

- Established 1867 -

IMJ
Official Journal of the Irish
Medical Organisation

Irish Medical Journal

NOVEMBER/DECEMBER 2015
Volume 108 ■ Number 10



IRISH MEDICAL
ORGANISATION
Ceardchumann Dochtúirí na hÉireann

291 This Month

292 IMJ Commentary

'The Patient Experience as a Catalyst for Change';
Doolin Lecture 2015: 5th December 2015

Editorial

293 Mental Health Policy in Ireland: A Decade after A Vision for Change, Where Are We Now?

BD Kelly

Original Papers

294 Paediatric Early Warning Trigger – A Cry for Help

T Bolger, N Clarke, S Crowe, C Martin, S Koe

296 The Role of Speech and Language Therapy in Assessing and Managing Pharyngo-esophageal Diverticula

E Holmes, C Kenny, M Samuel, J Regan, J O'Rourke, C McCoubrey

299 Utilisation of Clinical Networks to Facilitate Elective Surgical Workload; A Preliminary Analysis

T Burke, P Waters, RM Waldron, K Joyce, I Khan, W Khan, M Kerin, K Barry

302 Added Value of Stroke Protocol MRI Following Negative Initial CT in the Acute Stroke Setting

ML Gargan, HK Kok, J Kearney, R Collins, T Coughlan, D O'Neill, D Ryan, W Torreggiani, O Doody

304 Safety of Grass Pollen Sublingual Immunotherapy for Allergic Rhinitis in Concomitant Asthma

A Sahadevan, R Cusack, SJ Lane

Short Report

307 Young, Male and Feeling Suicidal in Ireland: Is Help or Harm Just One Click Away?

J Gilhooley, M Bolger, A Charles, E Cleary, A Lane, K Malone

309 Pregabalin Abuse amongst Opioid Substitution Treatment Patients

S McNamara, S Stokes, R Kilduff, A Shine

Case Report

310 Post traumatic Fat Embolism in Common Femoral Vein on CT

N Healy, K Billington, N Sheehy

311 Association of Oesophageal Hypertension with Bradycardia Mediated Deglutition Syncope

RY Lim, H Mulcahy, D Keane

Research Correspondence

312 'Malignant Phenylketonuria' (PKU) Due to Dihydropteridine Reductase (DHPR) Deficiency

A Ventzke, J Hoffmann, E Crushell, A Monavari, PD Mayne, I Knerr

Occasional Piece

316 Paget's Disease of Bone: Progress Towards Remission and Prevention

GM Healy, C Woods, E Heffernan, MJ McKenna

Letter to the Editor

318 'Life Saving Positioning' in Patients with Air Embolism

M Kooblall, SJ Lane, E Moloney

Book Review

318 Textbook of Clinical Gastroenterology and Hepatology. Second Edition

PA McCormick

319 Continuing Professional Development

Are you interested in your own GP practice?

Purpose built medical centre opening in North Wexford Feb/Mar 2016

Located in thriving and densely populated area

Fantastic opportunity for the right candidate

Contact:

northwexfordmedicalcentre@gmail.com



GP Partner or Salaried GP

Due to retirement we are looking for a full time GP to join our practice in beautiful Mid-Wales.

- Highly Innovative partnership agreement-Flexible working arrangements.
- Busy and profitable dispensary (85% of our population).
- Nurse led triage -GP skills are fully utilised with much of the day to day work being done by our excellent nursing team.
- Trained Administration Team relieves the GP's of much of the administration burden.
- Practice Income in upper quartile- finances are directly controlled by a Chartered Accountant with a special interest in GP finance.
- 15 minute appointments.
- Part of the North Powys Cluster, one of the most active Cluster groups in Wales. Fully computerised – we use digital dictation and voice recognition systems.
- Out of Hours work available at attractive pay rates.

Please contact Dr Simon Currin (Managing Partner) for more information.

Tel: 01686 668 217 Email: Simon.Currin@wales.nhs.uk

www.montgomerymedicalpractice.wales.nhs.uk

Editor

JFA Murphy, FRCPI

Assistant to the Editor

Lorna Duffy

Chief Operating Officer

Susan Clyne

IMO Executive Board

Dr Matthew Sadlier, Chair

Dr Illona Duffy, Treasurer

Dr Padraig McGarry

Dr Colm Loftus

Dr Peadar Gilligan

Prof Trevor Duffy

Dr John Donnellan

Dr Ann Hogan

Dr Patrick O'Sullivan

Subscriptions 2015

6 Month Subscription:

Ireland, UK, EU €125

Outside EU €200

Address: IMJ Editorial Office

IMO House, 10 Fitzwilliam Place, Dublin 2

Tel: (01) 676 7273. **Fax:** (01) 661 2758

E-mail: lduffy@imj.ie **Web:** www.imj.ie

In this Month's IMJ

Paediatric early warning trigger- a cry for help:

Bolger et al describe the efficacy of the PEWT. With its introduction the time from deterioration to senior clinical involvement reduced from 312 to 166 minutes. The rate of transfers to PICU of triage category 1 & 2 patients was more than halved.

Table 1: PEWT Parameters

A ACUTE AIRWAY OBSTRUCTION (seek prompt assistance)
 Stridor requiring rebuffed Adrenaline Q5 no improvement after rebuffed adrenaline
 Clinically rising or impending complete airway obstruction

B BREATHING
 1) SaO₂ ≤ 90% in any amount of oxygen
 2) SaO₂ ≤ 75% in any amount of oxygen (cyanotic heart disease)
 3) Persistent tachypnoea (RR ≥ 70 under 6 months; ≥ 60 6 - 12 months; ≥ 40 1 - 5 yrs; ≥ 30 over 5 yrs)
 4) Apnoea + /- bradycardia (HR ≤ 90 in children under 5 yrs)
 5) Marked increased effort of breathing (recession, tracheal tug, grunting)
 6) Respiratory depression RR < 20 0-3 months, < 1/2 normal value

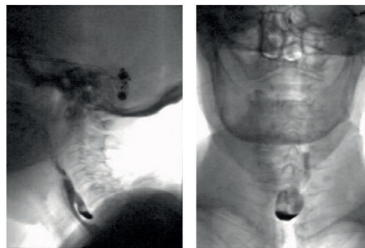
C CIRCULATION
 Persistent tachycardia following one bolus of 10mls / kg fluid (HR ≥ 160 under 5 yrs; HR ≥ 120 5 - 12 years; HR ≥ 100 over 12 yrs)
 QES Poor perfusion QES prolonged capillary refill (≥ 2 secs) + / - low systolic BP

D DISABILITY
 Acute change in neurological status. Children scored by AVPU, responding only to pain QIR unresponsive
 Child who is seizing ON not responding to prescribed anticonvulsants

E OTHERS
 1) Hyperkalaemia - K⁺ ≥ 6.0 mmol/litre
 2) Any child with pH < 7.2 whatever the cause, base deficit -5 or greater
 3) Any child with unresolved pain or escalating pain despite prescribed analgesia
 4) Any child whose condition is worrying - but is not triggering any of the parameters

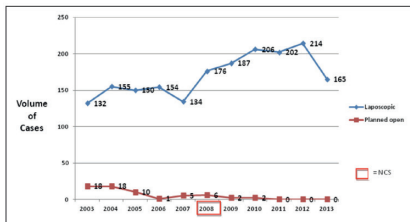
The role of speech and language therapy in assessing and managing pharyngo-esophageal diverticula:

Holmes et al describe 20 patients with pharyngeal-esophageal diverticula. Most had respiratory difficulties, dysphagia, voice changes and risk of aspiration. The authors describe the role of a swallow strategy in its management.



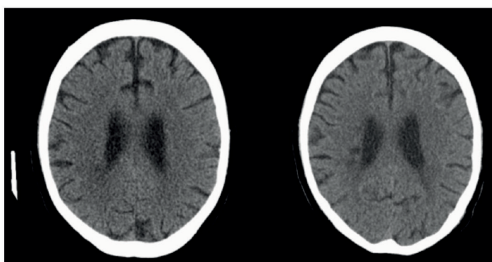
Utilisation of clinical networks to facilitate elective surgical workload: a preliminary analysis:

Burke et al state that the establishment of hospital networks provides an opportunity for certain elective surgical procedures to be undertaken in larger numbers in general hospitals. The authors illustrate this point with data showing an increase in the number of cholecystectomies annually from 134 (2008) to 214 (2012).



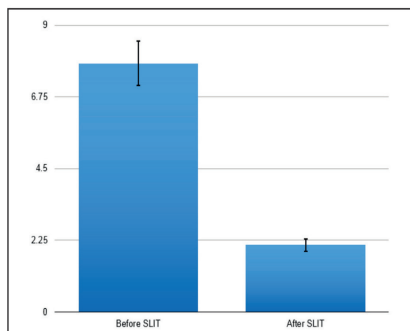
Added value of stroke protocol MRI following negative initial CT in the acute stroke setting:

Gargan et al studied 92 patients with a stroke with a negative CT scan who also had an MRI scan. In 20 patients the MRI contributed added value, acute or subacute ischaemia.



Safety of grass pollen sublingual immunotherapy for allergic rhinitis in concomitant asthma:

Sahadevan et al report on the use of sublingual immunotherapy in 30 patients with seasonal allergic rhinitis and mild asthma. Their rhinitis improved and their asthma remained stable.



Young, male and feeling suicidal in Ireland: is help or harm just one click away?

Gilhooley et al examined the internet help resources that are available to individual who feels suicidal. The authors found that the information provided was of variable quality and in some sites it was potentially harmful. They suggest that all the agencies should adopt a coordinated approach, produce a 'front page', and target the high-risk group 18 - 24 year old males.

Table 1: 'Front page' websites when searching the internet using the word 'suicide'

Name	Email	Face to face	Phone	Text	Post	Online chat	Other
Samaritans	Yes (Response 12 hrs)	No	No (24 hour helpline 24/7)	No	No (no internet response within 7 days)	No	No
Navigator Action	No	No	No	No	No	No	No
Helpline	No	No	No	No	No	No	No
Suicide Prevention	No	No	No	No	No	No	Other links to the Samaritans, LIPS, Access to contact (SP) A&E emergency
TuLar	No	No	No (24 hour helpline)	No	No (Qualifies 100%)	No	No
Methods	No	No	No	No	No	No	No
Suicide	Yes	No (11 central)	No (17 national, 24/7)	No	No	No	No
National Office for Suicide Prevention	Links to email 24	Links to 24hr Samaritans/Phone helpline	Links to 24hr Samaritans/Phone helpline	Links to 24hr Samaritans/Phone helpline	Links to Samaritans & Children	Links to Samaritans & Children	Links to Samaritans & Children
Suicide or not?	No	Links to 24hr Samaritans/Phone helpline	Links to 24hr Samaritans/Phone helpline	Links to 24hr Samaritans/Phone helpline	Links to Samaritans & Children	Links to Samaritans & Children	Links to Samaritans & Children
National Suicide Prevention	Multiple links to Samaritans, LIPS, A&E, 24/7	Links to Samaritans, LIPS, A&E, 24/7	Links to Samaritans, LIPS, A&E, 24/7	Links to Samaritans, LIPS, A&E, 24/7	Links to Samaritans, LIPS, A&E, 24/7	Links to Samaritans, LIPS, A&E, 24/7	Links to Samaritans, LIPS, A&E, 24/7
Stop Suicide	Links to the Samaritans	Links to the Samaritans, LIPS, A&E, 24/7	Links to the Samaritans, LIPS, A&E, 24/7	Links to the Samaritans, LIPS, A&E, 24/7	Links to the Samaritans, LIPS, A&E, 24/7	Links to the Samaritans, LIPS, A&E, 24/7	Links to the Samaritans, LIPS, A&E, 24/7
Suicide Advice	Email 'suicideadvice' provider	Advice provider contact SP or A&E 24/7	Advice provider contact SP or A&E 24/7	Advice provider contact SP or A&E 24/7	Advice provider contact SP or A&E 24/7	Advice provider contact SP or A&E 24/7	Advice provider contact SP or A&E 24/7

Pregabalin abuse amongst opioid substitution treatment patients:

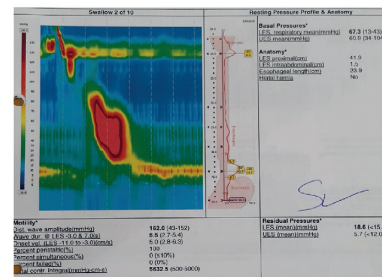
McNamara et al tested 440 drug abuse patients for Pregabalin use. The results were positive in 39 (9.2%) of individuals. Pregabalin induces a drunken state, its street name being Budweiser's. The authors emphasise that misuse of this agent is a serious issue.

Post traumatic fat embolism in the common femoral vein on CT:

Healy et al describe the CT presence of fat globules in the right common femoral vein following fracture of the right femur and right superior and inferior pubic rami. Management is supportive but steroids and albumin may have a role.

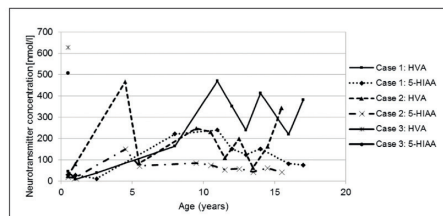
Association of oesophageal hypertension with bradycardia mediated deglutition syncope:

Lim et al describe recurrent syncope in a 77 year old woman. Investigations found that it was caused by swallow syncope. The mechanism is bradyarrhythmias from a functionally abnormal oesophagus. The patient was treated successfully with a permanent pacemaker.



Malignant phenylketonuria (PKU) due to dihydropteridine reductase (DHPR) deficiency:

Ventzke et al describe 4 cases of malignant PKU. DHPR deficiency is the underlying mechanism. The treatment is a life-long phenylalanine restricted diet together with L-dopa and 5- hydroxyl tryptophan.



Paget's disease of bone: progress towards remission and prevention:

Healy et al describe the clinical presentation, investigation, and management of Paget's disease. The authors state that the treatment of Paget's disease has advanced considerably since the introduction of intravenous Zoledronate, a nitrogen-containing bisphosphonate.



The Doolin Lecture 2015: 5th December 2015; 'The Patient Experience as a Catalyst for Change'

The 2015 Doolin Lecture was given by Ms Margaret Murphy, a leading advocate for patient safety. This year's talk dealt with error from the patient's perspective, while last year's Doolin Lecture delivered by the late Professor Aidan Halligan had dealt with error from the doctor's viewpoint. When introducing Ms. Murphy, Dr. Ray Walley IMO President, said that she had championed patient safety following the death of her son from a medical oversight.

Ms. Murphy opened by stating that the good doctor treats the disease, but the great doctor treats the patient with the disease. She emphasised the importance of the patient's experience of the healthcare system. Close co-operation between the patient and the healthcare worker should be encouraged. She quoted the patient safety framework suggested by the Irish Commission on Patient Safety and Quality Assurance. This supports safe and effective care from skilled professionals in an appropriate environment. It was established in 2007 following the Lourdes Inquiry and produced its report in July 2008. Its objective is to develop clear, and practical recommendations in order to ensure patient safety. The foreword to the Report begins with a quote from Atul Gawande 'we look for medicine to be an orderly field of knowledge and procedure. But it is not. It is an imperfect science, an enterprise of constantly changing knowledge, uncertain information, fallible individuals, and at the same time lives on the line'.

One of the tenets of the safety culture is to make the status quo uncomfortable, while making the future attractive. She serves as the External Lead Advisor of the WHO Patients for Safety which has a network of 500 champions from 52 countries. One of its aspirations is to harness untapped resources and utilize them for patient safety.

The core values for patient safety are openness, collaborative partnerships, meaningful engagement, and reduction in harm. Ms Murphy recalled Helen Keller's statement 'the one thing worse than being blind is having sight but no vision'. The future should find ways of separating disclosure and blame. Disclosure is about integrity and professionalism. No one should be hesitant to speak up on behalf of patients.

Ms. Murphy illustrated many of the previous points by discussing the death of her 21 year old son Kevin. It took both composure and fortitude to describe such personal, painful, and distressing events in public. She added that in the case of her deceased son, the healthcare system failed him at every point of contact. He had presented in 1997 with back pain. He was referred for hospital investigations. Blood tests were performed, but a raised serum calcium, and creatinine were not acted on. Ms Murphy had increasing concerns about Kevin. He was staying in bed more than usual, he had failed his exams. The family consulted a psychiatrist because of changed behavior. In response to her call, her son's blood test results were to the GP, but no verbal contact was made with her. The GP referred Kevin to the hospital medical department, and he attached a post-it with the blood test results to the back of the letter. These results, which showed the raised calcium and creatinine were misplaced and not seen by the hospital medical staff. He was admitted to hospital in 1999. A provisional diagnosis of nephritis was made. His condition deteriorated in hospital and he died. The postmortem revealed a solitary parathyroid adenoma, which in retrospect had been the cause of the hypercalcaemia.

Ms. Murphy and her husband sought an explanation for the events and circumstances leading up to their son's death. They found the interactions and communications with the hospital insufficient. They felt that they did not receive a satisfactory explanation about why the raised serum calcium level was not acted on and why

the results were subsequently misplaced. Following a period of communication with the hospital, the family decided to take legal action in order to get answers. Ms. Murphy found the litigation process unsatisfactory. She said that substantial efforts went into the defense of the lawsuit, rather than on improving the hospital's services. It needs to be appreciated, however, that this cannot change unless the current adversarial medico-legal system is reviewed.

In May 2004, the High Court found in favour of the action brought by the family against the hospital. The family subsequently donated the settlement to charity.

Ms Murphy explained to the audience that she had gone into such detail about her son's illness during her presentation because it helps to emphasise the core message. 'Tell me a fact and I will learn, tell me a truth and I will believe, tell me a story and it will live in my heart forever'. She thinks that the lessons that need to be learned are; simple measures save lives, and you ignore at your peril the concerns of a mother.

Ms. Murphy's concluding remarks are in common with other safety advocates who are involved with patient safety and the avoidance of error. 'It could not happen here' are the five most dangerous words in the practice of medicine. Everybody in healthcare should resolve to make patient care as safe as possible as soon as possible.

The safety issues raised in this lecture were about diagnosis, which is a critical step for all patients. Diagnosis can be very challenging for doctors. There are 13,000 diseases. Many have a straightforward pattern but a substantial number have a complex, multi symptom, multi system presentation. We all need to be frequently reminded about diagnostic vigilance. When things don't fit, ask the question 'what else could it be.'

The second issue raised was that of missing investigation results. This possibility makes all doctors uneasy, because we are aware that it can happen to any one of us. One promising development is the introduction of the electronic patient record, which will facilitate all laboratory and radiology results being entered as soon as they become available. The other potential is that abnormal results can be automatically flagged. The pilot programme is due to be rolled out next year in a number of Irish hospitals.

The third issue is how a hospital and its staff should best interact with relatives when a patient is perceived to have suffered an adverse, avoidable outcome. This is an area that doctors and other healthcare staff have struggled with for a long time. Neither the undergraduate or postgraduate training programme prepares one for these scenarios. The introduction of open disclosure policies and their structured governance offer the potential to bridge this communication deficit.

Ms Murphy's lecture was both thought provoking and challenging. It was a reminder of the importance of paying attention to the patient's details including history, examination, and investigations. Communication is of paramount importance. However when moving from individual cases to the global provision of healthcare, we need to accept, as recently pointed by Mr. Tony O'Brien HSE, that harm occurs and we must address the resulting needs in a sensible and pragmatic way.

JFA Murphy
Editor

1. Building a culture of safety. Report of the Commission on Patient Safety and Quality Assurance. Department of Health and Children. July 2008.

Mental Health Policy in Ireland: A Decade after A Vision for Change, Where Are We Now?

In 2006, the Irish government published *A Vision for Change: Report of the Expert Group on Mental Health Policy*, a comprehensive mental health policy document which sought to consolidate and deepen moves towards community-based mental health care in Ireland.^{1,2} Did it work?

Long before *A Vision for Change* was published, there was already a well-established commitment to community mental health care, dating from *The Psychiatric Services: Planning for the Future* (1984)³ and even the 1967 Commission of Enquiry on Mental Illness⁴ which recommended “radical and widespread changes” (p.xv), moving away from “barrack-like structures characterised by large wards, gloomy corridors and stone stairways” (p.xiii) and towards the provision of community care. As a result, well before *A Vision for Change* appeared in 2006, there was a strong emphasis on community care, at least in certain parts of the country, as reflected in the reduction of the number of “mentally ill” persons in institutions from 18,188 in 1966 to 4,522 in 2000.⁵

Since 2006, however, the rate of implementation of *A Vision for Change* has been commonly criticised as being too slow. In 2008, one study of 32 mental health services reported that just 16% of services had received the resources promised in order to implement the new policy; 32% had not been promised such resources and nor was there tangible evidence of the requisite enhancement of clinical teams; and there was significant concern about low levels of recruitment to multidisciplinary teams.⁶ In September 2009, a report by Indecon International Consultants, submitted to Amnesty International, made some similar points, highlighting that while definite progress had been made, significant deficits remained in relation to the number of community mental health teams and their composition.⁷ The report also pointed to an over-reliance on traditional acute and long-stay inpatient facilities, and presented a series of recommendations for future development of services, including setting new, realistic implementation targets. The rate of implementation was also a key concern of the Independent Monitoring Group (IMC) established as part of *A Vision for Change* in March 2006.⁸ In June 2012, the IMC, in its sixth annual report, concluded that implementation of the policy was still “slow and inconsistent” (p.3). The IMC pointed in particular to the “continued absence of a National Mental Health Service Directorate with authority and control of resources. Such a body has the potential to give strong corporate leadership and act as a catalyst for change”.

On a more positive note, there was “evidence of many local and regional initiatives being developed in line with [A Vision for Change]. These are principally ‘bottom-up’ developments led by local leadership”. Nonetheless, there was still much to be done. Many of the same themes recurred in a further, independent study of implementation published in 2014, which identified a significant body of opinion that saw implementation as slow, haphazard and uneven.⁹ This study identified a need for authoritative, accountable leadership as a key factor for implementation and, in 2013, the HSE duly appointed a National Director for Mental Health. The HSE Mental Health Division now has responsibility for all HSE mental health services. In addition, the National Clinical Programme for Mental Health was set up in 2010, in collaboration with the College of Psychiatrists of Ireland, to standardise high quality evidence-based practice across mental health services in relation to (a) management of patients presenting to emergency departments following self-harm; (b) early intervention for people developing first episode psychosis; and (c) eating disorders. While change of this magnitude is invariably complex, significant progress has been reported in several areas with, for example,

23 of the 35 posts identified to address self-harm in Emergency Departments in place by March 2015, and the remainder in the recruitment process.

