experience of inserting cannulas in different and difficult situations, the following practical tips and techniques are based on my experience of inserting cannulas as a foundation doctor and junior trainee in anaesthesia and intensive care.

Which cannula should I choose?
Once you get called to insert a cannula you should first find out why you have been asked to insert it. Maintenance fluids and most intravenous medications may be infused through any size of cannula, with larger cannulas only being required for rapid fluid administration. Blood may generally be transfused though 18G cannulas, and in some cases 20G may also be acceptable.

Gauge	Color	Maximal flow rate ml/min
24G	Yellow	13
22G	Blue	31
20G	Pink	67
18G	Green	103
17G	White	125
16G	Grey	236
14G	Orange	270

Table 1. Cannula size, color and flow rate

How do I prepare for inserting a cannula?
Prepare all the items necessary in a clean tray with a sharps container, these include:
- Cannula
- Sterile swabs
- Saline flush prepared in 5 or 10ml syringe
- Chlorhexidine in alcohol wipes
- Cannula fixator
- Tourniquet

The next step is preparing the patient. Explain why and what you will doing and remember that pain thresholds vary considerably and as anyone who has had a cannula inserted can tell you "tingiza zghira" or a "sharp scratch" doesn't quite do it justice!

Next, find a vein. Place the tourniquet proximally on the limb and begin your search, this is not always straightforward, and the following tips might help:

- Start distally and move proximally, this will ensure that any previous cannula sites or failed attempts at insertion do not result in infused medications "leaking" out of the vein.
- Letting the limb dangle below the level of the bed allows gravity to help but

ensure that your patient will remain safely on the bed.

- Fist clenching and unclenching helps by increasing venous return and engorging the veins.
- Briskly tapping on veins causes local irritation resulting in release of local vasodilators causing veins to visibly enlarge.
- Warming the hands by immersing in warm water or placing warm wet swabs on the arm encourages venodilatation.
- Choose your vein on feel not appearance. Veins should feel bouncy and spongy. A vein that feels like a rope under the skin is likely to be thrombosed despite being easily visible.
- Remember that the entire length of the plastic cannula should be inserted, this means that straight long veins are best.
- Let intravenous drug users guide you to their best veins.
- Lower limb veins are normally avoided as they are at higher risk of developing thrombophlebitis, however certain situations may require you to use the long saphenous vein or veins on the feet.
- Peripheral oedema may sometimes be severe enough to obscure any veins, in this case gradually compress the oedema away and the veins should come into view.

How do I insert the cannula?

Once you've found a vein, cleaned the overlying skin and let the cleaning solution dry it is time to insert the cannula. Use your dominant hand to hold the cannula and the other hand to tether the vein by putting traction on the skin distal to the vein. At an angle of about 5-15 degrees and the bevel facing up sharply slide the cannula through the skin into the vein until the first "flashback" of blood is seen. Once this is seen advance the cannula 2-3mm to ensure that the catheter itself is also in the vein and not just the needle. Keeping the needle still, advance the cannula. Apply pressure on the cannula tip as the needle is removed fully to prevent backflow of blood, and cap the cannula. Flush with 0.9% to confirm that the cannula is properly placed, and fix well.

I still haven't managed!

Cannulation is generally a straightforward task, however it may sometimes challenge even the most experienced doctor. Do not continue to struggle in vain as the more you struggle the less likely you are to succeed. Explain to the patient that through no fault of his or your own you've been unable to insert the cannula, and ask someone else to attempt it.

Goodluck !

Carl Tua
Trainee in Anaesthesia and Intensive Care

Impact of the Preoperative Controlling Nutritional Status (CONUT) Score on the Survival after Curative Surgery for Colorectal Cancer

Aim of Paper

- To assess whether the CONUT score could be a convenient way of predicting survival rates in patients suffering from Colorectal Cancer.
- To compare the results obtained from the CONUT score to the one obtained by using the Prognostic Nutritional Index (PNI)

Summary of Paper

- This is a retrospective study analysing a sample size of 204 patients who had been through curative surgery for stage II/III Colorectal cancer between the April 2004 and December 2009. These patients underwent surgery at the Department of Surgical Oncology, Osaka City University in Japan.
- Both the CONUT Score and PNI were found to have a significant relationship with age and tumour location. PNI was also found to correlate with adjuvant chemotherapy.
- This study concluded that the CONUT score is a strong predictor of survival in patients with colorectal cancer. Furthermore, it seems that the CONUT score is better than the PNI in predicting survival in such patients.

Details

- The people in this study were divided in two groups -low-risk and high-risk groups- according to the CONUT score and PNI. The cut-off value for the CONUT score for that of 3 whilst that of PNI was 40.
- The CONUT score is calculated by using the serum albumin concentration, total peripheral lymphocyte counts and total cholesterol concentration. The PNI is calculated from the total peripheral lymphocyte count and the serum albumin concentration.
- The preoperative blood samples were obtained 2 weeks before the operation.

Relevance to undergraduates

Colorectal cancer/ Survival after colorectal cancer surgery

Where to find it

PLoS One
July 6 2015; 10(7)

doi: 10.1371/journal.pone.0132488.

