President
Dr Peter Trewby

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Proceedings of the Association of North of England Physicians

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… excess mortality associated with vitamin d deficiency might be prevented by the replacement of vitamin D …

Abstracts of the meeting held on Wednesday 5th July 2017 at Freeman Hospital

THE EFFECT OF VITAMIN D LEVELS ON MORTALITY AND MOBILITY IN VITAMIN D DEFICIENT MEDICAL INPATIENTS

Atheer Al Haddabi, Hannah Fairclough, Clive Kelly
Queen Elizabeth Hospital Gateshead

The study examines the effect of replacement of vitamin D on mortality and mobility in a cohort of vitamin D deficient inpatients 3 months after discharge from hospital. We measured vitamin D levels in 90 consecutive admissions of patients aged 65 and over to a single medical ward over a 3 month period. Those whose levels were under 35 nmol/L were considered to be deficient and were offered vitamin D replacement therapy either IM (300,000 units stat) or orally (20,000 units bd for 10 days). Baseline mobility was measured. Patients were reassessed 3 months later and mobility was reassessed. Three month mortality was recorded. These data were compared to that obtained from an earlier cohort of vitamin patients where vitamin D replacement was not offered. Vitamin D deficiency was present in 47 patients (52%) and replacement was accepted by 46 (44 IM and 2 orally). Mean age was 78 and 23 were male. At three months, 7 patients had died (15%) and a further 9 could not be contacted. In the remaining 30, mobility had improved to a mean of 20 metres (from a baseline of 10 metres) 21 demonstrating improvement and 9 stability. These data compared favourably with the previous cohort with uncorrected vitamin deficiency where 3 month mortality was 31%.
Conclusion: This small study suggests that excess mortality associated with vitamin d deficiency might be prevented by the replacement of vitamin D. Such an approach may improve mobility and reduce the risk of readmission. Larger numbers studied over a longer period are necessary to test this hypothesis.

USING STOPP/START CRITERIA TO RATIONALIZE MEDICATIONS IN OLDER PATIENTS ADMITTED TO GENERAL MEDICAL WARDS

Azmi Mohammed, N O'Connell, P Peter, S Kamaruddin, M Carson, J Howells and C Matango
Darlington Memorial Hospital

We used the STOPP (Screening Tool of Older Person's Prescriptions)/START (Screening Tool to Alert doctors to Right Treatment) tool to rationalize prescribing for 50 patients (>= 65 years) admitted to the diabetes/general medical ward. 90% of patients satisfied the definition of polypharmacy being on 5 or more medications. The total number of medications for this group on admission was 487 compared with a total of 413 on discharge. We identified risk factors for non-compliance; namely cognitive impairment (18%), living alone (78%), more than 10 medications (33%). 52% of the patients met the criteria to stop at least one medication, 22% met the criteria to start a new medication. In the patients who met either criterion we performed the intervention during admission in 42%. In 58% of cases we recommended the GP carry out the intervention. The intervention was calculated to be cost neutral based on generic prices.
Conclusions: This work confirms the size of the polypharmacy problem. Using STOPP/START criteria helped rationalise medications in a safe and cost effective manner and might be expected to reduce readmissions, length of stay and ADRs.

THE USE OF MCP MINI-GENES TO INVESTIGATE ABERRANT SPLICING IN ATYPICAL HAEMOLYTIC URAEMIC SYNDROME

Jacobo Salvatore, Patrick Walsh, Valerie Wilson, David Kavanagh
Newcastle University, Great North Children's Hospital, Northern Genetics Service