Notwithstanding these positive developments, challenges remain in relation to *A Vision for Change*. In 2014, the Chairman of the Mental Health Commission¹⁰ pointed to some of the key issues: “The implementation of policy to date is still reliant on innovative and imaginative clinical and administrative leadership at regional and local levels. There is considerable commitment to the policy. Despite these actions the policy is being implemented unevenly and inconsistently across the country and there is a requirement for innovative actions to be supported and reinforced by strong corporate governance at national level” (p.6).

While acknowledging recent progress in relation to governance, budgetary assurances, physical infrastructure and certain other areas, the Commission was still “concerned regarding a number of specific areas of service provision which impinge on human rights and where, in 2013, standards fell below what is acceptable” (p.7). These areas included individualised care plans (implemented appropriately in an estimated 60% of approved centres), unacceptable use of seclusion and restraint, continued admission of children to adult facilities (22.3% of all child admissions in 2013), the absence of reformed, enacted mental capacity legislation, and various issues relating to staffing. Clearly, the decade since *A Vision for Change* was published has seen substantial progress. Equally clearly, however, the next decade needs to see further progress if the Vision is to be finally, fully realised.

BD Kelly

Department of Adult Psychiatry, UCD School of Medicine and Medical Science, Mater Misericordiae University Hospital, 62/63 Eccles St, Dublin 7
Email: brendakelly35@gmail.com

References

1. Expert Group on Mental Health Policy. *A Vision for Change: Report of the Expert Group on Mental Health Policy*. Dublin: The Stationery Office, 2006.
2. Guruswamy S, Kelly BD. A change of vision? Mental health policy. *Ir Med J* 2006;99:164-6.
3. Department of Health. *The Psychiatric Services: Planning for the Future*. Dublin: Stationery Office, 1984.
4. Commission of Enquiry on Mental Illness. *Report of the Commission of Enquiry on Mental Illness*. Dublin: The Stationery Office, 1967.
5. Brennan D. *Irish Insanity, 1800-2000* (Routledge Advances in Sociology). Abingdon, Oxon.: Routledge, 2014.
6. Barry S, Murphy P (on behalf of the Faculty of Clinical Directors of the College of Psychiatry of Ireland). *A Gloomy View: Rhetoric or Reality in Relation to the Advancement of A Vision for Change*. Dublin: College of Psychiatry of Ireland, 2009.
7. Indecon International Consultants. *Review of Government Spending on Mental Health and Assessment of Progress on Implementation of A Vision for Change*. Dublin: Indecon/Amnesty International, 2009.
8. Independent Monitoring Group. *A Vision for Change: Sixth Annual Report on Implementation (2011)*. Dublin: Department of Health, 2012.
9. Johnston H. *All Vision but No Change? Determinants of Implementation: The Case of Ireland and Mental Health Policy* (Issues in Public Administration). Dublin: Institute of Public Administration, 2014.
10. Mental Health Commission. *Mental Health Commission Annual Report 2013 Including Report of the Inspector of Mental Health Services*. Dublin: Mental Health Commission, 2014.

Paediatric Early Warning Trigger – A Cry for Help

T Bolger, N Clarke, S Crowe, C Martin, S Koe

Paediatric Emergency Department, AMNCH, Tallaght, Dublin 24

Abstract

In paediatrics, it is crucial to ensure that the child who is clinically deteriorating is rapidly recognised and treated. We implemented a Paediatric Early Warning Trigger (PEWT) in our unit to improve recognition of these patients. Our trigger was a series of physiological measurements with a PEWT call if any result was outside the accepted range. We retrospectively compared 12 months prior to the introduction of the trigger (January to December 2009) to the three years post the introduction of the trigger (January 2010 to December 2012). We compared the time from deterioration to involvement of senior staff during the two time periods. We also examined the rates of crash calls and PICU transfers in the two periods. We found that the time from deterioration to senior clinician involvement reduced from 312 minutes to 166 minutes and the rate of transfers to PICU among the triage category 1&2 patients reduced from 1:50 in 2009 to 1:129, 1:118 and 1:131 during the three years of the trial. The rate of cardiac arrest among this group reduced from 1:100 in 2009 to 1:129, 1:216 and 1:542 during the three years of the trial. This study demonstrates the effectiveness of a Paediatric Early Warning Trigger in an Irish setting. We have been able to maximise senior clinician input into our sickest children in a more timely fashion

Introduction

The old adage that sick children can deteriorate quickly remains true today. It is equally important to monitor for deterioration after making an accurate diagnosis. When a child has a cardiac arrest, this is most often at the end of a sustained period of deterioration¹. Early intervention in the deteriorating paediatric patient has been shown to improve clinical outcomes. The focus of treatment for all sick children should be on preventing rather than treating cardiac arrest. A number of paediatric early warning scores have been studied. Their aim is to identify the deteriorating patient before they are "in extremis". A recent UK based study found that 85% of inpatient paediatric units were using an Early Warning Score². An Early Warning Score is a set of algorithms relating to the findings of physiological parameters. In most scores, these parameters are scored based on severity. The overall score will result in a series of graded therapeutic interventions. An early warning trigger is a single trigger and single response system based on similar physiological parameters. Our hospital is a 66-bed inpatient paediatric unit with a Paediatric Emergency Department (PED). There are 33,000 attendances in the PED. While we do not have a Paediatric Intensive Care Unit (PICU), we are supported by anaesthetists on-site and we do not have ambulance by-pass for critically ill children. We noted, during our morbidity and mortality audits in 2008, that our transfer rates to PICU was rising and peaked at almost one transfer per week in 2009. Anecdotally, we felt that the time to escalate care to the sickest patients was suboptimal. We introduced a Paediatric Early Warning Trigger (PEWT) based on a modified Bristol PEWS. The response of a trigger breach was to instigate a full acute team review within 5 minutes. We compared the clinical outcomes before and after its introduction. Our hypothesis in this study was that the time taken to maximise the clinical input into these children would reduce following the introduction of the PEWT. We used the time of anaesthetic review as the time of maximising clinical input. An expected consequence of this improvement would also be less paediatric cardiac arrests in the hospital.

Methods

The PEWT was introduced in the hospital in December 2009. We undertook a retrospective audit of the patients' charts for the period January - December 2009 and compared them with the period December 2009 - December 2012. All charts of patients whose clinical condition resulted in a cardiorespiratory arrest, PEWT call or a critical illness transfer to another centre were included in the study. In the pre-PEWT group, we assigned a surrogate time of PEWT call at the time of first trigger breach and we compared this with the time of first anaesthetic team review. The parameters obtained from the charts included demographics, clinical diagnosis, elapsed times to first trigger breach, elapsed times to PEWT/crash call, elapsed times to anaesthetic review, which clinical parameter was triggering a PEWT, initial assessment

of patient at time of PEWT, any extra treatment instigated by the PEWT and the outcome following the PEWT. The PEWT was a single page document which listed baseline clinical parameters as documented in Table 1. If any one of these parameters were breached, then a PEWT call was made. The aim of the PEWT was to ensure that a rapid conglomeration of senior Medical, Surgical, ED and Anaesthetic staff were assembled at the bedside and making decisions regarding the level and place of care which the patient's condition was requiring.

Table 1: PEWT Parameters

A ACUTE AIRWAY OBSTRUCTION (seek prompt assistance)

Stridor requiring nebulised Adrenaline OR no improvement after nebulised adrenaline
Clinically tiring or impending complete airway obstruction

B BREATHING

- 1) SaO₂ ≤ 90% in any amount of oxygen
- 2) SaO₂ ≤ 75% in any amount of oxygen (cyanotic heart disease)
- 3) Persistent tachypnoea
(RR ≥ 70 under 6 months; ≥ 60 6 – 12 months; ≥ 40 1 – 5 yrs; ≥ 30 over 5 yrs)
- 4) Apnoeas +/- bradycardia (HR ≤ 90 in children under 5 yrs)
- 5) Marked increased effort of breathing (recession, tracheal tug, grunting)
- 6) Respiratory depression RR < 20 0-3 months, ≤ half normal value

C CIRCULATION

Persistent tachycardia following one bolus of 10mls / kg fluid
(HR ≥ 150 under 5 yrs; HR ≥ 120 5 – 12 years; HR ≥ 100 over 12 yrs)
OR Poor perfusion OR prolonged capillary refill (≥ 2 secs) + / - low systolic BP

D DISABILITY

Acute change in neurological status. Children scored by AVPU; responding only to pain OR unresponsive
Child who is seizing OR not responding to prescribed anticonvulsants

E OTHERS

- 1) Hyperkalaemia - K⁺ ≥ 6.0 mmol/litre
- 2) Any child with pH < 7.2 whatever the cause, base deficit -5 or greater
- 3) Any child with unresolved pain or escalating pain despite prescribed analgesia
- 4) Any child whose condition is worrying – but is not triggering any of the parameters

Results

Annual attendances in the PED went from 28,000 patients in 2008 to 34,000 in 2012. Figure 1 demonstrates that within this extra workload was more acuity as our Triage category 1&2 patients (who all require care within 10 minutes) were almost doubled in this period. Figure 2 demonstrates the overall increase in PEWT calls and crash calls from 2009 to 2012. There were 125 PEWT and crash calls in the three year period. This correlates with the increased acuity within the hospital during that time. Importantly, despite the increased acuity, both the overall number of crash calls and the proportion of these within the critically ill

hospital population reduced during the study. There were 149 trigger breaches by 137 patients since the introduction of the PEWT. 66 trigger breaches related to breathing while 50 breaches related to disability/neurological parameters. There were 27 due to circulation and 6 related to airway. We examined the outcomes in the PEWT group assess the accuracy of the trigger. Only 9/89 PEWTs resulted in the patient remaining on the ward where the call was triggered. 48/89 patients had their care escalated to the High Dependency Unit. Nine patients required transfer to a PICU for more intensive support. One patient died after the PEWT was called.

children. There have been multiple iterations of early warning scores for children. The first published data was from the Brighton PEWS by Monaghan et al³. The PEW System Score has been shown as a stronger predictor of cardiopulmonary arrest and can predict arrest by 11 hours⁴. The Bedside PEW System Score demonstrated a sensitivity of 82% and a sensitivity of 93% in predicting PICU admission⁵. The Bristol PEW tool has achieved a sensitivity of 99% in predicting escalation of care⁶. Rhandawa reported that cardiopulmonary arrests reduced by 37% in the cardiology/nephrology unit and 25% in general medical unit with an aggregate reduction in two pilot units of 31%⁷.

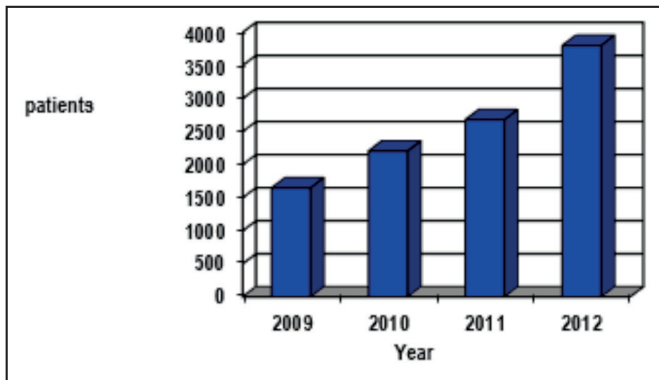


Figure 1: Category 1 & 2 patients 2009-2012

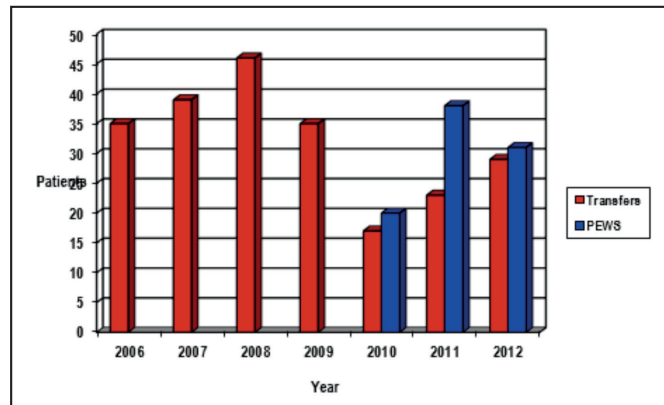


Figure 3: Impact of PEWT on critically ill transfers from Tallaght Hospital

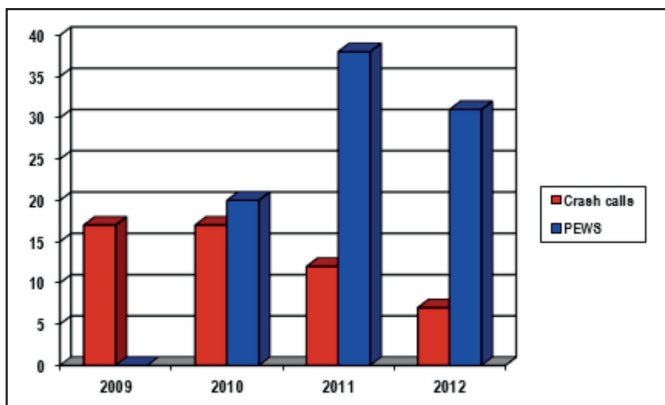


Figure 2: Crash calls and PEWT calls 2009-2012

Both the transfers and the PEWTs have risen during the study period in line with the increased acuity presenting to the ED. Figure 3 demonstrates the rising rate of critically ill transfers from 2006 to 2008. With the introduction of the PEWT system, the transfers reduced by 50%. In the triage categories one and two (i.e. all patients who require assessment by a doctor within 10 minutes of arrival to ED), the rate of transfer to PICU reduced from 1:50 prior to the introduction of the PEWT to 1:129, 1:118 and 1:131 during the three years after its introduction. Within the same group of sick patients, the rate of cardiac arrest similarly reduced from 1:100 prior to the introduction of the PEWT to 1:129, 1:216 and 1:542 in the three years after its introduction. When we examined the patient experience times within the hospital, we found that following introduction of the PEWT system, the time from first trigger breach to anaesthetic review reduced from 312 minutes to 166 minutes.

Discussion

This study demonstrates clearly, the usefulness and clinical impact of a simple, single-trigger, single-response Paediatric Early Warning System. We reduced our transfer rates of critically ill children and rates of crash calls through earlier recognition of the clinical state of these patients. We have also reduced the time taken to involve senior clinicians in the care of deteriorating

Our goal was to have a simple trigger which relied on information already being collected by nursing staff. We hoped to create a tool which would be useful in general and paediatric hospitals. We have achieved this by keeping the trigger to a single parameter resulting in a single, full team response. Studies have demonstrated that making a tool easier to use has a positive effect on the implementation of the tool in the Paediatric Emergency Department setting⁸. Studies have shown that 'For 17 PEW calls, one cardiac arrest might be prevented'⁹. This positive effect is reinforced in a number of systematic reviews on this topic. Tibbals et al demonstrated non-significant reductions in hospital-wide cardiac arrests and mortality¹⁰ post implementation of a PEWS-like system. Brilli et al was able to show that cardiorespiratory arrests on the general wards reduced for 0.27/1000 patient days to 0.11/1000 patients days ($p=0.03$)¹¹. Chan et al concluded in their systematic review that while cardiorespiratory arrest outside of ICU was reduced by 37% there is limited evidence to suggest improved survival¹². The use of PEWS in the Emergency Department setting is controversial. Bradman et al found that the Brighton PEWS had a low sensitivity (measured at 36%) for predicting those children needing admission¹³. While another study found that the same PEWS was unable to distinguish between those requiring ward or ICU admission¹⁴. Edgell et al. found a sensitivity of 70% and a specificity of 90% in predicting PICU admission using their Paediatric Advance Warning Score (PAWS)¹⁵. This demonstrates that the PEWS is not useful as a triage tool. Many of our patients would have been breaching the PEWS at triage but are suitable for routine emergency treatment and ultimately discharge from the Emergency Department. This may go some way to explaining why the time from breach to escalation of care remained at 166 minutes after the implementation of PEWS and the 50% reduction in this quantum is the more relevant result.

There was a fear that the introduction of this trigger would result in an excess of unnecessary reviews of patients. However, this was not experienced in our study. All patients who were reviewed following a PEW call had breached a physiological parameter. All demonstrated a deteriorating clinical condition and in the first year of operation, the total number of transfers and PEWT calls were the same as the previous year's transfers. Only 10% of the

patients had their care continued on a general paediatric ward indicating that the PEWT was generally appropriate. Both periods were examined retrospectively so we have shown significant reduction but we cannot claim a definite causal link. With the education surrounding the introduction of the PEWT, we can assume an increased awareness of the deteriorating child among the clinical staff. The education took place at the induction of new staff and sporadically throughout the period. There were no other alterations in staffing numbers experienced in the hospital during this time period which could have impacted on the outcomes.

This is the first study demonstrating the effectiveness of PEWT in an Irish hospital setting. We have demonstrated a significant reduction in the time to anaesthetic review for sick patients within our hospital. This early recognition has led to a reduction in transfers to paediatric ICU and crash calls during the study period. We have increased awareness of the need for closer monitoring of those patients who are not improving clinically and the PEW has become the standard of care within the hospital. The imminent arrival of the National PEWS document from the HSE is to be welcomed and the clinical improvements, which we have demonstrated, can be replicated across the Irish hospitals.

Correspondence: T Bolger

Paediatric Emergency Department, AMNCH, Tallaght, Dublin 24
Email: turlough.bolger@amnch.ie

References

- Zhai H, Brady P, Li Q, Lingren T, Ni Y, Wheeler DS, Solti I. Developing and evaluating a machine learning based algorithm to predict the need of pediatric intensive care unit transfer for newly hospitalized children. *Resuscitation*. 2014 Aug;85:1065-71.
- Roland D. Paediatric early warning scores: Holy Grail and Achilles' heel. *Postgraduate Medical Journal*. 2010 89: 358-365.
- Monaghan A Detecting and managing deterioration in children. *Paediatric Nursing* 2005 17:32-35.
- Duncan H, Hutchison J, Parshuram CS. The pediatric early warning system score: A severity of illness score to predict urgent medical need in hospitalized children. *Journal of Critical Care*. 2006 21:271-279.
- Parshuram CS, Hutchinson J, Middaugh K. Development and initial validation of the Bedside Paediatric Early Warning System score. *BioMed Central Critical Care*. 2009 13:R135.
- Haines C, Perrot M, Weir P Promoting care for acutely ill children – development and evaluation of a paediatric early warning tool. *Intensive and Critical Care Nursing*. 2006 22: 73-81
- Randhawa S, Roberts-Turner R, Woronick K, DuVal J. Implementing and Sustaining Evidence-Based Nursing Practice to Reduce Pediatric Cardiopulmonary Arrest. *Western Journal of Nursing Research*. 2011 33:443-456
- Seiger N, Maconochie I, Oostenbrink R, Moll HA. Validity of different pediatric early warning scores in the emergency department. *Pediatrics*. 2013.132:e841-e849
- Long term effect of a medical emergency team on cardiac arrests in a teaching hospital. D Jones et al *Crit care* 2005;9:R808-15.
- Tibballs J, Kinney S, Duke T, Oakley E, Hennessy M. Reduction of paediatric in-patient cardiac arrest and death with a medical emergency team: preliminary results. *Archives of disease in childhood*. 2005. 90: 1148-1152
- Brilli RJ, Gibson R, Luria JW, Wheeler TA, Shaw J, Linam M, Kheir J, McLain P, Lingsch T, Hall-Haering A, McBride M. Implementation of a medical emergency team in a large pediatric teaching hospital prevents respiratory and cardiopulmonary arrests outside the intensive care unit. *Pediatric Critical Care Medicine*. 2007 8: 236-246
- Chan PS, Jain R, Nallmothu BK, Berg RA, Sasson C RapidResponse Teams: A Systematic Review and Meta-analysis. *Arch Intern Med*. 2010 Jan 11;170:18-26
- Bradman K & Maconochie I. Can paediatric early warning score be used as a triage tool in paediatric accident and emergency? *European Journal of Emergency Medicine*. 2008 15:359-360
- Breslin K, Marx J, Hoffman H, McBeth R, Pavuluri P. Pediatric Early Warning Score at Time of Emergency Department Disposition is Associated with Level of Care. *Pediatric Emergency Care*. 2014 30:97-103
- Egdell P, Finlay L, Pedley DK. The PAWS score: validation of an early warning scoring system for the initial assessment of children in the emergency department. *Emergency Medicine Journal*. 2008 25:745-749.

The Role of Speech and Language Therapy in Assessing and Managing Pharyngo-esophageal Diverticula

E Holmes, C Kenny, M Samuel, J Regan, J O'Rourke, C McCoubrey
Speech and Language Therapy Department, AMNCH, Tallaght, Dublin 24

Abstract

This study explores the contribution of Speech and Language Therapists (SLTs) to the assessment and management of patients presenting on videofluoroscopic swallow studies (VFSS) with a suspected pharyngo-oesophageal diverticulum. Records for all patients who attended for VFSS in an acute hospital over an eleven-year period were examined (N= 1820). Twenty patients were identified on VFSS as having a suspected diverticulum. Symptoms suggestive of a diverticulum were found during both bedside clinical examination and radiographic examination e.g. respiratory difficulties (n=15; 75%), voice changes (n=14; 70%). VFSS confirmed a reduced risk of aspiration for 14 patients (70%) using a combination of fluid modification (n=9; 45%), food modification (n=13; 65%) and swallow strategies (n=14; 70%). VFSS confirmed aspiration directly related to the diverticulum in 11 patients (55%). Findings indicate that SLTs have the opportunity to identify potential diverticula and implement behavioural management to reduce associated health risks. This is of particular importance to patients who are awaiting, or cannot undergo, surgical repair of their diverticulum.