Eliezer Zahra MD5

Late Onset Neonatal Sepsis: Recent Developments

Aim of Paper

To conduct a systematic review of causes, prognosis and outcomes of late-onset neonatal sepsis (LOS) over the last decade

Summary

- This paper highlights major developments in LOS by review of published data and compilation of epidemiological and management trends associated with various clinical outcomes.
- Emphasis is placed on the frequent variations in pathogenic agents implicated in LOS, with the authors stressing the importance of constant guideline revision.

Details

- An accurate diagnostic tool for use in early LOS is not yet e available, while successful treatment of subsequently recognised LOS does not invariably protect against long-term neurological sequelae. Prevention of LOS should therefore be emphasized as a core strategy; a 47.3% decrease in bloodstream infections was observed in 19 UK PICUs following the Matching Michigan preventive strategy.
- This initiative involved;

> Appropriate hand-hygiene and personal barrier use
> 2% chlorhexidine gluconate in 70% isopropyl alcohol antisepsis wash
> Sterile precautions and full barrier drapes
> Avoiding the femoral route
> Central-venous catheter site review daily and assessment of aseptic technique

- Interspecialty collaboration inclusive of microbiological and immunological input in this regard has led to numerous novel approaches, ranging from antiseptic skin care and immune replacement therapy to the use of probiotics, synergistic bovine lactoferrin and early enteral trophic feeds with breast milk. The latter has shown promising effects thus far, although all require further investigation.
- Prophylactic antibiotics have shown promise in the context of antibiotic stewardships programs (ASPs), improving microbiological outcomes by 75%, with recommendation made for strict adherence to and frequent periodic revision of ASPs as a control measure in LOS

Relevance to undergraduates

Neonatology, paediatrics, sepsis, antibiotics, breast milk

Where to find it

Arch Dis Child Fetal Neonatal Ed 2015;100: F257-F623

doi: 10.1136/archdischild-2014-306213

Jamie Alexander Grech MD5

Study on Diastolic Dysfunction in Newly Diagnosed Type 2 Diabetes Mellitus and its Correlation with Glycosylated Haemoglobin (HbA1C)

Aim of paper

To study the incidence of left ventricular diastolic dysfunction (LVDD) in normotensive patients with newly diagnosed type 2 DM by using 2D echocardiography and finding out its correlation with HbA1C.

Summary

- This is a cross-sectional study conducted over a period of one year at the SVBP Hospital LLRM Medical College, Meerut, U.P. India
- The sample size comprised a total of 100 cases of newly diagnosed (within 1 month) type 2 DM between the age of 30 and 60 years
- The study concludes that higher HbA1C levels strongly correlate to the presence of LVDD. Age at the time of diagnosis of type 2 DM is however predicted to be the most important risk factor for LVDD in newly diagnosed patients

Details

- Chosen candidates had no clinical symptoms of cardiovascular involvement and blood pressures less than 130/80mmHg with normal ECG.
- The diagnosis of diabetes was made on the basis of clinical evaluation, biochemical and ancillary investigations which included: fasting and post prandial plasma glucose and HbA1C according to recent American Diabetic Association (ADA) criteria.
- HbA1C was estimated by Boronate affinity chromatography. Other relevant investigations included renal function tests, fasting lipid profile, ECG, urine and microscopy study, fundoscopy and chest radiography.
- Diastolic dysfunction was evaluated by pulsed Doppler echo according to the American Society of Echocardiography. Left overall ejection fraction was calculated by modified Simpson's method and left ventricular ejection fraction over or equal to 50% was considered as normal.
- All echo measurements were averaged over 3 consecutive cardiac cycles.

Relevance to undergraduates

Endocrinology/Cardiology

LVDD represents the first stage of diabetic cardiomyopathy preceding any changes in systolic function, reinforcing the importance of early evaluation of ventricular function in individuals with diabetes.

Where to find it

Journal of Clinical and Diagnostic Research 2015 Aug 1.

DOI: 10.7860/JCDR/2015/13348.6376

Diandra Mifsud MD4

Insulin pump therapy, multiple daily injections, and cardiovascular mortality in 18168 people with type 1 diabetes: observational study

Aim of Paper

To compare the cardiovascular mortality associated with long-term use of continuous subcutaneous insulin infusions versus multiple daily injections in type 1 diabetes patients.

Summary

- This is an observational cohort study with a sample size of 18,168 type 1 diabetes patients, entered in the Swedish National Diabetes Register. 2,441 patients were under insulin pump therapy and 15,727 were treated with multiple daily injections.
- Continuous pump therapy compared to multiple daily injections presented a significant reduction in fatal coronary heart disease (adjusted hazard ratio for pump therapy of 0.55, 95% confidence interval), fatal cardiovascular disease (0.58, coronary heart disease or stroke) and all cause mortality (0.73).