A 40 year old woman presented with microangiopathic haemolytic anaemia, thrombocytopenia and acute kidney injury. Investigation for shiga toxin HUS, thrombotic thrombocytopenic purpura and secondary causes of atypical haemolytic uraemic syndrome (aHUS) (normal homocysteine levels, negative autoantibodies, negative T-antigen) were negative. A diagnosis of primary complement mediated haemolytic uraemic syndrome was made. She was initially treated with plasma exchange and then transferred to eculizumab. Haemolysis stopped and she was discharged 10 days later with normal renal markers. Sequencing of known and aHUS genes (complement factor H, complement factor I, complement factor B and membrane co-factor protein (*CD46*)) revealed a new intronic variant in *CD46*. This new variant was predicted to alter the splice site of exon 3 of *CD46.* To confirm this we undertook site-directed mutagenesis using a *CD46* exon trap vector mini-gene. We demonstrated skipping of exon 3 and further functional work demonstrated reduced surface expression of CD46.
Conclusion: This case highlights the remaining diagnostic uncertainty behind aHUS. CD46 is a cell surface regulator of the complement system. Mutations in *CD46* are a known cause of aHUS. We have confirmed the functionality of this intronic *CD46* variant and identified this as the cause of aHUS in our patient.

GLUCOSE 6 PHOSPHATE DEFICIENCY MASQUERADING AS ATYPICAL HAEMOLYTIC UREMIC SYNDROME

Jacobo Salvatore, Patrick Walsh, Vicky Brocklebank, Sally Johnson, Martin Christian, David Kavanagh
Newcastle University, Great North Children's Hospital, Queen's Medical Centre, Nottingham,

A 4 year old boy presented to the paediatric nephrology unit with non-immune haemolytic anaemia, thrombocytopenia and acute kidney injury (AKI). A diagnosis of atypical haemolytic uraemic syndrome (aHUS) was made. He was treated with plasma exchange and subsequently eculizumab. Despite rapid improvement in renal function, there was evidence of continuing haemolysis. He re-presented twice whilst on eculizumab, despite adequate complement blockade, with haemolytic anaemia and thrombocytopenia, but on these occasions without renal involvement. Eculizumab was withdrawn after 6 months. Routine investigations for aHUS were performed, including the known aHUS related genes (*CFH, CFI, CFB, C3, CD46, THBD, DGKE*), factor H autoantibodies and the C5 polymorphism known to predict non-response to eculizumab. The investigations were negative, and the failure to respond to eculizumab led us to undertake whole exome sequencing. A pathogenic variant in glucose 6 phosphate dehydrogenase (G6PD) was identified. This was confirmed by functional analysis demonstrating decreased erythrocyte G6PD activity levels (0.4iU/1012 erythrocytes, normal 4.5-13.5). **Conclusion:** The pathogenic variant in G6PD identified in this child has previously been shown to result in chronic haemolytic anaemia with acute exacerbation following periods of oxidative stress. The AKI seen at presentation is likely due to heme-induced acute tubular necrosis. This case highlights the remaining diagnostic uncertainty in aHUS and the value of utilising next generation sequencing techniques in cases where the aetiology is unclear. We recommend G6PD deficiency is included in the differential diagnosis of patients presenting with aHUS.

A RAPID DECLINE IN MOBILITY

Aidan Whitehead, Emma Cox
Sunderland Royal Hospital

A 74-year-old female with a past medical history of hypertension, hypothyroidism and epilepsy presented to her GP with psychiatric symptoms, predominantly anxiety and depression. This was followed by a 3 month decline in mobility and function. Previously independent, she was disabled by progressive ataxia, tremor and weakness with later onset of cognitive impairment, requiring full time care for most ADLs. Her conscious level continued to decline after admission to hospital and with ongoing upper limb myoclonus. A CT head was normal and lumbar puncture biochemistry and immunology was normal. An EEG showed a diffuse encephalopathic pattern and MRI revealed increased signal in the basal ganglia, with cortical ribboning and “hockey stick sign”. A repeat EEG showed further deterioration, and the combination of these findings with MRI, and specific tests on CSF confirmed the diagnosis of Creutzfeld-Jakob Disease. **Conclusion:** Creutzfeld-Jakob Disease should be considered in all patients with rapid onset of symptoms suggestive of neurodegeneration.