Introduction

Diverticula (also known as 'pouches') are classified on the basis of anatomical location (pharyngo-oesophageal, midesophageal or epiphrenic) and mechanism of origin (pulsion or traction). The most common diverticulum encountered by Speech and Language Therapists (SLTs) is the Zenker's Diverticulum (ZD). This is a pulsion diverticulum between the cricopharyngeal muscle and the inferior constrictor muscle in an area of weakness known as

Killian's Dehiscence¹. ZD was first described by Ludlow in 1769². Despite over two centuries of research, controversy surrounds this condition with regard to aetiology and pathophysiology. The most widely accepted theory at present is that diverticula are formed when there is normal relaxation of the upper oesophageal sphincter but inadequate opening³. ZD is an acquired condition, occurring more often in the elderly (people typically become symptomatic in the sixth to seventh decade of life³). There

is an incidence reported of 2 per 100,000 in the UK⁴. For patients referred for an examination of the upper oesophageal tract, the incidence can reach 1 in 1000¹. Men are affected 2-3 times more commonly than women and in 90% of cases the diverticulum is found to protrude to the left of the midline⁵. Because gastroesophageal reflux contributes to cricopharyngeal dysfunction, a relation between gastro-oesophageal reflux disease and ZD has been assumed, but it has never been consistently investigated⁶.

One of the most prominent symptoms of ZD is a progressive dysphagia, occurring in excess of 90% of patients¹. Initially, the diverticulum is small and symptoms may be subtle, but with time, an increasing amount of food material becomes trapped in the growing pouch and symptoms become more pronounced. Common postprandial features suggestive of ZD include: regurgitation of undigested food particles (even hours post-meal); noisy deglutition; choking or coughing; tasting dissolved medications long after swallowing them; and halitosis. In the advanced stages, larger bolus volumes collect in the diverticulum. Patients may then additionally complain of the need to swallow with effort to clear residue; weight loss; apathy towards eating and drinking; and voice changes⁷. Aspiration can occur at any stage as the contents of the pouch are ejected and spill into the airway. Patients in the advanced stages may present with a history of recurrent pneumonia or other respiratory difficulties⁸. Many of the above features are evaluated by SLTs at bedside by taking a detailed case history from the patient and through the bedside clinical examination of swallow. This represents an opportunity for identification of a potential diverticulum before formal radiological imaging takes place.

Pharyngeal diverticula are often diagnosed or confirmed during barium studies which allow for discrimination of size and location⁹. Videofluoroscopic Study of Swallowing (VFSS) is one such study. VFSS are commonly carried out by SLTs to identify the presence of dysphagia in patients by examining oropharyngeal swallow function. Being a cineradiographic procedure, VFSS also allows for identification of diverticula, as cineradiography has been shown to more accurately delineate and discriminate between the types and behaviours of diverticula compared with single radiographs¹⁰. VFSS can include imaging of the oropharyngeal and oesophageal regions in both a lateral and anterior-posterior (A-P) view. It allows for observation of this region before, during and after the swallow for retrospective comparison. Thus, any potential diverticulum filling with food or fluids can be observed as the examination progresses⁷ (Figure 1, Figure 2). It is worth noting that the postprandial features of a ZD mentioned previously may be symptomatic of other illnesses¹¹. As such, VFSS presents itself further as a valuable diagnostic tool to establish whether a diverticulum exists, or whether alternative explanations for symptoms ought to be explored.

Research using oesophageal manometry has shown that evaluation of swallowing soft solids in the upright position reveals differences in motility abnormalities that are otherwise overlooked by liquid swallows alone¹². This adds further merit to the benefits of VFSS as a diagnostic tool, since a variety of food and liquid consistencies can be trialled during this examination. VFSS may in fact be more valuable than single-shot barium swallows, as it may highlight the presence of a small diverticulum, which might otherwise have been missed⁷. Few articles specifically address patient candidacy for surgical intervention for pharyngeal diverticula. However, it is documented that many elderly patients are wrongly considered to be unsuitable for surgical intervention¹³. Surgical ineligibility criteria include 'advanced comorbidity, pulmonary frailty or a difficulty assuming appropriate postural positioning for endoscopic management'¹¹. If surgical intervention for a diverticulum is not to be considered for a patient, behavioural intervention then remains as the treatment of choice¹¹. The primary aim of behavioural management of diverticulum ought to be to reduce the volume of material aspirated. Postural changes

may be effective in preventing aspiration. For example, a head rotation to the left or right during swallow may serve to reduce or eliminate the volume of material that can enter the diverticulum, preventing pocketing and later aspiration of this material, once ejected from the diverticulum.

This study explores the role of the SLT in contributing to the comprehensive evaluation and management of a cohort of patients with suspected pharyngo-oesophageal diverticula. It also examines the follow-up that these patients received once onward referral for medical/surgical consideration was suggested.

Methods

A retrospective review was conducted of all VFSS reports between the years 2000-2011 at an Irish acute care hospital. During this time period, 1820 procedures were carried out. Patients attending for VFSS presented with a diverse range of aetiologies, including stroke, progressive neurological diseases (e.g. Parkinson's disease, MND), age-related illnesses (e.g. Alzheimer's disease), COPD, tracheostomy and general medical conditions (most frequently, LRTI). Reports on the outcomes of these procedures containing any suspicion of pharyngo-oesophageal diverticula were collated and exclusion criteria subsequently applied to this set. Exclusion criteria were: known diagnosis of a diverticulum prior to SLT involvement; VFSS conducted for private care patients; and VFSS carried out for external agencies. The latter two criteria were applied, as there was limited access to full medical records for these patients. Twenty cases remained once exclusion criteria were applied. Information was collated from both medical and SLT records relating to demographics, medical history, SLT findings on bedside clinical evaluation, findings on VFSS, radiologic and/or surgical follow-up. The authors analysed the dataset using descriptive statistics to explore the diagnostic value of SLT clinical and radiographic evaluations in contributing to a comprehensive assessment and management of patients with pharyngo-oesophageal diverticula and concomitant dysphagia.



Figure 1: Lateral view of Zenker's Diverticulum during videofluoroscopy



Figure 2: A-P view of Zenker's Diverticulum during videofluoroscopy

Results

Twenty patients met inclusion criteria. 90% (n=18) of patients who met the criteria for inclusion were aged over 60 years with a mean age of 77.5 years and a range of 44-88 years. 20% (n=4) of patients were suspected by the medical/surgical team to have a diverticulum prior to referral to Speech and Language Therapy, while a further 25% (n=5) of patients were suspected to have a diverticulum upon bedside evaluation of swallow by the SLT. Diverticulum was therefore not suspected as a cause of symptoms of dysphagia in 55% (n=11) of patients prior to videofluoroscopy. The investigation during assessment of symptoms commonly

associated with diverticula was explored. Table 1 outlines typical symptoms of ZD. It captures the incidence rates within our cohort as well as the frequency with which symptoms were not documented. The most common symptoms documented in our cohort reflect the most prevalent symptoms reported in the literature. For example respiratory difficulties are commonly associated with ZD and 75% of the patients presented with a history of respiratory difficulties.

Table 1: Common symptoms of diverticulum and incidences reported (N = 20)

Symptom	Incidence (%)	% of Data recorded	Data not recorded (%)
History of respiratory difficulties (e.g. LRTIs)	75%	85%	15%
Voice changes	70%	85%	15%
Coughing	65%	85%	15%
Regurgitation	35%	45%	55%
Apathy for eating/drinking	35%	40%	60%
Sensation of pharyngeal residue post-swallow	25%	30%	70%
Reflux	25%	45%	55%
Unintended weight loss	25%	60%	40%
Belching	20%	50%	50%
Choking	10%	25%	75%
Hypopharyngeal mucous collection	5%	40%	60%

Table 2: Compensatory Strategies trialled on VFU

Strategy	Explanation
Head Turn	Turn head to the right or left in order to redirect the flow of the bolus away from the diverticulum
Head Tilt	Tilt head back in order to redirect the flow of the bolus away from the diverticulum
Chin Tuck	Tuck chin down in order to redirect the flow of the bolus away from the diverticulum
Mendelssohn	Hold larynx up at height of swallow to increase extent & duration of laryngeal elevation and hence duration & width of upper oesophageal sphincter opening
Volume Control	Reduce quantity of fluid bolus using 5cc or 10cc beakers
Slow drinking rate	Reduce speed of flow through sips with time lapses
Other	Not specified

Of note, on videofluoroscopic examination by the SLT, 55% of patients were noted to have aspiration that was directly related to the presence of a diverticulum. In order to manage dysphagia associated with the diverticulum, each patient was trialled during VFSS with an average of 2 compensatory swallow strategies¹⁴⁻¹⁶. Table 2 lists different compensatory strategies trialled on VFSS. Food modification was recommended in 65% (n=13) of patients and fluid modification was recommended in 45% (n=9) of patients. Based on positive outcomes during VFSS, 70% (n=14) of patients were recommended to implement a swallow strategy. An outcome was deemed positive if it reduced the risk of penetration or aspiration of bolus material into the airway. All patients suspected on VFSS of presenting with a diverticulum were recommended by the SLT for onward referral for further investigation of the diverticulum. 50% (n=10) of these did not receive any medical or surgical follow-up. Of patients who received follow-up, 60% (n=6) had a radiological investigation (e.g. Barium Swallow), while 40% (n=4) had endoscopic investigation. A diverticulum was confirmed in 60% (n=6) of patients who received follow-up investigation. The remaining investigations confirmed the absence of a diverticulum (20%) (n=2) or yielded inconclusive outcomes (20%) (n=2).

Discussion

While the sample size of the patient cohort included in the study is small, it should be considered that this is reflective of numbers encountered in actual clinical practice. In a recent prospective study, just 49 patients from a cohort of 2,430 (2%) presented with a pharyngeal diverticulum⁴. In terms of contributing to diagnosis, it is evident from the findings above that the SLT is well-placed to support medical/surgical teams, both in terms of identifying signs and symptoms subjectively through case history taking, bedside clinical exam and through objective study using videofluoroscopy. Early identification and management of ZD is important as long-term medical implications include dysphagia, malnutrition and chronic respiratory difficulties resulting from aspiration⁵. Also of note is a 'real, but low risk of carcinoma developing in a pharyngeal pouch'⁴. Of concern is the high percentage of relevant symptoms which do not appear to have been explored by the assessing clinician. Lack of documentation of symptoms associated with ZD ranged from 15%-75% (Table 1). Behavioural management of pharyngo-oesophageal diverticula is also an aspect of treatment in which SLTs may provide a valuable service. Behavioural management was explored in this study during VFSS. Within our cohort, 70% of patients were found to benefit from SLT-led behavioural management. We do however need to be cautious in interpreting this finding, as some of our cohort had a coexisting neurogenic dysphagia. As such, further research focusing on behavioural management of dysphagia caused by diverticula in isolation is required. Given the high percentage of patients who benefited from behavioural management, patients who are awaiting or are ineligible for surgery should be considered for referral to Speech and Language Therapy.

Finally, it is worth noting that 50% of patients recommended by SLT for follow-up due to a potential diverticulum did not receive any such follow-up. The reasons for this were not investigated in this study. Given the medical consequences of lack of treatment, room clearly exists for collaboration between medical/surgical teams and Speech and Language Therapists for patients presenting with a pharyngo-oesophageal diverticulum.

Correspondence: E Holmes

Speech and Language Therapy Department, AMNCH, Tallaght, Dublin 24

Email: liz.holmes@amnch.ie

References

- Scher R. Zenker's Diverticulum. In: Flint P, Bruce H, Haughey J, John K, Niparko M, Richardson K, Lund V. (ed.). Cummings Otolaryngology: Head and Neck Surgery Philadelphia: Mosby Elsevier, 2010, 987-997.
- Ludlow A. A Case of obstructed deglutition from a preternatural dilation of and bag formed in the pharynx. In: Johnson W. CT, (ed.). Medical observations and inquiries by a society of physicians in London. London 1769, 85-101.
- Sen P, Lowe D, Farnan, T. Surgical interventions for pharyngeal pouch. Cochrane Database of Systematic Reviews. 2011; 9.
- Murray I, Grimes D, Wilde A, Palmer J, Waters C, Dalton H. Incidence and predictive features of pharyngeal pouch in a dysphagic population. *Dysphagia*. 2014; 29: 305-9.
- Cook I. Cricopharyngeal function and dysfunction. *Dysphagia*. 1993; 8: 244-51.
- Ferreira L, Simmons D, Baron T. Zenker's diverticula: pathophysiology, clinical presentation, and flexible endoscopic management. *Diseases of the Esophagus* 2008; 21: 1-8.
- Siddiq MS S. Current management in pharyngeal pouch surgery by UK otorhinolaryngologists. *Annals Royal College of Surgeons of England*. 2004; 86: 247-52.
- Liu JJ, Kahrilas PJ. Pharyngeal and esophageal diverticula, rings, and webs. *GI Motility online*. 2006; Part 1 Oral cavity, pharynx and esophagus.
- Herbella FP, M. Modern pathophysiology and treatment of esophageal diverticula. *Langenbeck's Archives of Surgery*. 2012; 397: 29-35.
- Ekberg ON, G. Lateral diverticula from the pharyngo-esophageal junction area. *Radiology*. 1983; 146: 117-22.

11. Coyle J. Zenker Diverticulum (ZD). In: Jones H, Rosenbek, J. (ed.). *Dysphagia in Rare Conditions*. San Diego: Plural Publishing, 2010, p. 671-80.
12. Bernhard A, Pohl D, Fried M, Castell D, Tutuiian R. Influence of bolus consistency and position on esophageal high resolution manometry findings. *Digestive Diseases and Sciences* 2008; 53: 1198-205.
13. Crescenzo D, Trastek V, Allen M, Deschamps C, Pairolero P. Zenker's Diverticulum in the Elderly: Is Operation Justified? *The Annals of thoracic surgery*. 1998; 66: 347-50.
14. Mendelsohn MS MF. Function in the pharyngoesophageal segment. *Laryngoscope*. 1987; 97: 483-9.
15. McCullough GH, Kamarunas E, Mann GC, Schmidley JW, Robbins JA and Cray MA. Effects of Mendelsohn maneuver on measures of swallowing duration post stroke. *Top Stroke Rehabil*. 2012; 19: 234-43.
16. Bodén K HA, Witt Hedström H. Effects of three different swallow maneuvers analyzed by videomanometry. *Acta Radiol*. 2006; 47: 628-33.

Utilisation of Clinical Networks to Facilitate Elective Surgical Workload; A Preliminary Analysis

T Burke¹, P Waters², RM Waldron², K Joyce², I Khan¹, W Khan¹, M Kerin², K Barry¹

¹Department of Surgery, Mayo General Hospital, Castlebar, Co Mayo

²Department of Surgery, Galway University Hospital, Newcastle Rd, Galway

Abstract

Clinical networks have potential to increase elective surgical workload for benign conditions in non-cancer centres. The aims of this study were to determine outcomes for elective laparoscopic cholecystectomy in our unit and to evaluate early experience in managing benign surgical workload referred from the tertiary centre within our clinical network. An analysis of cholecystectomies performed at Mayo General Hospital was conducted (2003-2013). A review of elective procedures more recently referred from Galway University Hospital (GUH) waiting lists was also conducted. 1937 consecutive cholecystectomies were performed with an overall laparoscopic conversion rate of 1.7% (33/1875). The total major complication rate was 0.93% (18/1937). 151 selected procedures originating from GUH have been performed since December 2013 without adverse events. Laparoscopic cholecystectomy can be performed in significant volume in the general hospital environment. This and other appropriate benign surgical procedures may be performed outside of tertiary units according to network agreements.

Introduction

The recent establishment of hospital networks in Ireland combined with strategic policy changes outlined in the document "Securing the future of Smaller Hospitals" may facilitate the designation of certain benign procedures to be performed electively in large volumes in general hospitals¹. Potential changes to the delivery of elective surgical services within each hospital network will have implications for patients, hospitals and surgical training. Laparoscopic cholecystectomy is considered in many institutions as a non-specialist operation and a significant training procedure for aspiring laparoscopic surgeons. It has been suggested recently that improved outcomes and reduced conversion rates can be achieved if laparoscopic cholecystectomy is performed by specialist upper gastro-intestinal surgeons performing a high volume of cases annually. Furthermore the author advocates that

the procedure should be moved from the non-specialist surgeon to the exclusive domain of high volume upper gastro-intestinal surgeons². Against this background, the primary aim of this study was to perform a systematic review of the practice of laparoscopic cholecystectomy at our institution. The secondary aim of our study was to perform an analysis of elective surgical caseload transferred from the regional tertiary centre to our unit.

Methods

A comprehensive analysis was performed of all cholecystectomies performed at Mayo General Hospital (MGH) during the study period, January 2003-December 2013 inclusive. MGH is a teaching hospital within the Galway University Hospital Network (Saolta) and primarily serves a catchment population of 130,000 people. Our institution contains 325 in-patient beds across

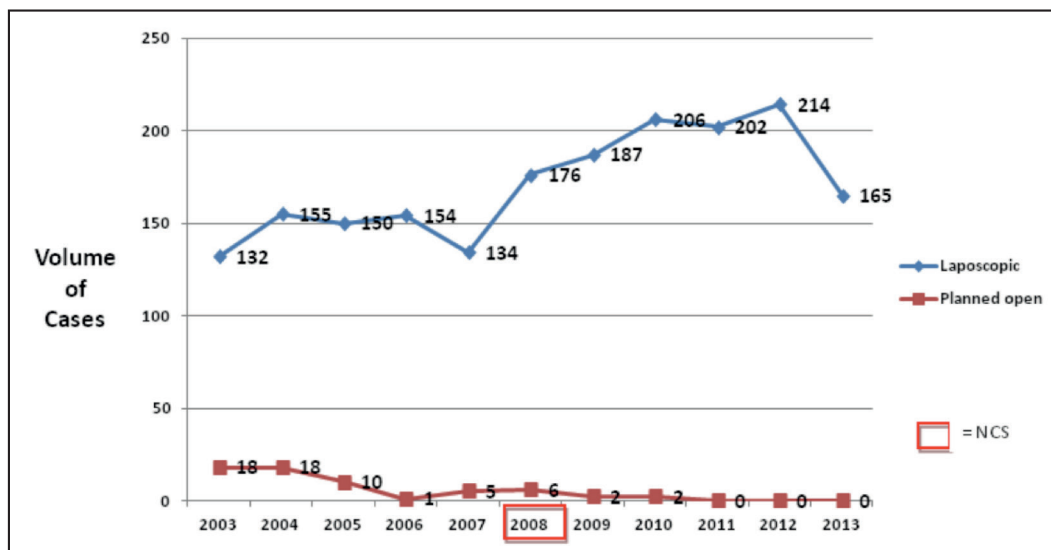


Figure 1: Impact of the introduction of the National Cancer Strategy (2007 – 2008) resulting in increasing volume of laparoscopic cholecystectomy with decreased planned open procedures performed

Table 1: 33 cases that were converted to an open procedure during the study period. The red box represents a decline in conversion to open cholecystectomy (<2%) from 2007 to 2013.

	Reason for Conversion												Total
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013		
Dense adhesions	4	2	2	2	-	-	1	-	-	-	-	-	11
Empyema/ Inflammation	5	1	-	1	-	1	-	1	-	-	-	-	9
Unable to define anatomy	1	2	-	2	-	-	1	1	-	-	-	-	7
Fibrosed Gallbladder	-	1	1	-	-	-	1	-	-	-	-	-	3
Elevated BMI	1	-	-	-	-	-	-	-	-	-	-	-	1
Bleeding	1	-	-	-	-	-	-	-	-	-	-	-	1
Abdominal Wall Unsuited	-	-	-	-	-	-	-	-	1	-	-	-	1
Total	12	6	3	5	0	1	3	2	1	0	0	0	33

multiple specialities and a 24 hour accident and emergency department (Model 3 hospital). The surgical unit previously consisted of 60 inpatient surgical beds. Seventeen of these beds were decommissioned in 2010 for budgetary reasons. The remaining 43 beds were then ring-fenced to elective and emergency general surgical patients, across two adjacent wards. The surgical department is staffed by four consultant surgeons without a declared interest in upper gastro-intestinal surgery. It is our unit policy to avoid cholecystectomy for the acutely inflamed gallbladder. Interval cholecystectomy for acute cholecystitis is performed routinely between four and six weeks after the index admission. Data was collected from the Health Information Patient Enquiry (HIPE) system, patient medical records and operating theatre registers. This included details of elective procedures referred from Galway University Hospital (GUH) waiting lists from December 2013 to date. Further information regarding laparoscopic conversion and complications rates was captured from analysis of monthly morbidity and mortality conference records. Statistical analysis was performed using SPSSV20. Ethical approval to conduct all aspects of this study was granted by the hospital research ethics committee.

Results

Volume and conversion rates for laparoscopic cholecystectomy
During the study period, 1937 patients (M-242, F-1695) underwent cholecystectomies with an average age of 46.8 years (16-90 years). 1875 elective laparoscopic procedures (M-217, F-1658) and 62 planned open cholecystectomies (M-25, F-37) were performed (Figure 1). The volume of laparoscopic procedures increased throughout the study with the greatest rise occurring between 2007 and 2008 coinciding with the introduction of the National Cancer Strategy (NCS). Furthermore, there was a corresponding decline in planned open procedures with no patients requiring a planned open cholecystectomy since 2011. A decline in the number of cholecystectomies performed in 2013 was secondary to departmental budgetary constraints. The overall conversion rate from attempted laparoscopic cholecystectomy to the open method for the study period was 1.7% (33/1875). The conversion rate was noted to decline during the study period from 8.3% in 2003 to <2% recorded in each of the years from 2007 – 2013 (Table 1). The single greatest reason for conversion to an open procedure was due to dense omental and gallbladder adhesions concealing the biliary anatomy and duodenum (n=11). Moreover, the presence of an empyema of the gallbladder or the inability to safely define the biliary anatomy prior to clipping the cystic duct and artery were also common reasons for conversion to open cholecystectomy (n=9, 7) respectively.