Details

- Type 1 diabetes was epidemiologically defined as all patients who received insulin treatment only (for diabetes mellitus) and were aged under 30 at onset.
- Baseline appointments commenced between 2005-2007 and the study was finalised in 2012, with an average follow-up period of 6.8 years.
- Complementary analyses revealed that the updated mean HbA1c and the difference seen in HbA1c readings throughout the study did not vary significantly between the two groups whereas much fewer hypoglycaemic incidents were recorded in pump therapy patients, which can partially explain the reduction in cardiovascular risk.

Relevance to undergraduates

Endocrinology, type 1 diabetes

Where to find it

BMJ
June 2015

DOI: 10.1136/bmj.h3234

Darren W. Rodgers MD4

Stroke following percutaneous coronary intervention: type-specific incidence, outcomes and determinants seen by the British Cardiovascular Intervention Society 2007-12

Aim of paper

To investigate changes in stroke complications over time as a result of percutaneous coronary intervention (PCI) and their effect on mortality and major adverse cardiac events (MACE).

Summary

- Population based case-cohort study involving 426,046 patients who underwent PCI in the UK between January 2007 and December 2012.
- Incidence of ischaemic stroke increased over the past years, whereas haemorrhagic stroke decreased. Stroke has a high 30-day mortality and in-hospital MACE rate.

Details

- 113 parameters (clinical variables, procedural parameters and outcomes) were analyzed.
- T-tests and one-way analyses of variables were used to compare means. Proportions were compared using Fisher's method and Chi Squared tests.
- The risk of stroke was predicted by simple logistic regressions.
- The incidence of ischaemic stroke was three-fold greater than that of haemorrhagic stroke.
- Ischaemic stroke increases 30-day mortality post-PCI 5-fold, while haemorrhagic stroke 14-fold. 60% remained with residual disability.
- The chance of stroke was twice as likely in patients undergoing PCI for ACS compared to elective PCI.
- Reasons for the increase in stroke complications rate included increasing age of patients, increased prevalence of valvular heart disease, increasing incidence of prior stroke, changing ACS indications for PCI and increase use of circulatory support devices.
- Some independent predictors of haemorrhagic stroke have increased e.g. warfarin use, valvular heart disease, STEMI PCI and age of patients while others have decreased e.g. thrombolysis. This could reflect the decreased rate of this complication.

Relevance to undergraduates

Cardiology/ Complications of PCI

Where to find it

European Heart Journal
July 2015; 36, 1618-1628

DOI:10.1093/eurheartj/ehv113

Rachel Xuereb MD4

Impact of Quetiapine Treatment on Duration of Hypoactive Delirium in Critically Ill Adults: A Retrospective Analysis.

Aim of Paper

This paper sought to determine whether the administration of low dose Quetiapine in critically ill patients reduces the duration of Delirium in this group when compared to the administration of no pharmacological agent.

Summary

This was a retrospective cohort study of 113 patients.

The Paper concluded that treatment of hypoactive delirium with the atypical antipsychotic Quetiapine reduced the duration of delirium when compared to standard care alone. Further prospective placebo-controlled studies are needed to more completely understand the role of atypical anti-psychotics in delirium

Details

All 113 patients were adults who had documented hypoactive Delirium and an Intensive Therapy Unit stay of at least 72 hours.

Patients were screened for hypoactive delirium using the Confusion Assessment Method-ICU (CAM-ICU) and the Richmond Agitation Sedation Scale (RASS).

Patients were assessed from August 2013 until September 2014.

Of the 113 patients, 52 patients received at least one dose of Quetiapine whilst 61 patients received no pharmacological Delirium Treatment.

Median duration of hypoactive delirium was shorter in the quetiapine-treated group compared with the no-quetiapine group (1.5 versus 2.0 days, p=0.04), and time to extubation after screening positive for delirium trended favourably toward quetiapine-treated patients (3 versus 5 days, p=0.08).

Patients were observed for adverse effects such as new onset of extrapyramidal symptoms or torsade de pointes

There were no significant differences in ICU or hospital LOS, and safety outcomes were similar between groups.

Relevance to Undergraduates

Hypoactive Delirium, Acute Organic Brain Syndrome, Psychiatry, Emergency Medicine

Where to find it

Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy
August 2015

doi: 10.1002/phar.1619.

Matthew Formosa MD5

Common SSRI Side-Effects in Older Adults Associated with Genetic Polymorphisms in the Serotonin Transporter and Receptors: Data from a Randomized Controlled Trial

Aim of Paper

- To determine whether SSRIs are associated with genetic variation in the serotonin system
- To determine whether concentration of the drug is a moderator of side-effects

Summary

- This is a 12-week, double-blind, randomized controlled trial, comparing escitalopram and a placebo. Subjects were 60 years or older, having a principal diagnosis of Generalized Anxiety Disorder but other co-morbidities such as unipolar depression and other anxiety disorders were allowed. Subjects were recruited from primary care, specialty mental health practices and advertisements
- The study showed that genetic variation in the serotonin system may predict which patients will develop common side-effects associated with SSRIs, however the findings should be considered as "preliminary" and further studies are needed to confirm this. Also, several pharmacogenetics effects were sufficient to be considered clinically significant, but not statistically significant
- There was also no statistically significant relationship between drug concentration and severity of side-effects