DEFINING THE GENETIC DETERMINANTS OF PANCREATIC BETA-CELL GLUCOSE SENSITIVITY

Harshal Deshmukh, Andrea Mari, Alison Heggie, Paul Franks, Ewan Pearson, Mark Walker and DIRECT and RISC consortium

Pancreatic beta-cell glucose sensitivity (GS), the slope of the glucose–insulin secretion relationship, is a key predictor of progression to abnormal glucose tolerance in non-diabetic individuals. We studied 780 patients with Type 2 diabetes (T2D), 1818 individuals at high risk of developing T2D from the DIRECT study and 1276 health controls from RISC study. GS was calculated from oral glucose tolerance or mixed meal tolerance tests. Heritability of GS was estimated with typed loci using genomic tetranucleotide composition analysis. Established significant single nucleotide polymorphisms (p value $\leq 10^{-15}$) and effect sizes for T1D, T2D, HbA1c and fasting glucose(FG) were identified from National Genome Human Research Institute catalogue. Association of GS with candidate genes and beta-weighted genetic risk scores (GRS) were then calculated with linear regression models after adjustments for age, sex and BMI. A genome-wide association study (GWAS) and GWAS-meta-analysis were performed with data imputed to 1000 genomes panel using standard methods. The narrow-sense heritability for GS was 34% (±17%). After correction for multiple testing several known loci (*HHEX, CDKAL1, HNF1A, FTO, C6orf57, IGF2BP2, KCNQ1, G6PC2*) were associated (p value $\leq 10^{-4}$) with GS across the three cohorts. GRS for HbA1c level was significantly associated with GS (p value=0.004) in patients with T2D. Genome-wide association scan

and meta-analysis of the three cohorts showed gastric inhibitory polypeptide receptor-glutaminyl-peptide cyclotransferase like (*GIPR-QPCTL*) SNP, *rs35541137* to be associated with GS (effect allele=T, beta=0.04 p value=7.43X10 $^{-9}$).
Conclusion: We have shown that several GWAS loci for T2D, HbA1c and impaired fasting glycaemia are potentially mediated through effects on beta-cell GS. We have identified *GIPR-QPCTL* as a new locus for GS in keeping with the evidence that variation in *GIPR* predisposes to type 2 diabetes.

DECREASING ERRORS IN MEDICATION HISTORIES

Morris G, Cox E.
Sunderland Hospital

Working overnight poses challenges, one of which is gathering accurate medication histories from new admissions. We demonstrated that through simple measures such as giving doctors access to summary care record and poster reminders on the admission unit we could improve the recording of medication histories from 73% to 94%. The number of incomplete medication histories dropped from 47% to 31% and patients missing doses of regular medications dropped from 42% to 24%.
Conclusion: Through simple, cost effective measures we can improve medication history recording in patients admitted overnight.

"SEPSIS" ?SOURCE

Rayner FR, Chapman K, Lorenzi AR, Hargreaves B, Platt P, Thompson B, Pratt A
Freeman Hospital Newcastle

We present a 76-year-old lady of Indian origin who was admitted with persistent fevers and hyperglycaemia. She was treated for presumed sepsis with courses of antibiotics but no source was identified and she continued to spike temperatures. Her inflammatory markers were persistently raised (CRP 150 ESR 130 WBC 10-12 Hb 110). Tests including blood and urine cultures, autoantibody screen, MRI, echocardiogram and labelled white cell scan were negative. A more detailed history elicited that she had been suffering from vague headaches. A temporal artery ultrasound (TA USS) was performed which was positive. A biopsy performed shortly after starting steroids confirmed temporal arteritis. An audit on the fast track giant cell arteritis (GCA) and TA USS service that we offer showed the number of referrals for GCA has doubled over 3 years (2014-2016) but the number of biopsies has decreased. We found the sensitivity and specificity of TA USS was comparable with the published literature.