Major complications encountered during cholecystectomy

During the study period, the total major complication rate was 0.93% (18/1937), (Table 2). There was no significant difference in morbidity experienced between the laparoscopic and planned open groups. Within the laparoscopic group, the complication rate was 0.8%. The most commonly encountered complication was

a bile leak (n=9, 0.48%). Eight bile leaks settled with radiologic drainage of the biloma/endoscopic insertion of common bile duct stent and temporary insertion of an abdominal drain. One case required transfer to a hepatobiliary unit for monitoring however the patient did not require further surgical intervention. There were four cases of haemorrhage requiring return to theatre within 24 hours of index surgery (n=2) or greater than 2 units of packed red cells transfused post-operatively (n=2). Furthermore there was one case of common bile duct injury requiring transfer to a specialist hepatobiliary unit for definitive open repair. Within the laparoscopic cohort, there was one case of small bowel ischaemia which was presumed secondary to increased intra-peritoneal pressure and prolonged operative time. There was a significant difference in mortality rates between both groups (p<0.05). Four cases of mortality were documented in the planned open group. One of these deaths was attributed to post operative myocardial infarction (ASA 3), one to multi-organ failure (ASA 3), and two were attributed to respiratory sepsis (ASA 4 and 3). Complications observed in the laparoscopic conversion group (n=33) included surgical site infection (n=5), retained common bile duct stone (n=1) and cardiac arrhythmia (n=1).

Table 2: The major complications encountered within both groups during the study period

Complication	Laparoscopic	Planned Open
Common bile duct injury	0.05% (1/1875)	0% (0/62)
Bile leak	0.48% (9/1875)	0% (0/62)
Bowel ischaemia	0.05% (1/1875)	0% (0/62)
Haemorrhage	0.21% (4/1875)	0% (0/62)
Death	0% (0/1875)	6.4% (4/62)

Table 3: The procedures performed as part of the initiative of redistributing cases within the Saolta Network

Inguinal Hernia Repair	60
Laparoscopic Cholecystectomy	49
Umbilical Hernia Repair	17
Haemorrhoidectomy	10
Soft Tissue Lesions	5
Varicose veins	4
Hydrocele repair	4
Pilonidal Sinus	2
Total	151

Details of procedures performed on patients referred from Galway University Hospital

Since the commencement of this initiative in December 2013, 151 selected elective procedures classified as intermediate level surgery have been performed at MGH. These cases were originally scheduled at GUH. The majority of the caseload consisted of hernia repairs, laparoscopic cholecystectomies and

haemorrhoidectomies. All patients were graded either ASA 1 or 2. No significant adverse events were recorded in this cohort.

Discussion

Clinical networks are an important pillar in the delivery of patient care in the UK³. Recent strategic policy documents in Ireland such as "Future Health" and the national clinical lead programmes have demonstrated a commitment to the development and implementation of clinical networks in this country^{4,5}. To date the most successfully implemented networks have concentrated on cancer, stroke and emergent cardiovascular care⁶. These have resulted in significantly improved patient outcomes. Numerous advantages have been outlined such as more effective use of scarce resources, enabling improved access, standardization of care, a faster spread of innovation, effective employment of proven quality and volume relationships and the combined expertise across the hospital group to be utilized to the fullest⁷. The transferring of patients between facilities within a network ensures that patients are assessed and treated in the most appropriate facility to their needs and in a timely fashion. This may lead to a substantial reduction in elective surgical waiting lists across networks and decrease or even negate the need for certain costly waiting list initiatives. The transfer of selected patients from tertiary facilities with long waiting lists to model 2 and model 3 facilities with availability of theatre time and competent staff may deliver improved patient care across hospital groups. The National Cancer Strategy was established in 2008, which led to the centralisation of cancer care services within eight large tertiary referral units. As a consequence, the nature of the surgical workload performed in our unit has altered to reflect a substantial reduction in surgical activity performed for malignant disease. Within our unit, this shift has facilitated a notable increase in the number of procedures performed for benign surgical disease including laparoscopic cholecystectomy⁸. Numerous studies have been published which demonstrate improved patient outcomes for surgical pathology when procedures are performed in high volume centres⁹⁻¹¹. The literature relating to improving outcomes for patients undergoing laparoscopic cholecystectomy in higher volume centres is varied. Several recent studies have reported reduced conversion rates and morbidity in higher volumes centres¹²⁻¹⁴. Alternatively, a recent study suggests that there is no association between surgeon volume and complication outcome after laparoscopic cholecystectomy¹⁵. In our study, rates of conversion were noted to decline inversely with increasing volume. With the continued introduction of clinical networks, any benefits in patient outcomes related to volume/outcome relationships can be fully exploited.

Departmental initiatives aimed at improving efficiency were introduced at MGH during 2011 including the development of a surgical pre-assessment clinic (PAC) and the introduction of a policy of day of surgery admission (DOSA)¹⁶. In addition, a number of technical refinements were introduced. These include the full implementation of a "10 Step Laparoscopic Cholecystectomy Checklist"¹⁷, judicious use of laparoscopic subtotal cholecystectomy and most recently transabdominal laparoscopic assisted regional anaesthesia¹⁸. These initiatives have streamlined the delivery of benign elective surgical care at our institution. As a consequence of discussions with local hospital management during 2014, additional capacity to perform between 180 and 200 inpatient surgical procedures for benign conditions per year was identified. A business case was prepared and accepted by GUH with selection of suitable procedures to be performed at MGH. Patients are identified who are waiting prolonged periods for elective benign procedures and offered the option of surgery at our institution. If accepted, they are reviewed at general surgical outpatient clinics at MGH, provided with an early date for surgery and assessed by the anesthetic team at the PAC. The transfer of surgical workload within clinical networks is a well-established practice in the United Kingdom. Benefits such as reduced cancellations, more predictable workflow, and enhanced patient

safety and experience have been identified¹⁹. Furthermore the new hospital activity based funding strategy in Ireland whereby the "money follows the patient" has potential to further incentivise the transfer of care for patients requiring certain procedures within clinical networks to hospitals most efficient in their provision²⁰. The process of selecting and transferring patients should be carried out however in a manner that is acceptable to patients, clinicians and administrative staff. This novel initiative is part of a regional strategy in evolution for the delivery of surgical services across the Saolta clinical network.

Laparoscopic cholecystectomy is considered an excellent training operation for aspiring laparoscopic surgeons²¹. The increased volume of benign surgical activity in our unit for procedures such as laparoscopic cholecystectomy combined with consultant commitment to improving and refining surgical techniques, employing modern surgical training tools and providing direct supervision for trainee-performed procedures has ensured an environment conducive to the development of basic laparoscopic skills²². A structured system of rotating surgical trainees through the different facilities within a clinical network has the potential to expose trainees to high volumes of both benign and malignant surgical cases. This will ensure maximization of available training opportunities and is in keeping with policies outlined in various health strategy documents^{1,4}. Laparoscopic cholecystectomy can be performed safely, effectively and in significant volume in the general hospital environment. This and other appropriate benign surgical procedures may be performed outside of tertiary units according to network agreements with numerous potential benefits for patients, hospitals and training of health care professionals.

Correspondence: T Burke
Wexford General Hospital, Wexford
Email: tpburke85@gmail.com

References

1. Securing the Future of Smaller Hospitals. <http://health.gov.ie/wp-content/uploads/2014/03/SecuringSmallerHospitals.pdf>
2. Andrews S. Does concentration of surgical expertise improve outcomes for laparoscopic cholecystectomy? 9 year audit cycle. *Surgeon* 2013;11;309-312
3. Edwards N. Clinical Networks. *BMJ* 2002;324:63
4. Future Health <http://health.gov.ie/blog/publications/future-health-a-strategic-framework-for-reform-of-the-health-service-2012-2015/>
5. Model of Care for Elective Surgery http://www.rcsi.ie/files/2013/20131216020529_Elective%20Surgery%20Implementatio.pdf
6. Boyle R. Clinical networks work and shouldn't be disbanded. *BMJ* 2013;346:25
7. Murphy JFA. *Ir Med J*. 2013; 106:68
8. Concannon ES, Robertson I, Bennani I, Khan W, Waldron R, Barry K. Life after the Cancer Strategy; analysis of surgical workload in the general hospital setting. *Ir J Med Sci* 2013;182;433-8
9. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, Batista I, Welch HG, Wennberg DE. Hospital volume and surgical mortality in the United States *N Eng J Med* 2002 346: 1128-37
10. Finks JF, Osborne NH, Birkmeyer JD. Trends in Hospital Volume and Operative Mortality for High-Risk Surgery. *N Eng J Med* 364:22 2011
11. McDermott AM, Wall DM, Waters PS, Cheung S, Sibbering M, Horgan K, Kearins O, Lawrence G, Patnick J, Kerin MJ, ABS Audit Committee. Surgeon and breast unit volume-outcome relationships in breast cancer surgery and treatment. *Ann Surg* 2013 258:808-13
12. Sakpal SV, Bindra SS, Chamberlain RS. Laparoscopic cholecystectomy conversion rates two decades later. *JSLs*. 2010 14: 476-483
13. Hobbs MS, Mai Q, knuiman MW, Fletcher DR, Ridout SC. Surgeon experience and trends in intraoperative complications in laparoscopic cholecystectomy. *Br J Surg*. 2006;2006;93:844-853
14. Harrison EM, O'Neill S, Meurs TS, Wong PL, Duxbury M, Paterson-Brown, Wigmore SJ, Garden OJ. Hospital volumes and patient

- outcomes after cholecystectomy in Scotland. Retrospective national population based study. 2012 May 23;344:e3330
15. Donkerervoort SC, Dijkman, Versluis PG, Clous EA, Vahl AC. Surgeon's volume is not associated with complication outcome after laparoscopic cholecystectomy. *Dig Dis Sci* (2014) 5;39-45
 16. Concannon ES, Hogan Am, Flood L, Khan W, Barry K. Day of surgery admission for the elective surgical inpatient: Successful implementation of the Elective Surgery Programme. *Ir J Med Sci* 2013;182;127-133
 17. Robb WB, Falk GA, Larkin JO, Waldron RM, Waldron RP. A 10 step intraoperative surgical checklist (ISC) for laparoscopic cholecystectomy. Can it really reduce conversion rates to open cholecystectomy. *J Gast Surg* 2012;16;1318-1323
 18. Elamin G, Waters PS, Hamid Het, O'Keefe HM, Waldron RM, Duggan M, Khan W, Barry MK, Khan IZ. Efficacy of a laparoscopically delivered Transversus Abdominus Plane block technique during elective laparoscopic cholecystectomy; a prospective double blind randomized trial. *J Am Col Surg* (Accepted for publication March 2015)
 19. Clinical Case for Reconfiguration of Surgical Services. <http://www.heartofengland.nhs.uk/wp-content/uploads/12.1-Surgery-Reconfiguration-Appendix-27-MAY-14.pdf>
 20. McElroy B, Murphy A. An economic analysis of money follows the patient. *Ir J Med Sci* (2014) 183:15-22
 21. Bockler D, Geoghegan J, Klein M, Weissmann Q, Turan M, Meyer L. Implications of laparoscopic cholecystectomy for surgical residency training. *JLS* 1999;3:19-22
 22. Robertson I, Traynor O, Khan K, Waldron R, Barry K. Higher surgical training opportunities in the general hospital setting: Getting the balance right. *Ir J Med Sci* 2013 182;589-93

Added Value of Stroke Protocol MRI Following Negative Initial CT in the Acute Stroke Setting

ML Gargan, HK Kok, J Kearney, R Collins, T Coughlan, D O'Neill, D Ryan, W Torreggiani, O Doody
AMNCH, Tallaght, Dublin 24

Abstract

The aim of the study was to determine the added value of stroke protocol MRI following negative initial CT brain in the acute stroke setting. A retrospective study was performed over a 6 month period in a tertiary referral stroke centre. Patients were selected from the stroke and radiology databases. Inclusion criteria: clinical stroke syndrome, negative initial CT with subsequent MRI study with diffusion weighted sequences. Ninety two patients were reviewed and 73 (M:F of 39:34, mean age 62.1 ± 14.0 years) met the inclusion criteria. Twenty MRI studies (27.4%) were positive for acute/ subacute ischaemia in the setting of a normal initial CT. The average time interval between initial CT and MRI brain imaging was 4.7 ± 2.6 days. Whilst CT continues to be the first line imaging investigation for acute stroke, MRI has substantial added value following negative initial CT in the diagnosis of stroke.

Introduction

Stroke is the third most common cause of death and the most common cause of acquired major physical disability in Ireland. Imaging plays a critical role in evaluating patients suspected of acute stroke, especially prior to initiating treatment. Guidelines from the Irish Heart Foundation on acute stroke assessment recommend that all Radiology departments involved in providing acute stroke services should provide 24 hour access to CT and fulfil three basic requirements of acute stroke imaging – to confirm the diagnosis and determine the type of stroke as either ischaemic or haemorrhagic, to exclude other conditions that can mimic stroke or present with stroke-like symptoms, to evaluate the appropriateness of acute treatment such as thrombolysis. A non-contrast computed tomography (CT) scan of the brain is the accepted standard of care imaging modality in the exclusion of intracranial haemorrhage (ICH). Advantages of CT include its availability, relative cost effectiveness and accuracy in detection of ICH. However, the diagnosis of early acute ischaemic stroke on CT is more challenging and relies on the detection of subtle signs such as parenchymal hypodensity, focal areas of cytotoxic oedema and mass effect and hyperdense vessels indicative of intravascular thrombus.^{1,2} Indeed, the reported overall sensitivity of CT in this setting is poor (46.9%)³. Interobserver agreement between neuroradiologists in the assessment of early CT signs of brain infarction has been shown to vary substantially, from 49% to 71%, with greatest variability achieved for the assessment of parenchymal hypodensity in the right hemisphere.²

Magnetic resonance imaging (MRI) of the brain with a tailored protocol to stroke imaging with diffusion weighted sequences (DWI) and perfusion is now established as a valuable problem solver in delayed or atypical clinical presentations of suspected stroke, or where there is diagnostic uncertainty after an initial CT. When compared to CT, MRI has a superior sensitivity and specificity of 96.6% and 100% respectively with MR perfusion and DWI sequences demonstrating ischaemia best.^{3,4} However, the provision of acute MRI in stroke presents its own challenges

including limited out of hours access and cost, longer imaging time, patient tolerability, and safety concerns out of hours. DWI based stroke protocol sequences also have limitations with false negative rates reported in the literature ranging from 0%-21% depending on infarct location and timing.⁵ One study, in particular, found that false negative studies occurred more often in cases of posterior (19%) versus anterior (2%) circulation strokes, or when DWI was obtained within 24 hours of symptom onset.⁵ Our aim in this study was to assess the number of acute strokes diagnosed on DWI imaging in the setting of a negative initial CT at presentation in a tertiary referral stroke centre in Ireland.

Methods

A retrospective study of all MRI brain imaging for acute stroke presentations over a 6 month period (January to June 2014) was performed. Data was obtained from the in hospital radiology information system and included patient demographics, indication for imaging, timing of the studies relative to clinical presentation and imaging findings. Patients were included if they had a clinical syndrome suggestive of stroke, a negative initial CT brain study performed within 12 hours of admission and if they underwent an MRI brain stroke protocol study within 2 weeks of presentation. Studies were excluded if there was no CT at initial presentation, if ischaemic changes were present at the initial CT examination or if the indication for MRI brain was not to diagnose an acute stroke. CT imaging was performed on a multidetector CT system (Aquilion 64, Toshiba, Japan) with a tube potential of 120kVp and tube current modulation. Images were acquired in 0.5 mm slice thickness and reconstructed using a soft tissue kernel in 5 mm slices in the axial, coronal and sagittal planes. MRI imaging was performed on one of two 1.5T magnets (Magnetom Aera or Symphony, Siemens AG, Erlangen) and our stroke protocol consists of a T1 spin echo sagittal sequence, axial T2 fast spin echo and fluid attenuation inversion recovery (FLAIR) sequences, axial T2* gradient echo sequence followed by echo planar DWI sequences in three b values (0, 500 and 1000) with apparent

diffusion coefficient (ADC) maps. Average imaging time for this protocol is approximately 15 minutes.

All studies were initially reported by general radiologists with experience in acute neuroimaging. Positive imaging findings on CT for acute stroke are well described in the literature and include parenchymal hypodensity, obscuration of the insular ribbon or basal ganglia, loss of grey-white matter differentiation, areas of cytotoxic oedema with sulcal effacement and mass effect and hyperdense intracranial vessels. Positive MRI findings for acute ischaemia include T2 and FLAIR signal hyperintensity with corresponding cytotoxic oedema, mass effect and evidence of diffusion restriction on DWI sequences. Subacute infarcts were diagnosed when a DWI abnormality was present with corresponding normalisation of ADC changes. Following inclusion to our study, further review was performed by two experienced radiologists in consensus. Data were expressed as mean \pm standard deviation where appropriate.

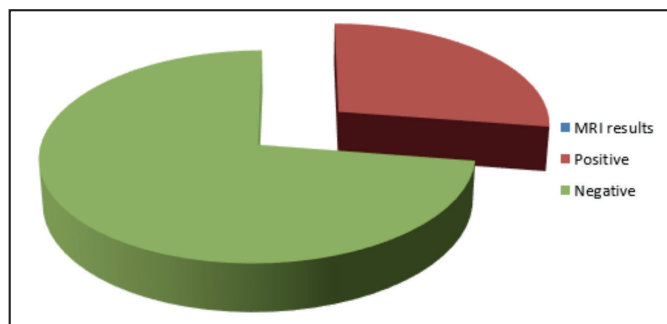


Figure 1: Chart depicting the percentage of MRI brain images that were positive on DWI

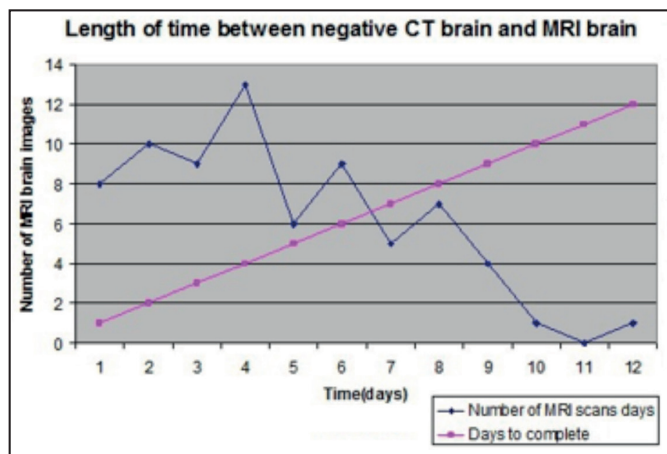


Figure 2

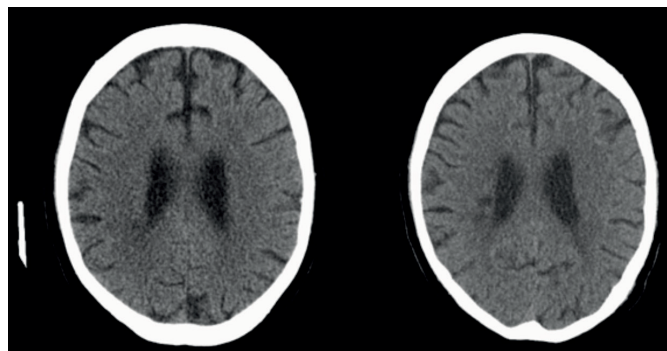


Figure 3 (A): Non contrast CT brain at presentation demonstrates mild background white matter vasculopathic changes without evidence of an acute infarct. (B) Follow up CT two weeks following initial presentation demonstrates interval development of a focus of hypoattenuation in the right centrum semiovale, consistent with an established lacunar infarct

Results

Seventy three patients met the inclusion criteria and were included in the study, comprising 39 male and 34 female patients with a mean age of 62.1 ± 14.0 years (range 29-86). All patients had a baseline negative CT brain for acute ischaemia performed within 12 hours of presentation to hospital. A total of 20 (27.4%) MRI studies were positive for stroke with 18 acute and 2 subacute infarcts diagnosed. Thirteen infarcts were left hemispheric and seven were right hemispheric. Lacunar infarcts involving the white matter, internal capsule or basal nuclei were the commonest ischaemic lesion diagnosed (13 patients) followed by anterior circulation infarcts involving the anterior and middle cerebral artery territories (7 patients). Fifty-three studies were negative for an acute infarct on DWI. Of these, 13 (24.5%) were diagnosed as TIA, 9 (17%) as migraine and 4 (7.5%) as sepsis. 7 (13.5%) were given a clinical diagnosis of stroke despite negative DWI findings. The remaining 20 (37.7%) had diagnoses of Bell's palsy, vertigo, head injury, seizure, symptomatic hypertension, peripheral neuropathy, L5/S1 disc bulge, TGA, functional disorder, viral encephalitis, vestibular neuronitis, manifestation of a prior stroke and a cavernoma. No posterior circulation infarcts were diagnosed in our cohort. The average time interval between initial CT and subsequent MRI brain imaging was 4.7 ± 2.6 days. None of the MRI studies were performed on the same day as the CT and therefore, no MRI imaging was performed in the hyperacute phase of stroke.

Discussion

The utility of imaging in stroke is evolving in tandem with technological advancements. CT remains the initial imaging modality in suspected acute stroke syndromes due to widespread 24 hour access, speed and familiarity with interpretation, and its' sensitivity in excluding haemorrhage, which is of greatest clinical significance to initial acute management of patients. However, a negative initial CT does not reliably exclude a diagnosis of stroke in a patient presenting with an acute neurological deficit. Our results support previous experience showing MRI to be superior to CT in reaching a diagnosis of acute ischaemia on imaging. When performed acutely within the thrombolysis window of 4.5 hours, this has the potential to better triage patients prior to intravenous thrombolysis, enabling the exclusion of patients in whom risky invasive treatment was not necessary.⁵ However, this is rarely achievable in practice with current competing clinical demands on a limited number of MRI scanners in the country. The main added value of MRI as demonstrated in our study, is in the 'problem solving' of clinically suspected stroke but with a negative initial CT for acute ischaemic change. This may have an important clinical impact in subsequent choice of and intensity of investigation, where an embolic pattern or 'shower' effect can be seen on the DWI. It may also have an important role in determining whether an actual infarction has occurred, which is necessary for many critical illness benefits, whereby patients claim after an event.