Description

- Participants were randomized into 1 group taking 10mg escitalopram (increased to 20mg after 4 weeks if tolerated and if needed) and 1 group taking the placebo
- Side effects were assessed using the Udvalg for Kliniske Undersøgelsger (UKU) rating scale taken upon starting (baseline), weekly from weeks 1 to 4 and once every 2 weeks from weeks 4 to 12. The UKU assesses 46 side effects scored from 0-3. Assessment was done by trained raters at the clinical visits
- Only 17 side effects were evaluated as preliminary analysis on patients treated with escitalopram showed higher mean scores on these side-effects compared to subjects taking the placebo- the four most prevalent were dry mouth, diarrhoea, decreased sexual desire, increased sleep
- DNA was extracted from blood using standard procedures. Sequenom™ technology was used the 5HT receptor polymorphisms- another protocol was followed for the 5HT transporter. The genotypes were dichotomized into "high-expressing" or "low-expressing"
- At weeks 2, 8 and 12 plasma escitalopram levels were obtained and assessed using liquid chromatography with UV detection

Relevance to Undergraduates

Psychiatry; Public Health

Where to Find It

American Journal of Geriatric Psychiatry
October 2014

doi:10.1016/j.jagp.2013.07.003

Elizabeth Grech MD5

Thrombectomy assisted by carotid stenting in acute ischaemic stroke management: Benefits and Harms

Aim of Paper

To analyse the benefits and consequences of thrombectomy assisted by carotid stenting through a cohort study. Furthermore, the study seeks to establish clinical and procedural factors associated with favourable outcomes and serious adverse effects.

Summary

- This is a prospective cohort study. A sample size of 361 stroke patients were taken from the Stroke centre of Rigshospitalet, Copenhagan University Hospital, with 47 of these patients being treated with both carotid stenting and thrombectomy.
- Intracranial thrombectomy assisted by carotid stenting proved to be beneficial; 87% had favourable re-canalisation with 46% experiencing early clinical improvement.
- Stenting aided clot retrieval, assisted in anatomic orientation and eased the intracranial thrombectomy procedure.
- Anti-platelet therapy administration proved to be a necessity for the prevention of intra-procedural stent thrombosis.
- Better outcome was noted with shorter procedural duration, with difficult vascular access and elongated procedure times compromising good clinical outcome.

Details

- The targeted vessel was assessed via Digital Subtraction Angiography (DSA) and CT angiogram for clot location and characteristics of occlusion.
- The patient received a loading dose of 500 mg aspirin with/ without a GPIIB/IIIa inhibitor at the interventionist's discretion.
- The extra cranial carotid lesion was accessed via the trans-femoral artery approach and a micro-guide wire was used to pre-dilate the lesion.
- Thrombectomy was performed using stent- retrievers with one/ several carotid stents being placed (balloon dilation).
- Successful re-canalisation was recognised through the thrombolysis in cerebral infarction scale.
- Early clinical improvement was defined by an NIHISS improvement of >= 10 or complete remission within 72 hours.
- Patients were assessed for 3 months for complications via neuro-imaging and disability via the modified Ranking scale.

Relevance to undergraduates

Neurosurgery / Benefits and Harms of Carotid Stenting

Where to find it

Journal of Neurology
September 2015; s00415- 015 - 7895 -0
DOI: 10.007

Matthew Laurence Zammit MD4

Sleep duration and risk of fatal and nonfatal stroke: A prospective study and meta-analysis

Aim of paper

To study the association between sleep duration and stroke incidence in a British population and to synthesize the findings with published results through a meta-analysis.

Summary

- This is a prospective study which included 9,692 stroke-free participants from the European Prospective Investigation into Cancer-Norfolk cohort. Age group set between 42-81 years.
- The participants reported sleep duration during 1998-2000 and 2002-2004. All strokes were recorded until March 2009.
- Ovid Medline, EMBRACE and Cochrane Library provided for the meta-analysis for prospective studies published until May 2014.
- Pooled effect estimates were done using a weighted random-effect model

Details

- The Norwich District Ethics Committee approved the study. All participants gave signed informed consent.
- All patients with doctor-diagnosed stroke were excluded, as were those who reported a stroke onset before the date of the sleep report.
- Sleep measurement was done answering the following questions:

1. "On average, how many hours do you sleep in a 24-hour period?" with 6 response options: <4, 4–6, 6–8, 8–10, 10–12, and >12
2. "Do you generally sleep well?" with answers being: yes or no

- Covariates were chosen a priori from recent literature and relevance to sleep and stroke
- For purposes of data analysis the categories for sleep were defined as: short (< 6hrs), average (6-8 hrs) and long (>8 hrs).
- Baseline characteristics of all participants were compared using X2 test. Models were constructed with progressive adjustments to covariates.
- The results suggest a significant increase in stroke risk among long sleepers and a modest increase among short sleepers.