Conclusion: This case shows the importance of taking a thorough history and that GCA should be considered in all case of PUO in the over 50s even in the absence of headache.

AN AUDIT EVALUATING A NEW NURSE-LED IMPLANTABLE LOOP RECORDER SERVICE FOR INVESTIGATING CARDIAC ARRHYTHMIAS.

T Rice, A Theakston, J Mudd, A Iglesias-Postigo, J Owen, C Wyatt, A Hall, S Taggart, AJ Turley, NJ Linker.
The James Cook University Hospital

A Cardiac Rhythm Management (CRM) nurse-led service was developed in 2015 using Medtronic Reveal LINQ ILR devices and advanced remote monitoring. Advances in technology have allowed for implantation in a procedure room by CRM specialist nurses. Following implant, all patients received remote monitoring equipment and access to a nurse-led telephone helpline. Daily assessment, management of patient transmissions and follow-up care by scheduled telephone appointments were coordinated by the CRM nurse team. Outcomes from the nurse-led service were compared with traditional pathways over the preceding 5 years. Over 12 months 125 loop recorders (ILRs) were implanted. Referral time to ILR implant reduced from 49 to 35 days. Implant to definitive diagnosis reduced from 270 to 56 days. The conversion rate from ILR to permanent pacemaker (PPM) was 20/125 (16%); 50% for AV node disease; 50% for sino-atrial node disease. Catheter laboratory time saved was 94 hours. Appointment time was reduced from 4 hours to 1 hour. No complications occurred. Audit of patient experience demonstrated high levels of satisfaction with the nurse-led service.

Conclusion: The development of a CRM nurse-led ILR service with use of remote monitoring has resulted in significant reductions in referral to ILR implant time; ILR implant to diagnosis times; a higher than average diagnostic yield for pacing indication and high levels of patient satisfaction.

IS BRONCHOSCOPY STILL A USEFUL TEST IN PATIENTS PRESENTING WITH HAEMOPTYSIS, WITH A NORMAL CT SCAN?

Carlin, H.J., Doe, S
Freeman Hospital Newcastle

Standard UK investigations of haemoptysis are thoracic CT scan and bronchoscopy. With increasingly sensitive CT scanners is bronchoscopy still needed if the scan is normal? We analysed retrospectively all patients undergoing bronchoscopy for investigation of haemoptysis over six months (n=52). CT scans were performed on helical 64-slice scanners and reported by specialist thoracic radiologists. Findings were classified as normal, abnormal without evidence of malignancy (e.g. bronchiectasis or emphysema), or probable cancer. CT n findings were normal in 19 (37%) patients. 21 (40%) had an abnormal scan without clear malignancy. 12 (23%) had findings of probable cancer. No patient with a normal CT scan had any suspicious bronchoscopic findings. 2 (9%) patients in the abnormal CT group (n=21) had abnormal bronchoscopy and were diagnosed with malignancy. 4 (7.6%) patients undergoing bronchoscopy were referred to ENT due to abnormal bronchoscopic findings in the upper airway. Of these 1 was diagnosed with tonsillar carcinoma.
Conclusion: With modern CT technology and specialist reporting, a normal scan may be sufficient to exclude thoracic malignancy, without bronchoscopy. Upper airway abnormalities were seen in patients presenting with haemoptysis; ENT examination should be considered if CT scan is normal.

NITROFURANTOIN LUNG – BEWARE THE BREATHLESS PATIENT WITH RECURRENT URINARY INFECTIONS

Palmer E, Simpson JS, Beattie A, Worthy S, Forrest IA
Royal Victoria Infirmary Newcastle