The time interval between initial CT and subsequent MRI can have an impact on overall diagnostic accuracy as it has been shown that significant events occur between the first 24 hours and the subacute follow-up, implying that a small infarct, not initially picked up on CT can increase in size. This is due to a number of factors including extension into the penumbra, lysis of proximal emboli with reperfusion/distal embolisation and spread of secondary oedema.⁶ It has also been proven that the reduction in ADC observed in human stroke persists after stroke onset up to 6 days on average with a significant reduction for at least 96 hours.⁷ Therefore, this study is not a direct comparison of CT and MRI in the same clinical setting. It must also be considered, that even when possible, the diagnosis of early stroke on CT is often relatively difficult, as the CT findings may be quite subtle. Fiebach et al looked at comparison of CT with DWI MRI in hyperacute stroke and found a moderate interobserver variability in interpretation of CT findings in acute stroke. There was consensus as to the extent of the infarct in only 8 out of 31 patients. In

one patient, all three raters made a different interpretation of where the stroke was. However, an area of high signal on DWI, consistent with early ischemic change was identified in all patients.⁸ False negative MRI studies are not uncommon during the first 24 hours of an ischaemic stroke, particularly with vertebrobasilar ischaemic strokes.⁵ It is likely that the optimal timing for MRI in this setting takes place between 24-72 hours following the initial CT. There are no guidelines at present in Ireland as to how quickly an MRI brain should be performed in the case of diagnostic uncertainty following a negative initial CT. The mean waiting time for an MRI in our series was 4.7 days. However, this does not accurately reflect inpatient access time to MRI for stroke as it does not distinguish between actual waiting time and the decision time interval involved prior to proceeding to further MRI evaluation.

Our study has a number of limitations. None of the investigators met the patients who were scanned to verify clinical findings and patients were selected on the basis of clinical information provided on the imaging request. There was also a variable time difference between the initial CT and subsequent MRI studies, which is perhaps a more accurate representation of an acute imaging case mix in a busy tertiary hospital. In conclusion, our study shows added value of performing a DWI-based stroke protocol MRI examination, in patients with a negative initial CT, in the setting of acute stroke. It is a powerful problem solving imaging modality.

Correspondence: ML Gargan
AMNCH, Tallaght, Dublin 24
Email: garganma@tcd.ie

References

1. Sunshine JL, Tarr RW, Lanzieri CF, Landis DM, Selman WR, Lewin JS (1999) Hyperacute stroke: ultrafast MR imaging to triage patients prior to therapy. *Radiology* 212:325-332
2. Von Kummer R, Holle R, Grzyska U, Hoffman E, Jansen O, Petersen D, Schumacher M, Sartor K (1996) Interobserver agreement in assessing early CT signs of middle cerebral artery infarction. *AJNR Am J Neuroradiol* 17:1743-1748
3. Davis DP, Robertson T, Imbesi SG (2006) Diffusion-weighted magnetic resonance imaging versus computed tomography in the diagnosis of acute ischemic stroke. *J Emerg Med* 31:269-277
4. Gonzalez RG, Schaefer PW, Buonanno FS, Schwamm L, Budzik R, Rordorf G, Wang B, Sorenson AG, Koroshetz W (1999) Diffusion-weighted MR imaging: diagnostic accuracy in patients imaged within 6 hours of stroke symptom onset. *Radiology* 210:155-162
5. Oppenheim C, Stanescu R, Dormont D, Crozier S, Marro B, Samson Y, Rancurel G, Marsault C (2000) False-negative diffusion-weighted MR findings in acute ischemic stroke. *AJNR Am J Neuroradiol* 21:1434-1440
6. Bryan RN, Levy LM, Whitlow WD, Killian JM, Preziosi TJ, Rosario JA (1991) Diagnosis of acute cerebral infarction: comparison of CT and MR imaging. *AJNR Am J Neuroradiol* 12:611-620
7. Schlaug G, Siewert B, Benfield A, Edelman RR, Warach S (1997) Time course of the apparent diffusion coefficient (ADC) abnormality in human stroke. *Neurology* 49:113-119
8. Fiebich J, Jansen O, Schellinger P, Knauth M, Hartmann M, Heiland S, Ryssel H, Pohlers O, Hacke W, Sartor K (2001) Comparison of CT with diffusion-weighted MRI in patients with hyperacute stroke. *Neuroradiology* 43:628-632

Safety of Grass Pollen Sublingual Immunotherapy for Allergic Rhinitis in Concomitant Asthma

A Sahadevan, R Cusack, SJ Lane

Respiratory Department, AMNCH, Tallaght, Dublin 24

Abstract

Seasonal allergic rhinitis (AR) occurs predominantly as a result of grass pollen allergy. Grass pollen sublingual immunotherapy (SLIT) has been proven effective in treating AR¹. SLIT is currently licensed for use in AR with concomitant stable mild asthma. There is evidence that SLIT improves asthma control when primarily used to treat AR². The aim was to assess the safety of SLIT in patients with severe seasonal allergic rhinitis who have co-existing stable mild asthma. The secondary aim was to determine whether asthma control improved post SLIT. There was no deterioration in asthma control after 6-36 months of SLIT. 27/30 (90%) patients' asthma control remained stable or indeed improved ($p < 0.021$). Of this 15 (50%) patients' asthma improved. There was no statistically significant change in their asthma pharmacotherapy after SLIT ($p = 0.059$). In conclusion, grass pollen SLIT is safe and can potentially treat dual allergic rhinitis- mild asthmatic patients.

Introduction

In the presence of innocuous environmental aeroallergens, B cells in atopic individuals mature into plasma cells which produce allergen-specific IgE as opposed to IgM or IgG. This is carried out in conjunction with T helper (Th) lymphocytes which secrete a cytokine profile including IL-5, GM-CSF and IL-13 i.e. Th2-restricted. This process is called sensitization and renders the atopic individual at risk of subsequently developing allergic diseases such as rhinitis, eczema, and asthma. The allergen-specific IgE so generated binds inter alia, to the high affinity IgE receptor on mucosal and cutaneous mast cells (FCεRI). When these cells come into contact subsequently with the same allergen inhaled via the airway, they degranulate and generate newly formed mediators of inflammation and pro-inflammatory cytokines. Allergen immunotherapy (AIT) has been practiced for more than 100 years to treat allergic diseases, particularly rhinitis, venom anaphylaxis and controversially, asthma. AIT has been traditionally administered as subcutaneous injections (subcutaneous immunotherapy or SCIT) over a period of up to 3 years or even longer. The mechanism of action of AIT is unknown; however, best available evidence indicates that that administration of high

dose allergen in sensitised individuals results in the production of allergen-specific inert IgG4 antibodies, as opposed to biologically active IgE, now under the control of T regulatory cells which produce IL-10 as opposed to the Th2 cytokines. In 1986, the UK Committee on the Safety of Medicines Report (CSM) reported 26 fatalities in primary care over the preceding 30 years involving SCIT³. They recommended that the use of SCIT be restricted to specialist hospital centers and that patients were observed for a period of time (then 2 hours; now 1 hour) post subcutaneous injection. As most of the fatalities occurred in patients with concomitant asthma, they advised strongly against its use in dual allergic rhinitis-asthmatic patients. The practice of SCIT in UK and Ireland dramatically decreased since that time. SCIT continued to be a common treatment for AR in other jurisdictions such as the USA, most of Europe and Australasia⁴.

Seasonal allergic rhinitis in Ireland occurs predominantly as a result of grass pollen allergy i.e. hay fever. Treatment currently is symptomatic with antihistamines and topical steroids^{5,6}. These treatments do not alter the natural history of the condition and some patients are poorly responsive. Interest in AIT has resurfaced

in the UK and Ireland in recent years as a result of availability of high dose sublingual immunotherapy (SLIT) in allergic rhinitis. Coexisting asthma is not a contraindication but must be mild, controlled and with a demonstrable FEV1 of 80% or more prior to SLIT administration^{7,8}. The primary aim of this study was to assess the safety of grass pollen sublingual immunotherapy in patients with severe seasonal allergic rhinitis who have co-existing stable and mild asthma. The secondary aim was to determine whether asthma control improved post grass pollen sublingual immunotherapy.

Methods

This was a cohort observational prospective study. 30 patients undergoing grass pollen SLIT with concomitant treated asthma were studied. SLIT in this study comprised of either a sublingual tablet Oralair™ or Grazax™. Asthma was diagnosed based on clinical history and lung function testing in a specialist asthma center. Patients' total nasal symptom score (TNSS) was recorded before and after SLIT as well. The TNSS comprised of the following symptoms of AR; sneezing, runny nose, and itchy nose. This was each graded on a 4-point scale, with the maximum severity of allergic rhinitis scored at 9⁹⁻¹¹. Asthma control was categorised as controlled, partially controlled, and uncontrolled using the GINA 2014 assessment tool¹². The assessment tool was based on whether a patient had daytime asthma symptoms more than twice a week, any night waking due to asthma, reliever needed for symptoms more than twice a week, and limitations of activity. The asthma control was also analyzed using patients' pharmacotherapy step based on GINA 2014 (GINA Step 1-Step 5) before and after SLIT¹². Individual data was plotted reflecting change from baseline asthma control status after at least 6 months of SLIT.

Each patient's change in asthma control from baseline to end of study was documented as either a positive difference or a negative difference. The change in categories (uncontrolled, partially-controlled and uncontrolled) was documented as a numerical difference e.g. +1 indicating when a patient's asthma control improved by 1 category; partially-controlled to controlled or uncontrolled to partially-controlled. Results for change in a patient's pharmacotherapy step (GINA Step 1-Step 5) before and after SLIT was documented in a similar method. Zero (0) indicates no change in their asthma pharmacotherapy step after SLIT. -1 indicates the level of reduction in their pharmacotherapy step; indicating improvement e.g. if patient went from GINA Step 3 to GINA Step 2 after SLIT. +1,+2,+3 indicates the patient required increased pharmacotherapy e.g. a patient moving from GINA Step 2 to GINA Step 4 asthma pharmacotherapy is +2. Data was analyzed using Minitab v.17. Wilcoxon signed rank test, and McNemar test was used to compare nasal symptoms and asthma control before and after SLIT. A p value of less than 0.05 was considered statistically significant.

Table 1: Patient demographics	
Total asthmatics with allergic rhinitis receiving SLIT(n)	30
Average age	36.6
Range in age	6-74
Polysensitised (Percentage of total asthmatics)	26(87%)
Mono-sensitised (Percentage of total asthmatics)	4 (13%)
Duration on SLIT (Range in months)	6-36
Mean duration on SLIT (Months)	18.5
Range in FEV1 (Percentage predicted)	79-130

Results

Patient demographics are summarized in Table 1. Average age was 36 years. The range of baseline FEV1 was 80-130% predicted for age and height. All showed strong positive reactions to grass pollen on skin prick testing. Of interest, most of the

patients were polysensitized to multiple allergens particularly house dust mite, tree pollen, and animal danders. Only 4/30 were monosensitized to grass pollen. The range in duration of SLIT therapy in patients was six to thirty-six months. Figure 1 shows the TNSS before and after SLIT. TNSS pre therapy was 7.3 and improved to a mean score of 2.1. This was a statistically significant using Wilcoxon signed rank test (p<0.05). Figure 2 shows the change in asthma control before and after at least 6 months SLIT. 0 indicates no change in asthma control; - represents a deterioration in asthma control; + represents an improvement in asthma control. Overall there was no significant deterioration in asthma control before and after SLIT using the McNemar test (p<0.021). 27/30 patients' asthma control remained stable or indeed improved. 12/30 showed no change in asthma control; 3 showed a 1 category deterioration. 15/30 patients showed an improvement in asthma score and out of this 7/30 showed a 2 category improvement and 8/30 showed a 1 category improvement. Using the Wilcoxon signed rank test, there was a significant improvement in overall asthma control after SLIT (p<0.005). Figure 3 shows the change in asthma pharmacotherapy after at least 6 months of SLIT. 0 indicates no change; - indicates an increase in pharmacotherapy; + represents a reduction in pharmacotherapy. Overall 26/30 patients remained stable or reduced their pharmacotherapy after SLIT (p=0.059). Four patients required a step up in their asthma pharmacotherapy.

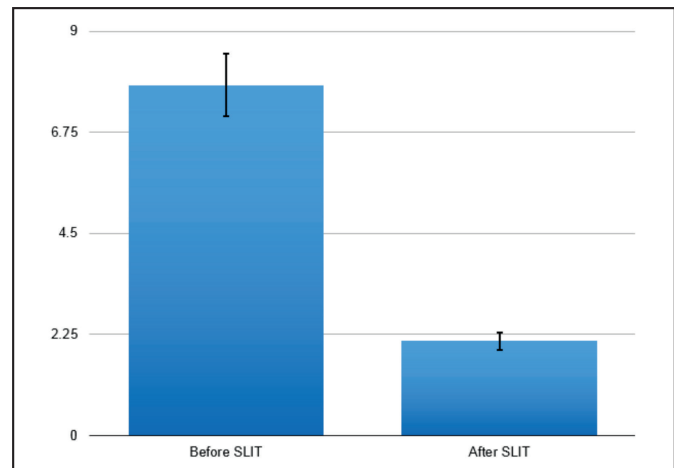


Figure 1: Mean total nasal symptom score (TNSS) before and after sublingual immunotherapy in 30 patients for a duration of 6 – 36 months. Results: Mean TNSS reduced from 7.8 to 2.1 using Wilcoxon signed-rank test (p<0.05).

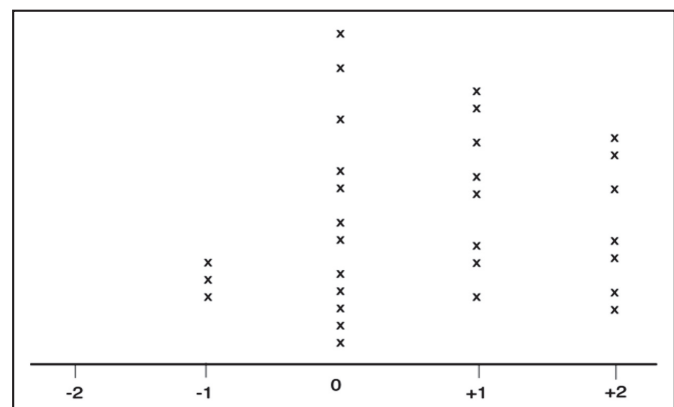


Figure 2: Change in asthma control using the GINA asthma control assessment (Categories: Controlled, partially uncontrolled, and uncontrolled) before and after at least 6-36 months of sublingual immunotherapy. Zero (0) indicates that a patient had no change in their asthma control after prolonged SLIT. +1 indicates the patient improved by 1 category (e.g. Uncontrolled to partially uncontrolled). +2 indicates patient improved by 2 categories.(e.g. Uncontrolled to controlled). -1 indicates patient's asthma control worsened by 1 category (e.g. partially controlled to uncontrolled). The improvements in asthma control were noted to be statistically significant P<0.005 using Wilcoxon signed rank test.

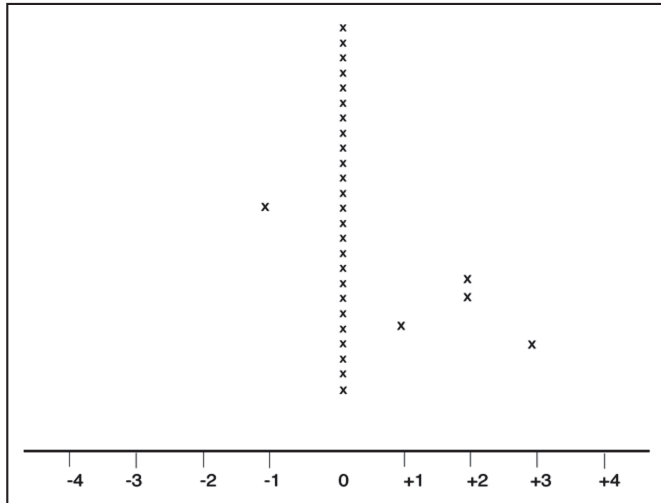


Figure 3: Change in asthma pharmacotherapy stepwise management (GINA Step 1-Step 5) before and after at least 6-36 months of sublingual immunotherapy. Zero (0) indicates no change in their asthma pharmacotherapy after prolonged SLIT. -1 indicates the levels of reduction in their pharmacotherapy step; indicating improvement. +1,+2,+3 indicates the patient required increased pharmacotherapy. There was no statistically significant change in pharmacotherapy after prolonged SLIT. $P=0.059$ using Wilcoxon signed rank test.

Discussion

This study demonstrates that grass pollen sublingual immunotherapy (SLIT) is safe in patients with controlled mild asthma while producing a significant improvement in their nasal symptom score (TNSS) for allergic rhinitis. In addition it demonstrated a significant improvement in asthma control with no significant change in asthma pharmacotherapy management. Furthermore, as most of patients demonstrated polysensitization, the importance of clinical allergy as opposed to sensitization in the blood is highlighted. The Oralair™ or Grazax™ tablet is placed under tongue for 1-2 minutes before swallowing it. Oralair™ is commenced pre grass pollen season in March and continued through to September for 3 consecutive years. It contains a mixture of freeze-dried extracts from the pollens of five grasses, including Timothy grass, Kentucky Blue Grass, Orchard, Perennial Rye, and Sweet Vernal. Grazax™ contains Timothy grass which is the major allergen in Ireland and UK and is commenced in March pre-season and continued each day for 3 years without an inter seasonal break. We avoid instituting SLIT during the grass pollen season as there is documented increase in bronchial hyper responsiveness during pollen season.¹³ This increase in bronchial hyper responsiveness is similarly noted in perennial allergic rhinitis e.g. house-dust mite atopic, where there are seasonal fluctuations in mite prevalence due to weather variations and temperature changes. Perennial allergic rhinitis is currently treated with either SCIT or SLIT without seasonal considerations. The first dose of both Oralair™ or Grazax™ tablet is initiated under medical supervision for one hour, however this is purely precautionary. Up dosing of Oralair is done over 3 days, while no up dosing is done with Grazax. SLIT is evidenced to be safer than SCIT, with no fatal events to date, and extremely rare reports of systemic adverse events.^{2,14} Commonly patients notice mild local reactions (e.g. perioral tingling, dyspepsia) during the first 2 weeks, which disappear with continued administration. If necessary, increased antihistamines can be dispensed to facilitate tolerance. Our findings replicate the findings of a recent systematic review by Lin et al, which found that sublingual immunotherapy was safe and associated with improvements in asthma symptoms². All placebo-controlled studies demonstrated a high strength of evidence in SLIT for the control of asthma symptoms. One of the studies included was Durham et al's multinational European study which documented a 39% reduction in 79 patients on daily grass

pollen SLIT's weighted asthma combined score when compared to placebo over the entire grass pollen seasons¹⁵. The research and evidence above builds on the 2010 Cochrane systematic review where SLIT was shown to be effective for allergic rhinitis and a safe method of administration¹. This systematic review had intentionally excluded research trials exclusively dealing with dual allergic rhinitis-asthma patients. The British Thoracic Society and Scottish Intercollegiate Guidelines Network (BTS/SIGN) has acknowledged the positive benefits of sublingual immunotherapy in their 2014 guidelines on asthma¹⁶. Despite this they did not advocate SLIT for routine management of asthma outside a specialist centre.

The 2014 Global Initiative for Asthma (GINA) consensus was that SLIT has potentially a role as add-on therapy for uncontrolled asthmatics with concomitant symptomatic allergic rhinitis. GINA also advises that potential benefits of SLIT must be weighed up against the risk of adverse effects, inconvenience and the cost of prolonged therapy e.g. 3 years in our centre¹². Our study is limited by our small cohort and the heterogeneity of our study population. This is mainly due to allergen-specific immunotherapy being a developing area in Irish allergy and asthma management. As current licensing also excludes SLIT from being used in patients with severe and uncontrolled asthma, we were limited to using SLIT in mild asthmatics. Furthermore this was an open label study which lends to treatment bias. There is also a lack of standardised scoring systems for asthmatic symptoms in patients with multiple allergic diseases. The standardisation of SLIT dosing (e.g. index of reactivity units) between different centres is another challenge to comparison of this papers' results with other similar trials. Professional societies like ARIA and BSACI are currently working on formalising in-vitro potency tests, dosing and treatment schedules to facilitate comparable research into the efficacy of SLIT.

The importance of our findings is consistent with WHO's position paper on allergen immunotherapy in 1998 which suggested that AIT can potentially be used in addition to asthma pharmacotherapy to get maximum benefit for asthmatics⁷. In conclusion, this study demonstrates grass pollen SLIT is clinically effective in allergic rhinitis and is both safe and may improve asthmatic control in patients with dual allergic rhinitis and asthma.

Correspondence: A Sahadevan
Respiratory Department, AMNCH, Tallaght, Dublin 24
Email: abhilash.sahadevan@gmail.com

Acknowledgements

J O'Callaghan (Respiratory Clinical Nurse Specialist), AMNCH.

References

1. Radulovic S, Calderon MA, Wilson D, Durham S. Sublingual immunotherapy for allergic rhinitis. *Cochrane Database Syst Rev*. 2010;CD002893.
2. Lin SY, Erekosima N, Kim JM, Ramanathan M, Suarez-Cuervo C, Chelladurai Y. Sublingual immunotherapy for the treatment of allergic rhinoconjunctivitis and asthma: a systematic review. *JAMA*. 2013;309:1278-88.
3. CSM Update: Desensitising vaccines. *Br Med J (Clin Res Ed)*. 1986;293:948.
4. Cox L, Jacobsen L. Comparison of allergen immunotherapy practice patterns in the United States and Europe. *Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology*. 2009;103:451-59; quiz 9-61, 95.
5. ARIA. ARIA Guidelines (Allergic rhinitis and its impact on asthma initiative) 2008 Update. <http://www.whiar.org/Documents&Resources.php>: 2008.
6. BSACI. BSACI Guidelines | Allergic and Non-Allergic Rhinitis. <http://www.bsaci.org/Guidelines/allergic-non-allergic-rhinitis>: 2015.