Relevance to undergraduates

Neurology

Where to find it

The official Journal of the American Academy of Neurology
2015 Feb
DOI 10.1212/WNL.0000000000001371

Diandra Mifsud MD 4

Accuracy of ultrasound in assessing cerebellar haemorrhage in very low birth weight babies

Aim:

To asses the accuracy when diagnosing cerebellar haemorrhages using cranial ultrasound through the anterior and mastoid fontanelle in very low birth weight babies.

Summary:

- All the very low birth weight neonates who were born in 'Istituto Giannina Gashni' and were admitted to the NICU between Febraury 2012 and September 2013 were included prospectively in the study.
- All neonates were examined by cranial ultrasonography through two windows; the anterior and the mastoid fontanelle.
- All the scans were performed twice, independently, by two expert ultra sonographers, according to the NICU routine protocol.

Details:

- At term equivalent age the results from each ultra sonographer were compared, after which an MRI was done.
- Cerebellar haemorrhages were classified into three grades; massive, limited and micro.
- The imaging used was susceptibility weighted imaging.
- All neonates were fed before the SWI to induce spontaneous sleeping before the procedure, while monitoring the parameters non-invasively during the SWI.
- The study started with 147 neonates but only 140 had the SWI done.
- The gestational ages were between 25 and 34 weeks; with birth weights between 435g and 1500g.
- To detect massive CBH, CUS sensitivity through both windows was 100%. In limited CBH, CUS sensitivity through AF dropped to 16.70%; through MF remained relatively good, 83.3%. All micro haemorrhages diagnosed by SWI were not diagnosed by CUS, even if the MF is used.

Relavance to undergraduates:

Paediatrics/Obstetrics/Neonatology; Premature birth complications

Where to find it:

Journal of the Royal College of Paediatrics and Child Health; Archives of Diseases in Childhood; Fetal and Neonatal edition.
January 2015
doi10.1136/archdischild2014-307176

Maria Christina Tabone MD4

Perinatal factors associated with long-term respiratory sequelae in extremely low birthweight infants

Aim:

To assess the lung function of 8 year olds who are extremely low birth weight survivors and identify any associated perinatal determinants with lung function impairment.

Summary:

- This is a retrospective cohort study set at level III NICU.
- The ELBW survivors born and admitted to the NICU at OMCRMCH between 1 June 1990 and 31 May 2004; and attended biyearly school-age follow-up from 1999 to 2011; were eligible for the study.
- ELBW was determined to be as lower than 1001g.

Details:

- To identify perinatal determinants associated with airway obstruction (FEV1/FVC of <80%), a multivariative logistic regression analysis was used.
- The airway obstruction was tested for at school-age as well as the predictive power of potential determinants.
- In this study the following risk factors and potential predictors were assessed: gestational age; birth weight; small for gestational age; sex; chorioamnionitis; premature rupture of membranes, antenatal steroids, surfactant administration, respiratory distress syndrome, post natal steroids, severe bronchopulmonary dysplasia and bubbly/cystic appearances of the lungs by X-Ray during the neonatal period.
- Out of 656 ELBW survivors, only 301 attended a school age follow up at the age of 8. 201 children only completed the lung function test.
- Bubbly/cystic appearance of the lungs on X-Ray was associated with decrease in FEV1/FVC ratio. These children had characteristics of immaturity and intrauterine inflammation.

Relavance to undergraduates:

Paediatrics – Respiratory outcomes in ELBW survivors.

Where to find it:

Journal of the Royal College of Paediatrics and Child Health; Archives of Diseases in Childhood; Fetal and Neonatal edition. March 2015
doi10.1136/archdischild2014-306931

Maria Christina Tabone MD4

Neurodevelopmental outcomes following late and moderate prematurity: a population-based cohort study

Aim:

This study was performed due to the need to conduct large prospective population-based studies, which tackle outcomes following late or moderate preterm birth.

Summary:

- 1255 term-born neonates and 1130 late or moderately pre term neonates were recruited at birth for this population-based cohort study.
- The sample was taken from a geographically defined region of the East Midlands (UK) and included all babies born LMPT from September 2009 to December 2010.
- The sample of term-born babies was chosen randomly from the same period and same geographical region.

Details:

- Mothers were interviewed exactly after birth and any other neonatal/obstetric data was acquired from medical records at discharge. At two years corrected age the mothers participated again by a follow-up questionnaire, so as to assess neurosensory impairments as well as cognitive impairment. These questionnaires were adjusted for sex, socio-economic status and small for gestational age.
- Parents of 638 LMPT infants and 765 controls completed the questionnaires.
- Neurosensory impairment was found in 1.6% of LMPT and 0.3% of controls. Cognitive impairment was found in 6.3% of LMPT and 2.4% of controls.
- LMPT infants were at twice the risk for neurodevelopmental disability.
- Independent risk factors for cognitive impairment: male sex, socio-economic disadvantage, non-white ethnicity, preeclampsia, not receiving breast milk at discharge.

