

Abstracts

78th Meeting of Ulster Society of Internal Medicine, Friday 19th October 2007.

Ulster Medical Society Rooms,
Belfast City Hospital, Belfast.



AGENDA

- 1.55pm Welcome - Chairman: Dr David Higginson
- 2.00pm Plenary I – presented abstracts
- 3.10pm Invited Lecture. “Management of Upper GI Bleeding”.
Dr Tony Tham, Ulster Hospital.
- 3.35pm Afternoon Tea
- 4.00pm Invited case from Belfast City Hospital
- 4.10pm Plenary II - presented abstracts.
- 4.35pm Presentation of prize for best abstract
- 4.40pm Guest lecture: “Biologic Therapies in Psoriatic Arthritis”
Prof Oliver Fitzgerald Consultant Rheumatologist,
St Vincent’s University Hospital Dublin.

PRESENTED ABSTRACTS

1. Prevalence of cardiac channelopathies in a tertiary referral centre in Northern Ireland

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Several primary cardiac arrhythmia syndromes are known to have a genetic basis and are caused by mutations in ion channel genes. These mutations cause abnormal ionic currents which can lead to ECG abnormalities and cardiac arrhythmias. These syndromes, known as cardiac channelopathies, include long QT syndrome (LQTS), short QT syndrome (SQTS), Brugada syndrome (BS) and catecholaminergic polymorphic ventricular tachycardia (CPVT), and are responsible for up to 40% of all cases of Sudden Adult Death Syndrome¹.

To date 32 families have been genetically diagnosed with LQTS. In these families 250 individuals have been genetically screened; 141 (56%) carry a mutation for LQTS and 95 (38%) are non-carriers (results pending in 14 (6%)). A further 10 families have a clinical diagnosis of LQTS with no gene mutation identified (sensitivity of 70% for picking up LQTS²). These families were identified following; investigation of syncope (35.4%), routine ECG (19.3%), screening following sudden death in family (16.1%), successful resuscitation of

cardiac arrest (13%), investigation of palpitations (13%) and investigation following a near drowning episode (3.2%). Nine families have been referred for investigation of likely BS; 3 have mutations in SCN5A detected by genetic screening (sensitivity of 30% for picking up BS²). One family has been diagnosed with CPVT on genetic screening and CPVT is a possible diagnosis in 1 other family. No SQTS families have been identified.

Cardiac channelopathies are important primary cardiac arrhythmia syndromes. Genetic testing aids in the identification of individuals carrying these gene mutations so that appropriate management can be implemented.

1. Tan HL, Hofman N, Van LI, Van der Wal AC, Wilde AA. Sudden unexplained death: heritability and diagnostic yield of cardiological and genetic examination in surviving relatives. *Circulation* 2005;**112**(2):1457-1459
2. Garratt CJ, Elliott PM, Behr E, Blair E, Connelly D, Cowan C, Davidson N, Grace A, Griffith M, Jolly A, Lambiase P, McKenna W. Heart Rhythm UK Familial Sudden Death Syndromes Statement Development Group. Clinical indications for genetic testing in familial sudden cardiac death syndromes: a HRRUK position statement. *Heart Online* 2007;doi:10.1136/hrt.2007.127761.

2. Anti-Xa activity with local treatment protocols for acute coronary syndrome.

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Abstract: Enoxaparin is now the recommended anti-thrombotic treatment for patients with acute coronary syndromes (ACS). While plasma monitoring of the biological activity of enoxaparin is not usually required due to its predictable pharmacokinetics and pharmacodynamics, it may be assessed by measuring plasma anti-Xa levels (therapeutic range 0.5-1.2IU/ml). In patients with ACS, low anti-Xa activity is independently associated with increased 30-day mortality.¹ Guidelines and licensing suggest an ACS treatment dose of 1 mg/kg bd, although in Northern Ireland, many local treatment protocols dose cap enoxaparin at 60mg bd to reduce bleeding risk. We studied 20 consecutive patients admitted with ACS. All received 60mg enoxaparin bd. Peak plasma anti-Xa activity was measured as described by Montelescot et al, 4-6 hours after administration of enoxaparin.