7. WHO. Allergen immunotherapy: therapeutic vaccines for allergic diseases. *Allergy*. 1998;53:1-42.
8. Calderón MA, Simons FE, Malling HJ, Lockett RF, Moingeon P, Demoly P. Sublingual allergen immunotherapy: mode of action and its relationship with the safety profile. *Allergy*. 2012;67:302-11.
9. Schiappoli M, Ridolo E, Senna G, Alesina R, Antonicelli L, Asero R, Costantino MT, Longo R, Musarra A, Nettis E, Crivellaro M, Savi E, Massolo A, Passalacqua G. A prospective Italian survey on the safety of subcutaneous immunotherapy for respiratory allergy. *Clin Exp Allergy*. 2009;39:1569-74.
10. Schatz M, Meltzer EO, Nathan R, Derebery MJ, Mintz M, Stanford RH, Dalal AA, Silvey MJ, Kosinski M. Psychometric validation of the rhinitis control assessment test: a brief patient-completed instrument for evaluating rhinitis symptom control. *Annals of allergy, asthma & immunology: official publication of the American College of Allergy, Asthma, & Immunology*. 104. 2010. 118-24.
11. Total_Nasal_Symptom_Score.pdf 2015. Available from: http://www.nwentallergy.com/docs/Total_Nasal_Symptom_Score.pdf.
12. From the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2014 <http://www.ginasthma.org/2014> [cited 2014 27.09.2014].
13. Tilles SA, Bardana EJ Jr. Seasonal variation in bronchial hyperreactivity (BHR) in allergic patients. *Clinical reviews in allergy & immunology*. 1997;15:169-85.
14. Larenas Linnemann DE, Blaiss MS. Selection of patients for sublingual versus subcutaneous immunotherapy. *Immunotherapy*. 2014;6:871-84.
15. Durham SR, Emminger W, Kapp A, de Monchy JG, Rak S, Scadding GK, Wurtzen PA, Andersen JS, Tholstrup B, Riis B, Dahl R. SQ-standardized sublingual grass immunotherapy: confirmation of disease modification 2 years after 3 years of treatment in a randomized trial. *J Allergy Clin Immunol*. 2012;129:717-25.e5.
16. BTS S. British guideline on the management of asthma. <https://www.brit-thoracic.org.uk/document-library/clinical-information/asthma/btssign-asthma-guideline-2014/>: British Thoracic Society, Scottis Intercollegiate Guidelines Network, 2015.

Young, Male and Feeling Suicidal in Ireland: Is Help or Harm Just One Click Away?

J Gilhooley¹, M Bolger², A Charles³, E Cleary³, A Lane⁴, K Malone³

¹AMNCH, Tallaght, Dublin 24

²Mater Misericordiae University Hospital, Eccles St, Dublin 7

³St Vincent's University Hospital, Elm Park, Dublin 4

⁴St John of God's Hospital, Stillorgan, Co Dublin

Abstract

Reports suggest an association between internet use and the elevated risk of suicide and self harm.¹ This study examined the resources a suicidal person might find when searching the internet 'front page' for help. Voluntary suicide help websites accounted for 7/12 front page hits. The National Suicide Research Foundation (NSRF) and the National Office for Suicide Prevention (NOSP), a blog and a newspaper article made up the remainder. Sites were difficult to navigate and highly variable in content. Phone credit was required in many cases in order to contact helplines; opening hours and locations were limited. Most statutory websites referred help-seekers to the voluntary sector, mainly the Samaritans. Information on fundraising and volunteering competed with other sources of help. Of concern, the front page also included links to methods to complete suicide. Irish professional medical bodies offered very limited advice. Our findings suggest that online information is variable and potentially harmful. There is an opportunity for all agencies and providers to generate a co-ordinated internet front page tailored for at-risk groups.

Introduction

Suicide is a major international public health problem and Ireland has the 4th highest youth suicide (15-24) in the EU.² The 'My World' survey (2012) indicates that the internet is one of the most preferred sources of mental health information for young people³ where it can provide support and empathy for those experiencing a mental health crisis. However, reports suggest that it can act as an incitement towards suicide.

Methods

We designed a survey of internet websites to determine the types of materials a suicidal person might find through a 'front page' internet search. Using the terms previously reported^{4,5}, we (JG,MB) simulated a person in suicidal distress⁶, going online. We keyed in the terms in previous international research, 'feeling depressed', 'feeling sad', 'suicide' into www.google.ie. We cleared our 'search history' and disabled 'Google ads', in order to decrease bias and content variability. We also examined the websites of a number of key Professional Medical Organisations to see what help they offered (Royal College of Physicians of Ireland, Irish College of General Practitioners, College of Psychiatrists of Ireland). Websites were coded by two raters together with consensus discussions with the two senior researchers who were independent of the research process and therefore 'blind' to the results.

Results

Voluntary suicide help websites accounted for 7/12 front page hits (Table 1). The front page included NSRF, NOSP, an anonymous and unregulated blog and a newspaper article regarding assisted suicide. Statutory agencies (NSRF, NOSP) referred help-seekers to the voluntary sector (6 of 8 links on NSRF and 4 of 8 links on NOSP). Most sites were difficult to navigate and required multiple 'clicks' to access helpful content. Most referred to GP, and to Emergency Departments during out-of-hour's. 'Face to face' support was minimal, most sites had limited opening hours, considerable geographical spread and were not cost-free. The Samaritans was the most common recommended onward site. On-line support was not tailored for specific groups. Sections on donations and volunteering were prominent and vied with or overshadowed help materials. Links to painless methods to complete suicide as well as other harmful and explicit content were prominent (Table 1). Irish Professional Medical organisations did not appear on the front page. When explored, the College of General Practitioners recommended "contacting a GP in your area" as well as journal articles and conferences on suicide prevention.

Discussion

For suicidal people, the internet front page information is variable in content and includes signposting for harm/suicide. Statutory and voluntary agencies refer to community help-sites with limited hours and often at some distance from the help-seeker. Overall,

Table 1: "Front page" websites when searching the Internet* using the word "suicide"

Name:	Email	Face to face	Phone	Text	Post	Online chat	Other
Samaritans	Yes (Response 12 hrs)	Yes	Yes (Local charge rates, open 24/7)	Yes	Yes (freepost, response within 7 days)	No	
Newspaper Articles	No	No	No	No	No	No	
Wikipedia	No	No	No	No	No	No	
Suicide Prevention	No	No	No	No	No	No	Offers links to the Samaritans, 1LIFE. Advises to contact GP/A&E in emergency.
1Life*	No	No	Yes 24 hour helpline	Yes (local rates apply)	No		
Metanoia	No	No	No	No	No	No	
Console	Yes	Yes (11 centre)	Yes (Freephone, 24hr)	No	No	No	
National Office for Suicide Prevention	Links to email the Samaritans/Pieta house	Links to Pieta house, Aware, Console.	Links to Samaritans, Aware, Console Childline.	Samaritans & Childline	Link to Samaritans	Links to Childline with 'online chat'	Online 'resources': Reachout, spunout, yourmentalhealth
Suicide or survive	No	'Eden Programme' Meetings held weekly for 6 weeks.	No	No	No	No	'Wellness Workshops' (practical tools and tips)
National Suicide Research Foundation	Multiple 'clicks' redirected to 'yourmental health' with email service	If urgent advised to go to GP and A&E	Links back to Samaritans	No	No	Multiple 'clicks' redirected to 'yourmental health' with 'twitter' and facebook options for instant message.	
Stop Suicide	Links to the Samaritans	Links to the Samaritans, GP service, A&E	Stopsuicide -Freephone, open 9am-6pm Mon-Fri. Links to Samaritans, 1life	Links to 1life. Headsup service which links to other help services.	No	No	
Suicide Aware	Email 'suicideaware@gmail.com'	Advises people to contact GP or A&E if in crisis.	Phone number for 'low cost counselling'.	No	No	No	'Amber Flag' initiative promotes 'Positive Mental Health' in Schools, Colleges by encouraging people to 'talk'.

*1life helpline now unavailable-advised to contact Samaritans if in crisis.

ehelp responses in other countries appear more coordinated, advanced and tailored to specific groups (www.mensline.org.au, www.breathingspacescotland.co.uk) and include Skype, hearing impaired and different language options. Front page signposting towards suicide is of concern. In 2005 the Australian Government banned 'inciting, promoting or teaching people how to commit suicide on the internet'⁴, as it may influence suicide risk in young people.¹ Like Recupero et al (2008)⁴ we found that professionally relevant medical bodies were not well represented among our results and did not guide people towards care. Recent technology initiatives by groups such as Reachout⁷, the Samaritans⁸, and sporting bodies⁹ are welcome but are not receiving prominence on the 'front page'. We suggest that professional, voluntary and statutory agencies should work together to generate an enhanced and coordinated, frequently updated and evaluated 'front page' presence, targeted for specific groups. This could start by focusing on 18 to 24 year old males who are at highest risk, are high internet information-seekers and where simulated patient experience could play a valuable role.⁶

Correspondence: J Gilhooley
Psychiatry Department, St Vincent's University Hospital, Elm Park, Dublin 4
Email: janeygilhooley@gmail.com

References

1. Daine K, Hawton K, Singaravelu V, Stewart A, Sinkin S, Montgomery P. The power of the web: A systematic review of studies of the influence of the internet on self-harm and suicide in young people *PLoS One* 2013 8: e77555
2. Central Statistics Office (www.cso.ie)
3. Dooley BA, Fitzgerald A: My World Survey: National Study of Youth Mental Health in Ireland. Headstrong and UCD School of Psychology, 2012-05.
4. Recupero PR, Harms SE, Noble JM. Googling Suicide: surfing for suicide information in the Internet. *J Clin Psychiatry*. 2008; 69: 878-888.
5. Huong Lai M, Maniam T, Fong Chan L. Caught in the Web: a review of web-based suicide prevention. *J Med Internet Res*. 2014; 16: e30
6. O'Connor K, King R, Malone KM, Guerandel A. Clinical examiners, simulated patients, and student self-assessed empathy in medical students during a psychiatry objective structured clinical examination. *Acad Psychiatry*. 2014; 38: 451-457
7. <http://ie.reachout.com/> 'Technology, Mental Health and Suicide Prevention'.
8. <http://www.samaritans.org/>
9. <https://www.gaelicplayers.com/WhatWeDo/HealthWellbeing.aspx>

Pregabalin Abuse amongst Opioid Substitution Treatment Patients

S McNamara, S Stokes, R Kilduff, A Shine

HSE National Drug Treatment Centre Laboratory, McCarthy Centre, 30-31 Pearse St, Dublin 2

Abstract

Pregabalin (Lyrica®) is used in treating epilepsy, nerve pain and anxiety. Pregabalin was initially thought to have a low misuse potential however there are emerging reports of Pregabalin being abused. A study was commenced at the National Drug Treatment Centre's (NDTC) Drug Analysis Laboratory to determine the level of usage of Pregabalin within the addiction services population in Ireland. A total of 498 urine samples representing samples from 440 individual opioid substitution patients, initially screened by immunoassay for drugs of abuse, were subjected to further analysis for Pregabalin by Liquid Chromatography/Mass Spectrometry (LC/MS). Of 440 patients tested, 39 tested positive for Pregabalin (9.2%). Only 10 patients from this group were prescribed this drug to our knowledge thus giving an estimated rate of misuse of 7.0%. Other drugs detected in the Pregabalin positive patients were Opiates (31.8%), Cocaine (11.4%), Benzodiazepines (79.5%) and Cannabis (77.8%). Our study confirms that Pregabalin abuse is taking place amongst the addiction services population. We believe that misuse of this prescription drug is a serious emerging issue which should be monitored carefully.

Introduction

Pregabalin (Lyrica®) is used in treating epilepsy, nerve pain and anxiety¹. Initially thought to have a low misuse potential it was classified in the US as a schedule V drug (i.e. lowest potential for abuse)². Recently however there are reports of Pregabalin being abused including abuse by Britain's opiate-using and prison populations and Belfast recreational users stating that Pregabalin induced a state similar to drunkenness, hence the street name 'Budweiser's'³⁻⁵. A 2014 PHE and NHS England expert group's advice note⁶ stated "Misuse of Gabapentin and Pregabalin has been noted for some years in clients attending substance misuse treatment and recovery services, and within secure environment settings. Currently, Pregabalin appears to be more sought after for misuse than Gabapentin."

Methods

Following requests for Pregabalin testing from clinicians in addiction services in Ireland who suspected its misuse, a method was developed to screen for this drug at our laboratory. A total of 498 urine samples initially screened by ISO17,025 accredited immunoassays tests for drugs of abuse were then subjected to further analysis for Pregabalin by LC/MS. Samples were tested from sequential sets of samples over the period June to August 2014 from 425 opioid substitution patients attending 6 clinics including NDTC clinics and clinics where clinicians had requested this testing. The number of patients in opioid substitution treatment in 2013 was 9,640 so this sample represents circa 4% of all patients.⁷

Results

Of 498 samples tested, 44 (8.8%) tested positive for Pregabalin with 39 of 425 patients testing positive for Pregabalin (9.2%). We consulted the relevant clinicians in relation to prescription of Pregabalin to patients with positive samples. Only 10 of the patients were prescribed this drug. Therefore 7% of the patients tested were using Pregabalin without prescription from the clinicians they attended. The age range of the individuals testing positive for Pregabalin was 21 to 61 years, with an average age

of 38 years. Of the 425 patients, 66% were male and 34% were female, while 41% of positive patients were male and 59% were female suggesting a possible gender based bias in usage. Table 1 shows a breakdown of the immunoassay results of the 44 Pregabalin positive samples. Most were prescribed Methadone (98%) and therefore positive for EDDP. One patient negative for EDDP was positive for Buprenorphine (2%) was prescribed Suboxone® as an alternative to Methadone. In summary, these results confirm that the abuse of Pregabalin is significant amongst this drug using population with 29 (7%) of 415 patients testing positive for Pregabalin in one or more samples despite their not being prescribed it. This is below the 12.1% of 124 patients reported by Grosshans et al⁴ nonetheless it extrapolates to potentially 675 patients based on 2013 figures of 9,640 in treatment.⁷

Discussion

Normal drug screening for patients in methadone maintenance does not include Pregabalin and so this drug may be taken in efforts to evade detection of drug use. The potential dangers of Pregabalin should not be underestimated. In 2013 there were 33 drug-related deaths in England and Wales where Pregabalin was mentioned on the death certificate.⁸ Of 10 patients attending a Belfast hospital following recreational Pregabalin abuse,⁶ presented with seizures (5 being 'first' seizures).⁵ We have seen that Pregabalin has significant abuse potential and is an attractive drug to opioid dependant drug users. We have confirmed that this drug is being misused by some addiction treatment patients. There is no information as yet in the public domain as to the numbers of deaths related to Pregabalin in Ireland, however we believe that misuse of this prescription drug is a serious emerging issue which should be monitored carefully.

Correspondence: S McNamara
HSE National Drug Treatment Centre Laboratory, McCarthy Centre, 30-31 Pearse St, Dublin 2
Email: smcnamara@dtcb.ie

Table 1: Summary of Immunoassay screening results of samples that tested positive for Pregabalin by LC/MS

	Alcohol	Benzodiazepines	Cocaine	EDDP*	Opiates	Amphetamine	Cannabis
No Tested	18	44	44	44	44	19	18
No. Positive	1	35	5	43	14	0	14
% Positive	5.6	79.5	11.4	97.7	31.8	0.0	77.8

NB: All of the immunoassay screening was performed using Cedia® kits

*EDDP – 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine is the specific metabolite of methadone

Acknowledgements

L Lawlor, M Kehoe, S Philbin, J Hannon, J Nolan, G Gaynor, E Burke, G Smith, S Conroy

References

1. <http://www.medicines.ie/medicine/9215/PIL>. (accessed 23rd April 2015)
2. Drug Enforcement Administration, Department of Justice. Schedules of controlled substances: placement of pregabalin into schedule V. Final rule. Fed Regist. 2005 Jul 28;70:43633-5.
3. Filipetto F, Zipp C, Coren J. Potential for Pregabalin Abuse or Diversion After Past Drug-Seeking Behavior. J Am Osteopath Assoc October 1, 2010 vol. 110 no. 10 605-7.
4. Grosshans M, Lemenager T, Vollmert C, Kaemmerer N, Schreiner R, Mutschler J, Wagner X, Kiefer F, Hermann D. Pregabalin abuse among opiate addicted patients. Eur J Clin Pharmacol. 2013 Dec; 69:2021-5.
5. Millar J, Sadasivan S, Weatherup N, Lutton S. Lyrica Nights—Recreational Pregabalin Abuse in an Urban Emergency Department. Emerg Med J 2013;30:874
6. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf (accessed on 23rd April 2015)
7. <http://www.emcdda.europa.eu/data/treatment-overviews/Ireland> (accessed on 14th July 2015)
8. <http://www.ons.gov.uk/ons/search/index.html?newquery=pregabalin>. (accessed on 23rd April 2015)

Post traumatic Fat Embolism in Common Femoral Vein on CT

N Healy, K Billington, N Sheehy

Radiology Department, St James's Hospital, James's St, Dublin 8

Abstract

Fat embolism syndrome usually occurs following trauma where fat globules from long bone fractures produce pulmonary, cerebral or cutaneous effects. This case illustrates the presence of macroscopic fat in the right common femoral vein secondary to a long bone fracture. This finding is rare but should be looked for on cross-sectional imaging to allow early, aggressive treatment of fat embolism syndrome.

Introduction

Fat embolism is the presence of fat globules in the circulation, which can affect trauma victims who sustain long bone fractures. In a minority of cases it causes fat embolism syndrome (FES), where the fat globules may produce pulmonary, cerebral or cutaneous effects. The treatment of FES is generally supportive but the mortality is high and therefore its presence should be recognised early and effective treatment instituted.

Case Report

A 20 year-old male was involved in a high-impact single vehicle road traffic accident. He sustained multiple injuries and was intubated on arrival at hospital. Initial chest radiograph revealed bilateral pneumothoraces and chest drains were inserted into both pleural cavities. Clinical and radiographic examination revealed open fractures of the right femur, left tibia and fibula, fractures of the right superior and inferior pubic rami and multiple rib fractures. A computed tomography (CT) of the thorax, abdomen and pelvis was performed with intravenous contrast enhancement to allow a detailed search for solid organ damage. CT of the pelvis demonstrated an unsuspected area of low attenuation in the right common femoral vein (Figure 1 and 2). This was in contrast to the right common femoral vein which revealed a uniform enhancement pattern. Based on the negative Hounsfield units of the low attenuation material, CT findings indicated a macroscopic venous fat embolism in the right common femoral vein. The presumed source was from the ipsilateral right femoral bone fracture. Over the course of the admission the patient developed dense bilateral airspace opacification on chest radiograph, and clinically an acute respiratory distress syndrome (ARDS) picture. The x-ray findings and the patient's clinical condition improved with supportive therapy.

Discussion

Fat embolism is due to blood vessel blockage by fat globules released from a long bone fracture following trauma. Up to 90% of individuals with fractures of the lower limbs can get embolisation of microglobules of fat, however most patients remain asymptomatic. The effects of fat embolisation are most apparent in the skin, brain and the lung parenchyma. 3-4% of individuals proceed to develop fat embolism syndrome, which is a triad of petechial haemorrhages,



Figure 1: Coronal Image from contrast enhanced CT abdomen/pelvis showing a low attenuation focus in the right common femoral vein (arrow) with a normally enhancing left common femoral vein

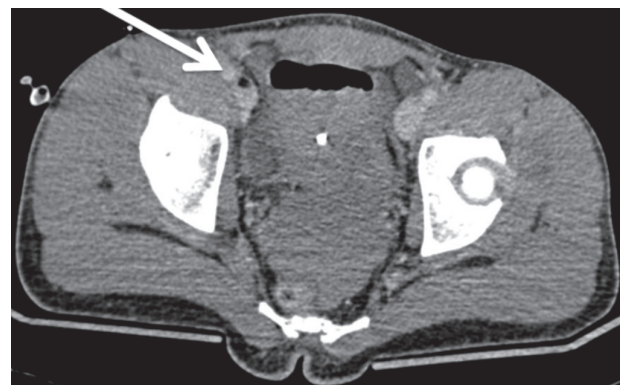


Figure 2: Axial Image from contrast enhanced CT abdomen/pelvis showing a low attenuation focus in the right common femoral vein (arrow)

cerebral abnormalities and respiratory distress¹. Severe cases of fat embolism occur in 10-20% of patients in whom the diagnosis is made and of these, mortality can reach as high as 20%¹. Fat embolism syndrome (FES) is clinically challenging based on the diverse aspects of its pathophysiology and management. It is postulated that FES is due to mechanical obstruction of pulmonary blood vessels or that hormonal changes cause toxic endothelial damage to pulmonary capillary beds^{2,3}. Young age, closed and multiple fractures increase the risk of FES, with higher mortality rates seen in bilateral lower limb fractures⁴. Chest radiograph may be normal or display diffuse alveolar infiltrates. Groundglass opacities with interlobular septal thickening or centrilobular nodular opacities can be seen on CT thorax⁵. The treatment of FES is generally supportive, with maintenance of adequate oxygenation, hydration and provision of sufficient nutrition, in addition to prevention of deep vein thrombosis and gastrointestinal bleeding. High-dose corticosteroids have been effective in preventing the development of FES in several studies but their use still remains controversial⁶. Albumin may have a role in therapy as it restores blood albumin levels and combines fatty acids which may limit lung injury⁶.

To our knowledge only two papers to date have illustrated the presence of macroscopic fat emboli within the common femoral vein and inferior vena cava^{7,8}. Given the gravity of the sequelae of fat embolism, the syndrome should always be considered in individuals following significant trauma with associated lower limb fractures. It is essential that radiologists monitor for the presence of fat in the lower limb veins or inferior vena cava on CT to warn clinicians of the impending syndrome and allow for early diagnosis and aggressive supportive treatment.

Correspondence: N Healy
Radiology Department, St James's Hospital, James's St, Dublin 8
Email: nualahealy@hotmail.com

References

1. Mudd KL, Hunt A, Matherly RC, Goldsmith LJ, Campbell FR, Nichols GR, Rink RD. Analysis of pulmonary fat embolism in blunt force fatalities. *J Trauma* 2000;48:711-5.
2. Gossling HR, Pellegrini VD, Jr. Fat embolism syndrome: a review of the pathophysiology and physiological basis of treatment. *Clin Orthop Relat Res* 1982;68-82.
3. Schemitsch EH, Turchin DC, Anderson GI, Byrick RJ, Mullen JB, Richards RR. Pulmonary and systemic fat embolization after medullary canal pressurization: a hemodynamic and histologic investigation in the dog. *J Trauma* 1998;45:738-42.
4. Nork SE, Agel J, Russell GV, Mills WJ, Holt S, Routh ML, Jr. Mortality after reamed intramedullary nailing of bilateral femur fractures. *Clin Orthop Relat Res* 2003;272-8.
5. Malagari K, Economopoulos N, Stoupis C, Daniil Z, Papiris S, Muller NL, Kelekis D. High-resolution CT findings in mild pulmonary fat embolism. *Chest* 2003;123:1196-201.
6. Porpodis K, Karanikas M, Zarogoulidis P, Konoglou M, Domvri K, Mitrakas A, Boglou P, Bakali S, Iordanidis A, Zervas V, Courcouthsakis N, Katsikogiannis N, Zarogoulidis K. Fat embolism due to bilateral femoral fracture: a case report. *Int J Gen Med*;5:59-63.
7. Harris AC, Torreggiani WC, Lyburn ID, Zwirewich CV, Ho SG, Munk PL. CT and sonography of traumatic fat embolism in the common femoral vein. *AJR Am J Roentgenol* 2000;175:1741-2.
8. Liu P, Armstrong P, Skippen P. Post-traumatic fat embolism in the inferior vena cava. *Can Assoc Radiol J* 1990;41:303-4.