Relavance to undergraduates:

Paediatrics/Obstetrics/Neonatology; Neurodevelopmental outcomes in LMPT neonates

Where to find it:

Journal of the Royal College of Paediatrics and Child Health; Archives of Diseases in Childhood; Fetal and Neonatal edition.
April 2015
doi10.1136/archdischild2014-307684

Maria Christina Tabone MD4

Case based teaching: Acute Myeloblastic Leukaemia in Pregnancy

Patient Demographics
JS is 40-year-old primagravida, currently unemployed and living with husband in Cardiff, South Wales

Presenting Complaint
Preoperative assessment for elective lower segment Caesarean section at 32 weeks

History of Presenting Complaint
JS went to antenatal clinic at 10 weeks to book her pregnancy. The routine CBC showed pancytopenia, with platelets being particularly low (c. 30 x 109/L). Her blood investigations were repeated, along with a blood picture, which showed myeloblasts. A bone marrow aspirate was then performed, which showed >30% myeloblasts. Further tests confirmed that this was acute myelobastic leukaemia.

JS was asked if she would like to terminate the pregnancy and she chose to proceed with the pregnancy. She was started on daunorubicin and cytarabine but remission was not achieved so a second and a third combination were started (she could not remember the names of the drugs). However she still did not achieve remission. In the meantime, she was going for fortnightly growth scans and a multidisciplinary review at antenatal clinic with a haematologist and obstetrician. The growth scans showed that the foetus was growing steadily along the 2nd centile but between weeks 28 and 30 growth had levelled off- "static growth"

It was decided to have an elective C-section at 32 weeks- in this time, she was to be admitted to hospital so that she could be observed because of the decision to give steroids to help foetal lung maturation, and due to the worry of neutropenic sepsis (she had a high-grade fever a few weeks prior).

Past Medical and Drug History
No previous medical, surgical, gynaecological/obstetric history.
No known drug allergies

Social History
JS has a supportive family, even after quitting her job shortly after diagnosis.

Plan of Management
Between weeks 30 and 32, the following were to be done

- Take blood for X-match
- Liaise with paediatric intensive care unit and special care baby unit to arrange a place for the baby to be transferred to, depending on his/her condition- immediate CBC to check white cell count and differential (looking especially at neutrophil count)
- Steroids for foetal lung maturation
- Daily CTG until the day of the C-section, to keep monitoring foetus's condition
- Liaise with anaesthetist to assess fitness for general anaesthesia, and if not, to optimise her condition

Discussion

Introduction
Leukaemia during pregnancy is uncommon. Acute leukaemia accounts for the majority of leukaemia cases in pregnancy. Of these, approximately one third of women will have acute lymphoblastic leukaemia, and two thirds will have acute myeloblastic

leukaemia (Hurley et al, 2005).Women face a dilemma when diagnosed at a gestation when delivery is not feasible, raising a maternal-foetal struggle. Patients and their families need enough time and support to make decisions regarding not only their own health, but that of their child.

Diagnosis

Diagnosis is also more difficult in pregnancy, because anaemia and thrombocytopoenia are common in pregnancy, however, the diagnostic criteria for AML are the same as for non-pregnant women i.e. the WHO classification (Vardiman et al, 2009). Another classification system that is used is the FAB:

Type	Name	Cytogenetics	Percentage of adult AML patients
M0	acute myeloblastic leukemia, minimally differentiated		5%
M1	acute myeloblastic leukemia, without maturation		15%
M2	acute myeloblastic leukemia, with granulocytic maturation	t(8;21)(q22;q22), t(6;9)	25%
M3	promyelocytic, or acute promyelocytic leukemia (APL)	t(15;17)	10%
M4	acute myelomonocytic leukemia	inv(16)(p13q22), del(16q)	20%
M4eo	myelomonocytic together with bone marrow eosinophilia	inv(16), t(16;16)	5%
M5	acute monoblastic leukemia (M5a) or acute monocytic leukemia (M5b)	del (11q), t(9;11), t(11;19)	10%
M6	acute erythroid leukemias, including erythroleukemia (M6a) and very rare pure erythroid leukemia (M6b)		5%
M7	acute megakaryoblastic leukemia	t(1;22)	5%

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Risks, Management and Foetal Survival

Management should be multidisciplinary-haematologists, obstetricians and later on anaesthetists and neonatologists. Although there are risks to the foetus with treatment, studies have shown that delaying treatment compromises the mother's outcome, and there is no benefit for the foetus either (Greenlund et al, 2001). Chemotherapy may result in growth restriction of the foetus or loss of the foetus, but so does leukaemia in itself, and without treatment, and maternal death can occur in weeks or months (Reynoso et al, 1987; Cardnoick & Iacobucci, 2004; Cheghoum et al, 2005). The earlier in gestation this diagnosis is made, the higher the incidence of miscarriage, growth restriction and premature labour.