Nitrofurantoin is recommended as first line prophylactic treatment for non-pregnant women with recurrent urinary tract infections. Nitrofurantoin induced pulmonary toxicity “nitrofurantoin lung” (NL) is rare but can lead to fibrosis and progressive respiratory failure. Cessation of nitrofurantoin can lead to complete recovery. We present a case series of patients with NL from the regional interstitial lung disease centre at the Royal Victoria Infirmary (RVI).We identified 11 patients between January 2012 and April 2017 with evidence of pneumonitis or fibrosis on CT imaging likely to be related to nitrofurantoin treatment. Mean age was 76 years (range 60 to 92), male to female ratio 1:10. On stopping nitrofurantoin there was radiological improvement in 54% of patients (n=6). In many cases, even those with patterns of apparent established fibrosis, the improvement was dramatic. Patients’ symptoms and pulmonary function tests improved.
Conclusion: NL should be considered in patients taking nitrofurantoin who present with progressive breathlessness and clinical or radiological signs of pulmonary fibrosis. Stopping nitrofurantoin can result in dramatic improvement in radiological features and symptoms.

ASSESSMENT OF NASOGASTRIC TUBE PLACEMENT

Christopher Taylor, Christopher Wells
North Tees Hospital

An audit had identified lack of documentation of 4 safety elements needed to accurately confirm correct nasogastric (NG) placement. Issues were identified regarding pH testing and use of trust guidelines. Following this, in conjunction with a practical assessment of Foundation-year doctors, an e-learning module was developed. This has been reviewed to assess the impact on

documentation and compliance with guidelines. There were improvements. However, the trust is continuing to review and educate staff regarding NG use and safety checks after placement.
Conclusion: This project identifies ways to support doctors to check the position of nasogastric tubes without complete reliance on chest x-rays.

CURRENT DEXAMETHASONE PRESCRIBING PRACTICE FOR CEREBRAL METASTASES

Samantha Foreman, Christopher Taylor, Benjamin Prudon,
North Tees Hospital

Cerebral metastases are common and can present with neurological symptoms from vasogenic oedema. Dexamethasone is the first line treatment but has side effects including hyperglycaemia, gastritis, psychiatric disturbance and myopathy. We noted inconsistency in the dose of dexamethasone, how it was weaned and side effects consented for. The available literature suggests appropriate regimes best represented by the Edinburgh Cancer Centre Guidelines. These suggest starting dose and subsequent weaning should be tailored to symptom severity and evidence of oedema, mass effect or coning on CT scan. We reviewed over 6 months patients admitted and managed for new cerebral metastases. We noted inconsistencies in starting doses, weaning regimes, PPI co-prescription, complication screening and follow up.
Conclusion: We have introduced new guidelines for dexamethasone prescribing and plan to audit the changes to assess impact.

Association Business

Date of next meeting: Wednesday 8th November 2017 6.00 pm Freeman Hospital.
This will take place after the GIM teaching. The format will remain unchanged with 9 slots for oral abstracts and 6 for poster presentations. There will be a free buffet meal to allow posters to be inspected and concentration to be maintained! Please do come and encourage your juniors to come after the GIM teaching.
The meeting is **approved for 3 hours CME.** Abstracts for poster or oral presentations from consultants, trainees and medical students are all welcome. Presentations should reflect the full range of clinical medical practice including research, clinical series, audit and case reports. Please submit by email (around 250 words including a short conclusion) **before 2nd October** to the secretary clive.kelly@ghnt.nhs.uk.
The Margaret Dewar prize for the best junior doctor or medical student's presentation will be awarded for the best oral presentation of the year (£150), runner-up (£100) and best poster (£50).
Had you considered joining the committee? Our meetings with refreshments take place 3 times a year. We are particularly seeking enthusiastic representatives from James Cook, Northumbria and Carlisle. If interested, please contact Clive Kelly clive.kelly@ghnt.nhs.uk.
Also please e-mail the names of any new consultant colleagues or your own name if you are not already on the mailing list to the secretary and consider presenting your research for the Hewan Dewar prize awarded annually for the best research paper submitted by a junior doctor or medical student.
We look forward to seeing you at the Freeman Postgraduate Centre on Wednesday 8th November 6.00 p.m.