Association of Oesophageal Hypertension with Bradycardia Mediated Deglutition Syncope

RY Lim, H Mulcahy, D Keane
Cardiology Department, St Vincent's University Hospital, Elm Park, Dublin 4

Abstract

Swallow syncope is a rare form of situational syncope. We report a case of swallow syncope with invasive confirmation of oesophageal hypertension (spasm) and invasive confirmation of a bradycardia mechanism. Awareness of this uncommon disorder is important as a treatable cause of syncope.

Introduction

The exact prevalence of swallow syncope is unknown. Its recognition is important as once diagnosed, its treatment is often effective.

Case Report

A 77 year old woman was referred for cardiac evaluation by the gastroenterology service for assessment of recurrent syncope and presyncope upon deglutition of solids. These episodes were always preceded by symptoms of dysphagia following ingestion of solid food. She was found to have a structurally normal upper GI tract, however, a high resolution oesophageal motility study had detected a hypercontractile oesophagus (see Figure 1). She was on no rate lowering cardiac medications and she had no other relevant medical history. Initial investigation in the form of cardiac monitoring during meals failed to reveal any cardiac abnormalities. We proceeded to insertion of an implantable loop recorder (ILR). Approximately 1 month later, two episodes of patient activated events on the ILR revealed sinus arrests of 6 seconds (see Figure 2). Both episodes correlated with symptoms of presyncope preceded by dysphagia after ingestion of solid food. A permanent pacemaker was implanted. On follow up the, patient has not reported any recurrence of presyncope or syncope.

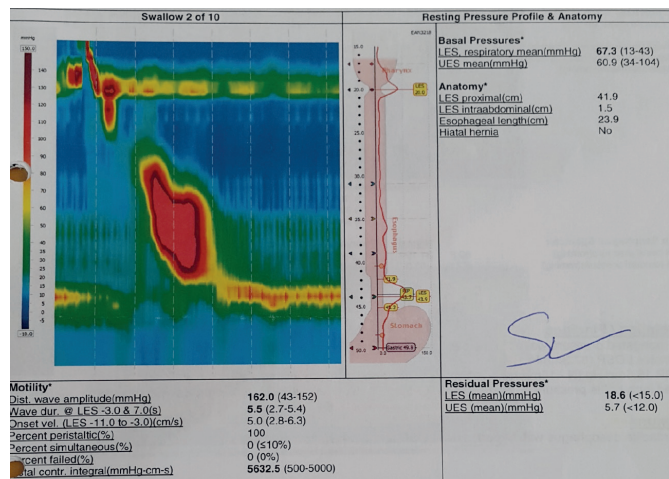


Figure 1: Oesophageal hypercontractility on High Resolution Oesophageal Motility Study in Our Patient

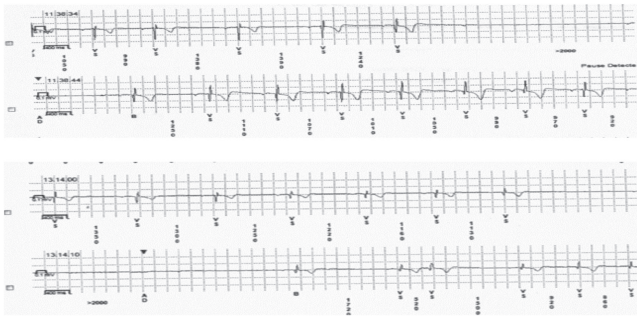


Figure 2: Two episodes on ILR interrogation in our patient confirming significant sinus pauses correlating with symptoms of presyncope during meals

Discussion

The pathophysiology of swallow syncope is postulated to be caused by common innervation of the oesophagus and the heart. Food boluses stretching the mechanoreceptors in the oesophagus result in afferent impulses to the brainstem via the oesophageal plexus, followed by efferent impulses to the SA and AV node of the heart resulting in bradyarrhythmia.^{1,2} Abnormal or excessive connections of the afferent nerves from the GI tract and efferent innervation to the heart in the brainstem may exist in patients with swallow syncope. Bradyarrhythmias in the form of sinus arrest, sinus bradycardia, SA block or AV block have been identified in swallow syncope¹. As the occurrence of these events are unpredictable more permanent forms of cardiac monitoring may be required in the form of an ILR, as demonstrated in our case. Once bradyarrhythmias are identified and a temporal relationship with symptoms established, pacemaker insertion is usually an effective form of treatment¹. Swallow syncope is often associated with underlying cardiac or GI abnormalities. In a literature review of 80 reported cases of swallow syncope, 38.8% had underlying

GI disease while 15% had underlying cardiac disease¹. While bradyarrhythmias are common, structural abnormalities such as hiatus hernia causing compressive effects leading to syncope when distended have also been described^{3,4}. Establishing these structural abnormalities as a cause is important as pacemaker insertion would not be effective in these situations.

We report a case of swallow syncope caused by bradyarrhythmias from a structurally normal, but functionally abnormal oesophagus. The symptoms of swallow syncope can have significant detrimental effects to patients' lifestyle, and should be suspected in patients with a convincing history of syncope associated with ingestion of food. The use of ILRs are helpful in establishing the presence of an arrhythmic component to the disease. Pacemakers provide symptomatic relief if bradyarrhythmias are the underlying cause to syncope.

Correspondence: RY Lim

Cardiology Department, St Vincent's University Hospital, Elm Park, Dublin 4

Email: limrenyik@gmail.com

References

1. Subashis Mitra, Tiffany Ludka, Shereif H Rezkalla, Param P Sharma, Jiangming Luo Swallow Syncope: A Case Report and Review of the Literature. *Clin Med Res.* 2011 Nov; 9: 125–129.
2. Kang KH, Cho WH, Kim MC, Chang HJ, Chung JI, Won DJ. Cases of swallow syncope induced by the activation of mechanoreceptors in the lower esophagus. *Korean J Intern Med* 2005;20:68–71
3. Oishi Y, Ishimoto T, Nagase N, Mori K, Fujimoto S, Hayashi S, Ochi Y, Kobayashi K, Tabata T, Oki T. Syncope upon swallowing caused by an esophageal hiatal hernia compressing the left atrium: a case report. *Echocardiography* 2004;21:61–64
4. Maekawa T, Suematsu M, Shimada T, Go M, Shimada T. Unusual swallow syncope caused by huge hiatal hernia. *Intern Med* 2002;41:199–201

'Malignant Phenylketonuria' (PKU) Due to Dihydropteridine Reductase (DHPR) Deficiency

A Ventzke, J Hoffmann, E Crushell, A Monavari, PD Mayne, I Knerr

National Centre for Inherited Metabolic Disorders, Children's University Hospital, Temple St, Dublin 1

Abstract

DHPR deficiency is a rare autosomal recessively inherited metabolic disorder of tetrahydrobiopterin (BH4) regeneration. Clinical symptoms may comprise microcephaly, developmental delay, ataxia and seizures. BH4 is the cofactor for the enzyme phenylalanine (Phe)hydroxylase (PAH), and for tryptophan and tyrosine hydroxylases, both of which are essential for serotonin and dopamine biosynthesis. We present four patients in two families who are being treated at the National Centre for Inherited Metabolic Disorders (NCIMD). All are members of the Irish Traveller population. We have identified a homozygous mutation, c.353C>T, in the DHPR (QDPR) gene which, to the best of our knowledge, has not been previously described. The mainstay of treatment is a life-long Phe-restricted diet together with supplementation of L-dopa and 5-hydroxy tryptophan (5-HT) and folinic acid. In Ireland, there is neurological comorbidity in our adult DHPR patients, although the overall outcome is satisfactory and one affected female has three healthy children.

Introduction

Phenylalanine (Phe) hydroxylase (PAH) is a key enzyme in amino acid metabolism, converting Phe into tyrosine, using tetrahydrobiopterin (BH4) as its co-factor. Defects in BH4 metabolism, including dihydropteridine reductase (DHPR) deficiency, are referred to as 'malignant' or atypical phenylketonuria (PKU) as distinct from classical PKU which refers to a defect in PAH apo-enzyme. DHPR is involved in a salvaging process of BH4. There are other BH4-dependent enzymes involved in neurotransmitter synthesis including tyrosine hydroxylase, which converts tyrosine to L-dopa and tryptophan

hydroxylase, which converts tryptophan to 5-hydroxy tryptophan (5-HT). Ireland was the first country worldwide to have a national Newborn Bloodspot Screening (NBS) Programme, including PKU, commencing in February 1966. Similar to patients with classical PKU, patients with atypical PKU due to DHPR deficiency present with elevated Phe levels on NBS. In general, classical PKU is characterized by neurotoxicity due to excessively elevated Phe concentrations, leading to severe mental retardation, microcephaly, and epilepsy if left untreated. Patients with 'malignant' PKU due to DHPR deficiency may also present clinically with microcephaly, hypotonia, mental retardation and seizures¹. In DHPR deficiency

there is not only an accumulation of Phe but also a profound deficit in the neurotransmitters dopamine and serotonin. There can be also alterations in the CNS folate status along with intracranial calcifications^{2,3}. Treatment comprises a Phe-restricted diet along with L-dopa, 5-HT and folic acid supplementation. In this study, we report on diagnosis, management and clinical outcome in four DHPR-deficient patients. Diagnosed in Ireland on NBS for PKU, they represent only 0.56% of our total cohort of 718 PKU patients being treated at the NCIMD.

Methods

Ethics approval and patient consent were obtained for this study. We retrospectively collected anonymized data from our patients with DHPR deficiency who had been diagnosed and treated at the NCIMD from 1966 until 2014, using medical charts and the laboratory database. Descriptive statistics were performed using MS Excel 2010.

Case 1

This is a 28-year-old woman from the Irish Traveller population. She has been treated from day 20 of life following abnormal NBS. Work-up for PKU which included measurements of amino acids (Phe 1333µmol/l), pterins and DHPR in blood revealed an absence of DHPR enzyme activity. She was started on a Phe-restricted diet together with L-dopa/carbidopa (ratio 4:1), 5-HT and folic acid (Table 1). Developmental assessment showed language delay and mild motor deficits for which she received speech and language therapy and physiotherapy. The girl had a high-stepping gait which resolved at the age of three years. Phe levels were monitored according to our policy for PKU patients with a target range of 120-400µmol/l in childhood; neurotransmitter supplements were adjusted according to CSF levels (Figure 1) and body weight. At 12 years of age, psychology assessment (Wechsler Intelligence Scale for Children, 3rd Ed. UK) showed a Full Scale IQ of 51 indicating an intellectual ability within the Exceptionally Low Range. At age 20, she became pregnant with her first child. During pregnancy, her Phe levels were mostly in the desired range of 150-250µmol/l. The baby was born by emergency LSCS due to foetal distress. The baby's NBS screening was normal. Aged 23 years, she had a miscarriage at 14 weeks gestation. In a non-pregnant state, her elevated prolactin levels of 610-6577 mU/L (normal range 116-585) may reflect adherence issues in taking the medications. At 24 years of age, she gave birth to her second child. During this pregnancy, she had elevated Phe levels in the range of 271-599 µmol/l requiring

hospital admission. At 26 years of age clinical examination revealed some lower limb pyramidal findings. She had another pregnancy and her third child was clinically well.

Case 2

This is a male patient who was identified with high Phe levels on high-risk NBS. His sister (case 1) is the index case. Absence of DHPR enzyme activity in blood confirmed the diagnosis biochemically. After molecular genetic testing became available to us, we could demonstrate a pathogenic c.353C>T mutation in the DHPR (QDPR) gene in this family. The boy was started on a Phe-restricted diet, L-dopa/carbidopa, 5-HT and folic acid; CSF neurotransmitter metabolite concentrations subsequently increased to near normal levels (Figure 1). He had mild speech delay and an episode of intermittent tremor during childhood but neurological exam was otherwise unremarkable. A psychological assessment at the age of 15 years showed an IQ within the Mild General Learning Disability range. During childhood his Phe levels were in the range of 200-700µmol/l. His prolactin levels were in the range of 820-2360 mU/l (mean 1483, reference range 100-400). At age 20 he did not attend any further outpatient appointments at the NCIMD. His care was mainly managed locally and advice was provided over the phone. He had a seizure at 23 years of age; his EEG at the time was normal. Neuroimaging revealed very mild sulcal dilatation along with very mild degree of cerebral atrophy. Additional medical issues in this case were behavioural issues, alcohol abuse, and recurrent dental abscesses.

Case 3

The third patient is a 17 months old boy. He presented with high Phe levels on NBS and was admitted to the NCIMD at 10 days of age. On admission, his plasma Phe level was 1608µmol/L and he underwent work-up for PKU including blood DHPR activity and pterins. He was subsequently started on a Phe-restricted diet. Within the first month he was diagnosed with DHPR deficiency (DHPR activity <0.1 µmol/min/g). The diagnosis was also confirmed genetically. He was started on L-dopa/carbidopa (2-8 mg/kg/day), 5-HT(2-7 mg/kg/day) and folic acid (10 mg/day). His Phe levels are within the therapeutic limits so far. Serum prolactin concentrations came down with treatment (max. 1129 mU/l prior to treatment, min. 180 mU/l whilst on treatment). His development is normal.

Case 4

This baby girl is the sister of case 3. She was diagnosed on high-risk NBS on day 3 of life with a Phe level of 668µM/l.

	Case 1	Case 2	Case 3	Case 4
Age	28 yrs.	27 yrs.	17 months	3 months
Gender	female	male	male	female
Age at diagnosis	20 days	3 days	10 days	3 days
Clinical symptoms	hypotonia, frizzy hair, mild transient tremor, mild developmental delay, mild speech delay, high-stepping gait, mild motor defects, double vision, fainting episode, headaches	developmental delay, mild speech delay, transient tremor, epileptic seizure, behavioural issues. On CT brain: very mild sulcal dilatation/ cerebral atrophy.	asymptomatic	asymptomatic
Ethnicity	Irish traveller population	Irish traveller population	Irish traveller population	Irish traveller population
IQ	mild range of learning disability	mild range of learning disability	NA	NA
Treatment summary	L-dopa/ carbidopa (4-10 mg/kg/day), 5-HT (5-8 mg/kg/day), folic acid (10-15 mg/day), phe-restricted diet	L-dopa/ carbidopa (4-10 mg/kg/day), 5 HT (5-8 mg/kg/day), folic acid (10-15 mg/day), phe-restricted diet	L-dopa/ carbidopa (2-8 mg/kg/day), 5-HT (2-7 mg/kg/day), folic acid (10 mg/day), phe-restricted diet	L-dopa/ carbidopa (2-7 mg/kg/day), 5-HT (2-6 mg/kg/day), folic acid (10 mg/day), phe-restricted diet

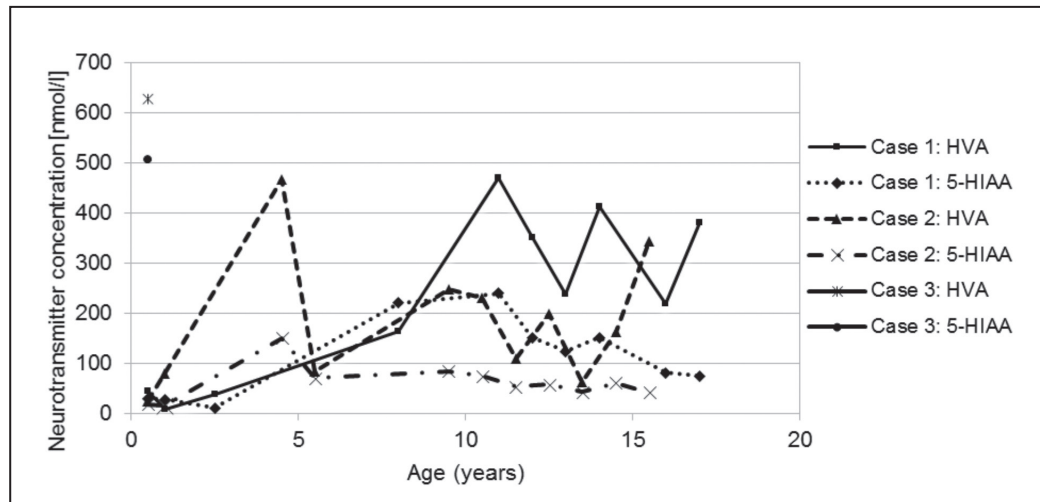


Figure 1: Neurotransmitter (HVA, 5-HIAA) concentrations in follow-up examinations (n=3)

Her maximum Phe level was 1198 μ M/l on day 8 of life before treatment was fully implemented. Her initial prolactin level was 2212 mU/l; it came down after she had been commenced on medications. Since day 9 of life, her blood Phe levels were within therapeutic limits thus far. She is homozygous for the same pathogenic c.353C>T mutation in the QDPR gene. At her most recent visit, she was clinically well and neurologically asymptomatic.

Discussion

All our patients with DHPR deficiency presented with raised Phe levels on NBS. In principle, a very low/absent DHPR enzyme activity in blood in the setting of an elevated Phe level confirms the diagnosis biochemically. Molecular genetic testing is available. In addition to Phe-restricted diet, patients with DHPR deficiency need life-long L-dopa/carbidopa and 5-HT as well as folinic acid supplements to prevent/reduce severe neurological symptoms^{2,4,5}. In addition to neurotransmitter studies in CSF for monitoring, serum prolactin measurement was introduced at the NCIMD in 2006 which is a sensitive marker for hypothalamic dopamine content and, therefore, a suitable biomarker for optimal dosage of L-dopa in DHPR-deficient patients^{6,7}. Taken together, DHPR deficiency is an extremely rare metabolic disorder. In Ireland to date, only members of the Irish Traveller population have been affected, a population constituting <1% of the total Irish population⁸, in which a high rate of consanguinity is a common finding. All four patients harbour the same pathogenic c.353C>T mutation in the QDPR gene that, to the best of our knowledge, has not yet been described. Despite the low frequency, 'malignant PKU' or DHPR deficiency has to be considered in each newly diagnosed PKU patient as approx. 2% of all patients with high Phe levels have an underlying disorder of BH4 metabolism⁹. Following the identification of an index case in the family, early high-risk NBS is recommended for future pregnancies. An early diagnosis soon after birth enables early initiation of treatment with the best possible outcome¹⁰. There is neurological comorbidity in our adult patients, although the overall outcome is so far satisfactory.

Correspondence: I Knerr

National Centre for Inherited Metabolic Disorders (NCIMD),
Children's University Hospital, Temple St, Dublin 1
Email: ina.knerr@cuh.ie

Acknowledgements

The medical and nursing staff, psychologists, dieticians, and laboratory staff at NCIMD CUH for their excellent collaboration and assistance; the lifelong work of E Naughten in caring for patient 1 and 2, and in implementing the 'Diet for Life' policy. Molecular genetic analysis of the QDPR gene was performed at the Centre for Genomics and Transcriptomics, Tübingen Germany.

References

- Blau N, Barnes I, Dhondt JL. (1996) International database of tetrahydrobiopterin deficiencies. *J Inherit Metab Dis* 19:8-14.
- Woody R, Brewster M, Glasier C. (1989) Progressive intracranial calcification in dihydropteridin reductase deficiency prior to folinic acid therapy. *Neurology* 39:673-5.
- Goldstein D S, Hahn S H, Holmes C, Tiff C, Harvey-White J, Milstien S, Kaufman S. (1999) Monoaminergic effects of folinic acid, L-dopa and 5-hydroxytryptophan in dihydropteridine reductase deficiency. *J Neurochem* 65:2810-3.
- Opladen T, Hoffmann G F, Blau N. (2012) An international survey of patients with tetrahydrobiopterin deficiencies presenting with hyperphenylalaninaemia. *J Inherit Metab Dis* 35: 963-7.
- Dhont JL. (2005) Defects in dihydropteridin reductase, Orphanet encyclopedia, <http://www.orpha.net/data/patho/GB/uk-dhpr.pdf>
- Concolino D, Muzzi G, Rapsomaniki M, Moricca MT, Pascale MG, Strisciuglio P. (2008) Serum prolactin as a tool for the follow-up of treated DHPR-deficient patients. *J Inherit Metab Dis Suppl* 2:S193-7.
- Birnbacher R, Scheibenreiter S, Blau N, Bieglmayer C, Frisch H, Waldhauser F. (1998) Hyperprolactinemia, a tool in treatment control of tetrahydrobiopterin deficiency: endocrine studies in an affected girl. *Pediatr Res* 43:472-7.
- Central Statistics Office, census 2011, <http://www.cso.ie/en/census/census2011reports/census2011profile7religionethnicityandirishtravellers-ethnicandculturalbackgroundinireland/>
- Blau N, Thöny B, Cotton RG, Hyland K. (2001) Disorders of tetrahydrobiopterin and related biogenic amines in: Scriver C R, Beaudet A L, Sly W S, Valle D, Childs B, Vogelstein B (Eds.), *The Metabolic and Molecular Bases of Inherited Disease*, McGraw-Hill, New York, 2001, 1725-76.
- Jaeggi L, Zurfluh MR, Schuler A, Ponzone A, Porta F, Fiori L, Giovannini M, Santer R, Hoffmann GF, Ibel H, Wendel U, Ballhausen D, Baumgartner MR, Blau N. (2008) Outcome and long-term follow-up of 36 patients with tetrahydrobiopterin deficiency. *Mol Genet Metab* 93:295-305.