Contributing factors to foetal death due to untreated AML are severe maternal anaemia and disseminated intravascular coagulation and leukaemic cells within the placenta, affecting blood flow and exchange of nutrients, oxygen from mother to foetus (Cardonick and Iacobucci, 2004).
When a diagnosis is made in the first trimester, because of the higher risk of miscarriage, malformation and foetal death, it is considered reasonable to offer a termination of pregnancy in countries which allow it (because it is considered safer to have an elective termination rather than a spontaneous abortion because platelet count and coagulation can be controlled better in an elective situation, thus posing less risk to the mother). Chemotherapy in the 2nd and 3rd trimesters also increases the risk of late miscarriage, growth retardation, neonatal neutropoenia and thus sepsis, but it rarely causes congenital malformation (Cardonick and Iacobucci, 2004; Doll et al 1988; Ebert et al, 1997), however it is also well documented that non-malformed, healthy babies are still the most likely outcome.

Survival is around 90% for babies born at 28 weeks or more, and even higher for babies born at 32 weeks or more (around 95%). In fact, it may be advisable to deliver immediately if a mother is diagnosed with leukaemia at this gestation. Despite short-term morbidity being low at these gestational

ages, minor cognitive impairment decreases linearly as gestational increases towards 36 weeks. It is not advisable to start chemotherapy after 36 weeks gestation if a mother is diagnosed at this stage, because spontaneous delivery will probably occur before the bone marrow has recovered- here delaying treatment may be of benefit to the child, but this needs to be discussed with the mother.

Combination chemotherapy with daunorubicin and cytarabine as in standard AML protocols-

- Daunorubicin 60mg/m2/day IVI on days 1, 3 and 5
- Cytarabine 100mg/m2 IV every 12 hours on day 1, all the way through to day 10 (day 10 inclusive)

This is the standard combination in the UK. Other anthracycline based regimens may be favoured but there is no data to support the use of one regimen over the other. Dose adjustments must be made, for although dosing should be by weight, it depends on the actual weight of the mother, not the weight gained during pregnancy, also keeping in mind that blood volume and renal clearance increase during pregnancy (Cardnik and Iacobucci, 2004).

Complications

It is debatable whether in utero exposure to anthracyclines (e.g. daunorubicin) causes cardiotoxicity as it does in the adult but foetal cardiac function monitoring using serial US assessment might play a role in prevention of foetal cardiac toxicity and subsequent heart failure (Meyer Wittkopf et al, 2001).

The patient's doctors should also have a low threshold for fever- immune changes in pregnancy itself make a woman susceptible to infection, but the pregnant woman with AML is also at risk due to neutropenia due to the disease itself, or secondary to chemotherapy (RCOG 2012a; RCOG 2012b).

Antibiotics may be considered as prophylaxis and as treatment- penicillins (but not co-amoxiclav), metronidazole and cephalosporins can be used. Co-amoxiclav should be avoided because it is associated with neonatal necrotizing entercolitis. Other antibiotics to avoid are quinolones, tetracyclines and sulphonamides (Lynchn et al, 1991). If antifungals are required, fluconazole is commonly used, provided the dose is less than 150mg per day (King et al, 1998). Amphotericin B is however preferred, because there is less renal and infusion-related toxicity.

Delivery

Delivery should be planned- as soon as foetal maturity allows, and preferably not immediately following chemotherapy as the mother's blood count would be poor. Delaying delivery by 2-3 weeks after chemotherapy not only allows the mother's blood count to improve, it also allows time for drug excretion from the placenta, thus reducing the risk of foetal neutropoenia and sepsis.

Vaginal delivery is preferable to caesarean section as the later has a higher infection risk and longer recovery. If the 2-3 week delay has been observed, than foetal scalp

electrode monitoring, ventouse or forceps may be used. Dexamethasone is given when delivery is expected to occur between 24-35 weeks, for 2 days within the week prior to the delivery. MgSO4 has also been shown to reduce chance of cerebral palsy when given in the 24 hours prior to delivery (RCOG 2010; RCOG 2011). Also because women with AML are more prone to bleeding, the risk of postpartum haemorrhage is greater, so besides giving syntocinon before the cord is clamped and cut, it may be worth giving a syntocinon infusion over 4 hours after delivery.

After Delivery

Consolidation therapy should be completed as soon as possible following delivery. Because of the risk of venous thromboembolism in the puerperium a risk assessment should be done at delivery- if LMWH is required, it should be started 4 hours after delivery for 10 days or 6 weeks depending on risk. This should only be done if the platelet count is over 50 x 109/L (RCOG. 2009). Breast feeding is not recommended until at least 2 weeks following chemotherapy completion.