(SMO36-15) Gynaecologic Oncology Consultant

Wellington, New Zealand

Wellington Hospital is one of New Zealand's largest tertiary hospitals and is renowned for its teaching and research opportunities.

Our new regional hospital offers state of the art technology and systems to support you and the care you deliver.

We are seeking a **Gynae-Oncology Specialist** to join our team on a permanent basis. The successful applicant will hold either a RANZCOG or RCOG sub specialist qualification in Gynae-Oncology or significant experience in Gynae-Oncology with appropriate equivalent qualification. This is not a training position, but may be of interest to those completing their CGO training.

The position will help develop the Regional Gynae-Oncology Tertiary Service providing care to women from the Central Region. The population covered by the service is roughly 1 million.

The service is based at Wellington Hospital in a purpose built facility with recently added surgical and ward facilities.

This position requires a high level of communication skills and the ability to interact with various populations from diverse backgrounds. Our multi-disciplinary model demands our team members to be quality focused, constantly working towards improving outcomes and giving meaning to the strategic direction of the service through specialist experience and broad approach to future planning.

It is also vital to our service that the successful applicant assists with the supervision and instruction of junior doctors within the Women's Health Service.

Wellington is the capital of New Zealand and is situated geographically at the lower tip of the North Island of New Zealand. As well as being the political capital, Wellington also is highly regarded for its cultural and café activities. It is a vibrant, cosmopolitan, sophisticated city with waterfront developments, inner city apartments, new venues and restored cultural centres. The city is encircled by a "Greenbelt", which ensures plenty of green spaces and tracks for rambling on your days off.

For more on this exciting opportunity, contact Sean Hill, SMO Recruitment Advisor sean.hill@ccdhb.org.nz or +64 4 806 2552.



CCDHB is committed to equal employment opportunities and supports the professional development of all its employees.

capitalhealthcareers.org.nz

Paget's Disease of Bone: Progress Towards Remission and Prevention

GM Healy^{1,2}, C Woods^{1,3}, E Heffernan^{2,4}, MJ McKenna^{1,3,4}

¹St Michael's Hospital, Dún Laoghaire, Co Dublin

Departments of ²Diagnostic Imaging and ³Endocrinology, St Vincent's University Hospital, Elm Park, Dublin 4

⁴School of Medicine and Medical Sciences, UCD, Dublin

Abstract

Paget's disease of bone is a focal disorder of bone remodelling leading to areas of enlarged weakened bone manifesting with chronic pain, bone deformity, and fracture. Predominantly a disease of older adults, its prevalence is strongly linked to European ancestry. Pre-disposing factors include exposure to viruses such as measles and mutations in the SQSTM1 gene. PDB is diagnosed on plain radiograph, the extent of disease is delineated by radionuclide bone imaging, the degree of activity is quantified biochemically, and it is treated with a nitrogen-containing bisphosphonate, most effectively by a single intravenous infusion of zoledronate 5mg. Lifelong specialist follow-up is advocated because some patients require repeated infusions. Current clinical research is focusing on genetic factors in order to identify patients suitable for prevention.

Introduction

Paget's disease of bone (PDB), an eponym after Sir James Paget who described the condition in the nineteenth century, is a chronic metabolic disorder of bone remodeling at a focal level. It may affect one bone (monostotic) or many bones (polyostotic)¹. It is often diagnosed incidentally, but otherwise presents late, with slowly progressive, non-specific and common symptoms that challenge a physician's acumen. We present a review of epidemiology, diagnosis and management of this condition and look to the future of disease prevention.

Aetiopathogenesis of PDB

PDB is a disease of older adults (rare before 40), most commonly of European heritage, with highest prevalence found in Britain, Ireland and mainland Europe. Its prevalence varies widely throughout the world from 0.7% to 4.6%². This has led to the theory that PDB originated in Britain and has spread with migration. The true prevalence is unknown, because patients frequently have minimal or no symptoms. Recent data suggests a reduction in the incidence globally, with some groups reporting that the age at diagnosis is increasing, while the level of serum total alkaline phosphatase (ALP) at the time of diagnosis is reducing. The reasons behind this reduction in occurrence are not understood but unknown environmental factors are believed to be responsible. The normal adult skeleton undergoes remodelling in multicellular units with about 10% of the skeleton being replaced yearly. Remodelling balance may be positive, negative or neutral depending on the degree of bone resorption with respect to the degree of formation. In PDB, bone remodelling is chaotic, leading to woven bone, which is weaker than lamellar bone. The axial skeleton including skull, spine (lumbar more than thoracic more than cervical), pelvis and long bones of the extremities are the most frequently affected. These foci of abnormal weakened bone result in pain and associated complications. This tends to be slowly progressive, and has the potential to cause significant disability.

Abnormal osteoclastic activity is thought to be responsible for the development of PDB². The disease can be divided into three pathological phases, all of which may be present simultaneously in the same bone. The initial osteolytic stage is characterized by abnormal osteoclastic bone resorption, and is typically followed by a period of compensatory disorganized osteoblastic bone formation (mixed osteoclastic-osteoblastic stage) while the bone marrow is replaced by connective tissue. A burnt-out osteosclerotic stage eventuates with greatly expanded but weakened and deformed bone. Genetic and environmental factors are believed to play important roles in PDB development. Among many possible predisposing genes, SQSTM1 influences osteoclast activation and is thought to be strongly associated with developing PDB but is also a risk factor for disease progression and severity².

Exposure to infection such as paramyxoviruses are thought to be key factors in the development of abnormal bone remodelling and subsequent PDB². The declining incidence of PDB in recent decades also supports the theory that infections are causative or contributory to PDB development, since vaccination programs have expanded and certain infections are better controlled.

Diagnosis

PDB often goes undiagnosed for years, because symptoms can be absent or mild. Commonly, the diagnosis is made incidentally following blood or radiological tests for other reasons. The most preeminent symptom is pain, usually localized to the affected bone. Secondary complications such as hearing loss, osteoarthritis or neuropathy can occur as a result of bone expansion. Rare complications include osteosarcoma, hypercalcaemia (in patients who are immobilised), high output cardiac failure, paraparesis and basilar invagination with brainstem compression². Imaging is critically important in diagnosing PDB. On plain film, enlarged bones with cortical thickening and coarse trabecular pattern are commonly seen³. Each of the osteolytic, mixed and osteosclerotic stages have distinct features, the earliest being a local radiolucency indicative of osteolysis. While plain imaging is often sufficient for diagnosis in the appropriate clinical setting, radionuclide bone scanning has a higher sensitivity and has the advantage of identifying the total extent of disease. However, radionuclide imaging may fail to identify the osteosclerotic phase of disease, as a consequence of low remodelling activity. Computed tomography and MRI are helpful if there is concern about metastases, pathological fracture, osteosarcoma or neurological complications².

Monostotic disease is more difficult to diagnose radiologically. Historically, this has led to a higher rate of bone biopsies to confirm diagnosis. MRI is of particular use in this area and is usually able to exclude disorders that may mimic PDB, such as metastatic bone disease, hyperostosis frontalis, fibrous dysplasia and pustulotic arthrosteitis⁴. A characteristic feature of PDB on MRI is the presence of prominent islands of preserved fatty (yellow) marrow in the involved bone⁵ (Figure 1). In metastatic bone disease the yellow marrow is replaced by metastases. Laboratory testing should include measurement of calcium, phosphorus, total ALP, parathyroid hormone and 25-hydroxyvitamin D (25OHD). Depending on clinical suspicion and indication, liver dysfunction or underlying malignancy will need to be excluded. Bone turnover markers of resorption (serum C-terminal telopeptide of type I collagen) and formation (serum pro-collagen type I N pro-peptide) are readily available and should be measured at diagnosis, especially in cases of liver dysfunction when interpretation of total ALP as a bone marker is not possible². It is important to have a baseline measure of bone remodelling activity, because this has a role in assessing the response to

treatment. Of note, osteocalcin, which is a marker of the late phase of normal bone formation, is usually within the reference range, in keeping with the absence of normal mineralization in the woven bone of PDB.



Figure 1: MRI lower thoracic and lumbar spine.

Left: Sagittal T1 weighted image with diffuse signal abnormality throughout L2 vertebral body and also within S1, L1 and L5. Arrows illustrate 'fat islands' that are typical of Paget's disease.

Right: Short-tau inversion recovery image for fat suppression – fat islands become dark on this image (arrows).

Treatment

The treatment of PDB has advanced immeasurably following the introduction of nitrogen-containing bisphosphonates (N-BP), in particular intravenous zoledronate^{2,6}. They produce a sustained reduction in bone remodelling at active sites, which usually results in improvement in pain, although the long term clinical benefits of this therapy have not yet been established². Biochemically there is a rapid and prolonged drop in ALP to the reference range. Nothing emulates the degree and durability of the response in total ALP that is seen with zoledronate⁷. Assuming that there is no contraindication, the patient should be treated with a single 5 mg dose of intravenous zoledronate. The goal of treatment is to achieve remission, which is defined as achieving bone turnover below the midpoint of the reference range for the chosen bone turnover marker⁷. We aim to achieve and maintain a total ALP below 75 IU/L. Clinical review with measurement of total ALP should be at 6-monthly intervals. The need for subsequent infusions depends on clinical judgment based on appraisal of symptoms and total ALP response. In our experience about 25% of patients need repeat infusion of zoledronate⁸. There are two clinical considerations at the time of the infusion: risk of hypocalcaemia, and the acute phase reaction. The former is called the "hungry bone"; where shutting off bone resorption in the setting of a high bone turnover state like PDB with ongoing high bone formation leads to net transfer of circulating calcium into bone resulting in hypocalcaemia, which may be severe and prolonged^{9,10}. The acute phase response is a non-specific physiologic immune-driven reaction to a challenge; patients are apt to develop flu-like symptoms with fever and myalgia within 1-2 days following the infusion, most commonly after the first infusion¹¹. This response may be prevented by ensuring adequate vitamin D status^{11,12}. So, for both these reasons, prior to zoledronate infusion we favour pre-treating our patients for at least 3 months with an oral bisphosphonate (alendronate 70mg

weekly, or risedronate 35mg weekly) and supplementation with calcium (1000mg daily) and vitamin D (20µg daily). Also, at the time of the first zoledronate infusion, we prescribe paracetamol 1000mg and advise patients to repeat this dose about 8-hourly until symptoms settle.

By the time that PDB is diagnosed, it is already at an advanced stage with bone enlargement and deformity; therefore, we are currently participating in a randomised controlled trial of genetic testing and targeted zoledronate therapy to prevent SQSTM1-mediated Paget's disease¹³. The main aim of this trial is to determine if targeted intervention with zoledronate can prevent the development of raised bone turnover or focal bone lesions in subjects who carry mutations in SQSTM1.

Correspondence: G Healy
Department of Diagnostic Imaging, St Vincent's University Hospital, Elm Park, Dublin 4
Email: gmhealy@gmail.com

References

1. Ralston S. Clinical practice. Paget's disease of bone. *New England Journal of Medicine* 2013;368:644-50.
2. Singer F, Bone H, Hosking D, Lyles KW, Murad MH, Reid IR, Siris ES. Paget's Disease of Bone: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology and Metabolism* 2014;99:4408-22.
3. Cortis K, Micallef K, Mizzi A. Imaging of Paget's disease of bone - From head to toe. *Clinical radiology* 2011;66:662-72.
4. Theodorou D, Theodorou S, Kakitsubata Y. Imaging of Paget's disease of bone and its musculoskeletal complications: review. *American Journal of Roentgenology* 2011;196:S64-75.
5. Smith SE, Murphey M, Motamedi K, Mulligan M, Reskin C, Gannon F. From the archives of the AFIP. Radiologic spectrum of Paget disease of bone and its complications with pathologic correlation. *Radiographics* 2002;22:1191-216.
6. Bolland M, Cundy T. Paget's disease of bone: clinical review and update. *Journal of Clinical Pathology* 2013;66:924-7.
7. Reid IR, Miller P, Lyles K, Fraser W, Brown JP, Saidi Y, Mesenbrink P, Su G, Pak J, Zelenakas K, Luchi M, Richardson P, Hosking D. Comparison of a single infusion of zoledronic acid with risedronate for Paget's disease. *N Engl J Med* 2005;353:898-908.
8. Mahmood W, McKenna M. Proposed new approach for treating Paget's disease of bone. *Irish Journal of Medical Science* 2011;180:121-4.
9. Smith D, Murray BF, McDermott E, O'Shea D, McKenna MJ, McKenna TJ. Hungry bones with hypocalcaemia following parathyroidectomy. *J Bone Miner Metab* 2005;23:514-5.
10. Crowley RK, Kilbane M, King TF, Morrin M, O'Keane M, McKenna MJ. Hungry bone syndrome and normalisation of renal phosphorus threshold after total parathyroidectomy for tertiary hyperparathyroidism in X-linked hypophosphataemia: a case report. *J Med Case Rep* 2014;8:84.
11. Bertoldo F, Pancheri S, Zenari S, Boldini S, Giovanazzi B, Zanatta M, Valenti MT, Carbonare LD, Cascio VL. Serum 25-hydroxyvitamin D levels modulate the acute-phase response associated with the first nitrogen-containing bisphosphonate infusion. *Journal of Bone and Mineral Research* 2010;25:447-54.
12. Srivastava T, Dai H, Haney CJ, Alon US. Serum 25-hydroxyvitamin D level and acute-phase reaction following initial intravenous bisphosphonate. *Journal of Bone and Mineral Research* 2011;26:437-8.
13. ISRCTN11616770 - Zoledronate in the Prevention of Paget's: the ZiPP study. <http://www.controlled-trials.com/ISRCTN11616770>.

'Life Saving Positioning' in Patients with Air Embolism

Sir,

Air embolism is an uncommon, but potentially catastrophic, event that occurs as a consequence of the entry of air into the vasculature.¹ The following illustrates such a case; an 82 year old lady, COPD with an FEV1 of 0.6 L (40%) was admitted following an exacerbation of her COPD. Her CXR showed a right sided density and her CT thorax confirmed a 4 x 3 cm mass in the right upper lobe. She was booked for a CT core biopsy. Patient was initially scanned in the prone position but was turned into the left lateral decubitus position as it was felt that this was a better access into the mass. Under aseptic technique and CT fluoroscopic guidance, core biopsy was obtained using an 18 gauge core biopsy needle. 3-4 samples were sent to pathology.

Upon removal of the needle the patient was fully coherent. After a couple of minutes, the patient appeared to be confused and dysarthric. A scan was performed of the entire chest to exclude a pneumothorax. No pneumothorax was seen. However there was a large amount of intra cardiac air pocket in the left atrium. Based on this, the patient was positioned in the left lateral decubitus position with the right side up and the head tilted down. The patient's sedation was reversed and after a few minutes patient began more coherent and lucid with no residual deficit. Patients was put under observation and repeat CT thorax one day later showed complete resorption of the intracardiac air. Patient made a full recovery without any sequela.

There has always been a debate about the correct positioning of patient during such event. As arterial air embolisation is of concern in lung biopsies, the use of right lateral decubitus position is used because this maintains air in the superior aspect of the left ventricle away from the left ventricular outflow tract. However

this only applies if the air pocket is in the left ventricle. In our case the biopsy was performed in the left decubitus position. As the air bubble pocket was found to be confined to the left atrium, a left lateral decubitus position was used with head-down angulation to prevent systemic embolisation. Reflecting on the above case, recognition of the symptoms by the interventional radiologist and positioning the patient in the left decubitus position was certainly a big contribution for the full recovery of the patient. Air embolism has a reported incidence of 0.02% – 0.07% and can be associated with major morbidity and mortality. Early recognition and prompt initial management such as 100% high flow oxygen and the correct position can save the patient's life by preventing air embolisation into the cerebral circulation. Early hyperbaric oxygen therapy if available can also be used as it promotes exchange of oxygen for nitrogen in the air bubbles.^{2,3}

M Kooblall, SJ Lane, E Moloney
Respiratory Department, AMNCH, Tallaght, Dublin 24
Email: mineshamnch@gmail.com

References

1. King MB, Harmon KR. Unusual forms of pulmonary embolism. *Clin Chest Med* 1994; 15:561.
2. Hare SS, Gupta A, Goncalves AT, Souza CA, Matzinger F, Seely JM. Systemic arterial air embolism after percutaneous lung biopsy. *Clin Radiol* 2011;66:589-596
3. Wu CC, Maher MM, Shepard JA. Complications of CT-guided percutaneous needle biopsy of the chest: prevention and management. *ARJ Am J Roentgenol* 2011;196: W678-W682

Textbook of Clinical Gastroenterology and Hepatology. Second Edition

Editors: Hawkey CJ, Bosch J, Richter JE, Garcia-Tsao G, Chan FKL.

This is a large textbook with the stated aim of focusing 100% on the clinical management of patients with gastrointestinal or hepatobiliary disease. Having some time recently I read this textbook from cover to cover. It was the first time in many years that I systematically read a major textbook. I found it to be an enlightening and enjoyable experience and would recommend this text book to both colleagues and trainees in gastroenterology.

This textbook aims to provide practical, essential information in the fields of gastroenterology and hepatology. To this end the editors assembled a strong team of writers, most of whom are international authorities in their field. Containing 1,246 pages it is a substantial volume. The book is divided into four sections. The first has 26 chapters on symptoms, syndromes and scenarios. The second has 95 chapters dealing with specific disorders of the G.I tract including liver and pancreas. The third section is a primer of diagnostic methods and contains chapters on diagnostic endoscopy, imaging, tissue biopsy and functional testing. The final section is a primer of treatments, which includes therapeutic endoscopy, radiological interventions and some surgical treatments. There is little medical therapy in this section, but most medical treatments are discussed in specific disease chapters in section 2.

Each chapter begins with three three summary text boxes. These contain "Essential facts about causation", "Essential of Diagnosis"

and "Essentials of Treatment". These summaries are particularly well written and useful and would certainly provide a quick means of revision for candidates preparing for examinations. The main body of the chapters include discussion of basic science concepts and pathophysiology but the main emphasis is on clinical presentations, diagnosis and management. The chapters are clearly written, informative and well illustrated. Many of the chapters also have associated videos, which may be viewed on-line. The therapeutic endoscopic videos are particularly useful as an additional teaching aid. The book is generally well edited and there is relatively little overlap between chapters. Unfortunately one chapter on prescribing in liver disease is reproduced verbatim in both sections 2 and 4.

This is a well-written comprehensive textbook and I hope it will run to many editions. I would strongly recommend it to trainees in gastroenterology and hepatology, particularly those in their first two years. It gives an excellent over-view of the subject. I would also recommend it to "long in the tooth" practitioners like myself who may need a refresher in areas out-side of our normal areas of practice. Having read this book I am re-assured that the comprehensive textbook still has an important place in medical education.

PA McCormick
Liver Unit, St Vincent's University Hospital, Elm Park, Dublin 4

Continuing Professional Development

To receive CPD credits, you must complete the question online at www.imj.ie.

The Role of Speech and Language Therapy in Assessing and Managing Pharyngo-esophageal Diverticula

E Holmes, C Kenny, M Samuel, J Regan, J O'Rourke, C McCoubrey. *Ir Med J.* 2015; 108: 296-9.

Question 1

The study period was

- a) 3 years
- b) 5 years
- c) 7 years
- d) 9 years
- e) 11 years

Question 2

The total number of patients who attended for videofluoroscopic swallow studies was

- a) 1780
- b) 1790
- c) 1800
- d) 1810
- e) 1820

Question 3

Among the confirmed cases the proportion with respiratory symptoms was

- a) 60%
- b) 65%
- c) 70%
- d) 75%
- e) 80%

Question 4

Videofluoroscopic studies confirmed aspiration in

- a) 8 patients
- b) 9 patients
- c) 10 patients
- d) 11 patients
- e) 12 patients

Question 5

The mean age of the patients was

- a) 74.5 years
- b) 75.5 years
- c) 76.5 years
- d) 77.5 years
- e) 78.5 years

Utilisation of Clinical Networks to Facilitate Elective Surgical Workload; A Preliminary Analysis

T Burke, P Waters, RM Waldron, K Joyce, I Khan, W Khan, M Kerin, K Barry. *Ir Med J.* 2015; 108: 299-302.

Question 1

The number of cholecystectomies performed was

- a) 1907
- b) 1917
- c) 1927
- d) 1937
- e) 1947

Question 2

The overall laparoscopic conversion rate was

- a) 1.1%
- b) 1.3%
- c) 1.5%
- d) 1.7%
- e) 1.9%

Question 3

The major cholecystectomy complication rate was

- a) 0.93%
- b) 1.93%
- c) 2.93%
- d) 3.93%
- e) 4.93%

Question 4

Among the cholecystectomy patients the number of females was

- a) 1675
- b) 1685
- c) 1695
- d) 1705
- e) 1715

Question 5

The catchment population for Mayo General Hospital is

- a) 120,000
- b) 130,000
- c) 140,000
- d) 150,000
- e) 160,000

Safety of Grass Pollen Sublingual Immunotherapy for Allergic Rhinitis in Concomitant Asthma

A Sahadevan, R Cusack, SJ Lane. *Ir Med J.* 2015; 108: 304-7.

Question 1

The number of patients in the study was

- a) 26
- b) 28
- c) 30
- d) 32
- e) 34

Question 2

The average age of the patients was

- a) 34.6 years
- b) 36.6 years
- c) 38.6 years
- d) 40.6 years
- e) 42.6 years

Question 3

The proportion of patients whose asthma remained stable during the therapy was

- a) 84%
- b) 86%
- c) 88%
- d) 90%
- e) 92%

Question 4

The mean duration of sublingual immunotherapy (SLIT) was

- a) 16.5 months
- b) 18.5 months
- c) 20.5 months
- d) 22.5 months
- e) 24.5 months

Question 5

The range of baseline FEV1 was

- a) 70-130%
- b) 80-130%
- c) 90-130%
- d) 90-140%
- e) 90-150%



IMO
FINANCIAL SERVICES

Financial planning for doctors

- IMO Group Schemes
- GMS Pension Protection
- Pensions
- Protection
- Wealth Management
- IMO Surgery Package
- Mortgage Services

www.imofs.ie

10 Fitzwilliam Place, Dublin 2, Ireland.

Tel: (01) 661 8299 Fax: (01) 661 8332 Email: imofs@imo.ie

Fitzserv Consultants Ltd., t/a IMO Financial Services is regulated by the Central Bank of Ireland.