References

- Ali et al, 2015 Guidelines for the Diagnosis and Management of Acute Myeloid Leukaemia in Pregnancy
- Br J Haematol. 2015 Aug;170(4):487-95. doi: 10.1111/bjh.13554. Epub 2015 Jun 17.
- Cardonick, E. & Iacobucci, A. (2004) Use of chemotherapy during human pregnancy. Lancet Oncology, 5, 283-291
- Cheghoum, Y., Vey, N., Raffoux, E., Huguet, F., Pigneux, A., Witz, B., Pautas, C., de Botton, S., Guyotat, D., Liore, B., Fegueux, N., Garban, F., Saad, H. & Thomas, X. (2005) Acute leukaemia during pregnancy: a report on 37 patients and a review of the literature. Cancer, 104, 110-117
- Doll, D.C., Ringenberg, Q.S. & Yarbro, J.W. (1988) Management of cancer during pregnancy. Archives of Internal Medicine, 148, 2058-2064.
- Ebert, U., Löffler, H. & Kirch, W. (1997) Cytotoxic therapy and pregnancy. Pharmacology and Therapeutics, 74, 207-220.
- Greenlund, L.J., Letendre, L. & Tefferi, A. (2001) Acute leukemia during pregnancy: a single institutional experience with 17 cases. Leukemia & Lymphoma, 41, 571-577.
- Hurley, T.J., McKinnel, J.V. & Irani, M.S. (2005) Hematologic malignancies in pregnancy. Obstetric and Gynecology Clinics of North America, 32, 595-614.
- King, C.T., Rogers, P.D., Cleary, J.D. & Chapman, S.W. (1998) Antifungal Therapy During Pregnancy. Clinical Infectious Diseases, 27, 1151-1160.
- Meyer-Wittkopf, M., Barth, H., Emons, G. & Schmidt, S. (2001) Fetal cardiac effects of doxorubicin therapy for carcinoma of the breast during pregnancy: case report and review of the literature. Ultrasound in Obstetrics & Gynecology, 18, 62-66.
- Reynoso, E.E., Shepherd, F.A., Messner, H.A., Farquharson, H.A., Garvey, M.B. & Baker, M.A. (1987) Acute leukemia during pregnancy: the Toronto Leukemia Study
- Group experience with long-term follow-up of children exposed in utero to chemotherapeutic agents. Journal of Clinical Oncology, 5, 1098-1106.
- Royal College of Obstetricians and Gynaecologists (2009) Reducing the Risk of Thrombosis and Embolism during Pregnancy and the Puerperium. Green-top Clinical Guideline No. 37a.
- Royal College of Obstetricians and Gynaecologists (2010) Antenatal Corticosteroids to Reduce Neonatal Morbidity and Mortality. Green-top Clinical Guideline No. 7. London: Royal
- Royal College of Obstetricians and Gynaecologists (2011) Magnesium Sulphate to Prevent Cerebral Palsy. Scientific Impact Paper No. 29.
- Royal College of Obstetricians and Gynaecologists (2012a) Bacterial Sepsis in Pregnancy.
- Green-top Clinical Guideline No. 64a. London: Royal College of Obstetricians and Gynaecologists
- Royal College of Obstetricians and Gynaecologists (2012b) Bacterial Sepsis following Pregnancy. Green-top Clinical Guideline No. 64b.
- Vardiman, J.W., Thiele, J., Arber, D.A., Brunning, R.D., Borowitz, M.J., Porwit. A., Harris, N.L., Le Beau, M.M., Hellström-Lindberg, E., Tefferi, A. & Bloomfield, C.D. (2009) The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukaemia: rationale and important changes. Blood, 114, 937-951

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Magnetic resonance imaging of male and female genitals during coitus and female sexual arousal

Discovery

Schultz, VanAndel, Sabelis, and Mooyart showed that it is feasible to perform magnetic resonance imaging of male and female genitals during coitus. This allows for more exploration of such living anatomy, since studying coital and arousal anatomical changes has been no easy task. The authors won the Ig Noble Prize in medicine for the study in the year 2000.

This section is inspired by the concept of the Ig Noble Prize which helps spur people's interest in science. It is a parody of the actual Noble Prize, which gives awards annually to "honour achievements that first make people laugh, and then make them think".

Summary

The images capturing intercourse in the "missionary position" (face to face coitus with the male in superior position) show the penis adapting into the shape of a 'boomerang' with a third of its length being made up of the root. Therefore, the erect penis makes an angle of around 120° to its root. Imaging also revealed that in three out of four couples with full penetration there was a preferential contact of the penis with the anterior fornix and vaginal wall. In female sexual arousal without intercourse, the uterus was raised and the anterior vaginal wall lengthened. Sexual arousal did not increase the size of the uterus, in contrast to previous findings suggested by Masters and Johnson (1966) which were based solely on bimanual palpation.

Details

The observational study was carried out at a University hospital in the Netherlands. It involved a total of thirteen experiments with eight couples and three single women to assess changes during coitus and arousal with clitoral stimulation. The imaging was done using a 1.5 Tesla magnet system (Gyroscan S15) and a 1.5 Tesla magnet system from Siemens Vision. Males had more problems than females with sexual performance in the scanner. In fact just one couple managed to perform coitus adequately without Sildenafil. All females had complete sexual arousal although they described their orgasm as 'superficial'.

Clinical Relevance

Reproductive Medicine, Radiology, humor

Where to find it

British Medical Journal, 1999;319:1596

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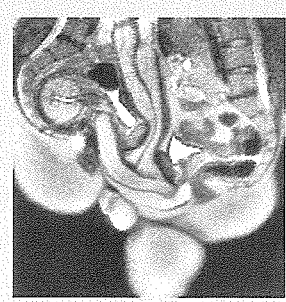

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