Results: Of the 20 patients, 14 were male, mean TIMI risk score was 4.2/7 and mean weight was 81.9kg. One third (35%) of patients (5 male, 2 female) were found to have

sub-therapeutic anti-Xa levels (mean 0.35 IU/ml, range 0.2–0.49 IU/ml). The remainder had anti-Xa levels within the therapeutic range (mean 0.73 IU/ml, range 0.5 – 1.12 IU/ml). Mean weight was higher in those with sub-therapeutic compared with therapeutic anti-Xa levels (89.9 vs 77.6kg; p value = 0.041). 5 patients in the therapeutic group and 1 patient in the non-therapeutic group had impaired renal function (eGFR 30-60 mls/min). In conclusion, dose capping of enoxaparin at 60mg bd in ACS patients may result in a significant proportion achieving sub-therapeutic anti-Xa levels, potentially correlating with poorer outcome.

1. Montalescot G, Collet JP, Tanguy ML, Ankri A, Payot L, Dumaine R, Choussat R, Beygui F, Gallois V, Thomas D. Anti-Xa activity relates to survival and efficacy in unselected acute coronary syndrome patients treated with enoxaparin. *Circulation* 2004;**110**:392-398.

3.A randomised placebo-controlled interventional trial of omega-3-polyunsaturated fatty acids on endothelial function and disease activity in systemic lupus erythematosus

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We aimed to determine the clinical effect of dietary supplementation with low dose omega-3-polyunsaturated fatty acids on disease activity and endothelial function in patients with systemic lupus erythematosus.

A 24 week randomised double-blind placebo-controlled parallel trial of the effect of 3g of omega-3-polyunsaturated fatty acids on 60 patients with SLE was performed. Serial measurements of disease activity using the revised Systemic Lupus Activity Measure (SLAM-R) and British Isles Lupus Assessment Group index of disease activity for SLE (BILAG), endothelial function using flow mediated dilation of the brachial artery (FMD), oxidative stress using platelet 8-isoprostanes and analysis of platelet membrane fatty acids were taken at baseline, 12 and 24 weeks.

In the fish oil group there was a significant improvement at 24 weeks in SLAM-R (from 9.4±3.0 to 6.3±2.5, $p<0.001$); in BILAG (from 13.6±6.0 to 6.7±3.8, $p<0.001$); in FMD (from 3.0% (-0.5-8.2) to 8.9% (1.3-16.9), $p<0.001$) and in platelet 8-isoprostanes (from 177pg/mg protein (23 – 387) to 90 pg/mg protein (32 – 182), $p = 0.007$).

Low dose dietary supplementation with omega-3 fish oils in SLE not only has a therapeutic effect on disease activity but also improves endothelial function and reduces oxidative stress and may therefore confer cardiovascular benefits.

4. Effect of ingestion of food on the inhibition of DPP-IV activity by oral metformin in type 2 diabetes.

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The incretin hormones glucagon-like peptide-1 (GLP-1) and

glucose-dependent insulinotropic polypeptide (GIP) constitute the enteroinsular axis which promotes postprandial insulin secretion. The therapeutic potential of these hormones in diabetes is limited by their rapid inactivation by the enzyme

dipeptidylpeptidase-IV (DPP-IV). Here we investigated the acute effects of metformin in the presence and absence of food on DPP-IV activity in type 2 diabetes

Ten subjects with type 2 diabetes (6 male/4 female, age 65.8±15.8 years (mean±SEM), body mass index 30.0±7.5kg/m², HbA1c 6.3±1.2%) received metformin 1g orally or placebo together with a standard mixed meal (SMM) in a random crossover design. Six subjects reattended fasting and received metformin 1g without a SMM.

Following SMM (n=10), DPP IV activity was not suppressed by metformin compared with placebo (area under curve AUC_{0-4h} 1574±4 and 1581±8 µmol/min respectively). No differences were observed in plasma glucose, insulin and total GLP-1. After fasting (n=6), DPP IV activity was suppressed ($P<0.02$) when compared to those given metformin with a SMM (AUC_{0-4h} 1494±9 vs 1578±4 µmol/min). Metformin plasma levels were significantly higher ($P<0.03$) after fasting than SMM (AUC_{0-4h} 457±55 vs 350±66 mcg/ml).

Thus metformin inhibits DPP IV activity in type 2 diabetic patients in the fasting state but not when taken with a standard mixed meal. Metformin plasma concentrations are lower if taken with food. Metformin may have potential for combination therapy with incretin hormones.

5. An interesting cause of hypopituitarism: infiltrative versus idiopathic

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Hypopituitarism usually occurs as the result of a pituitary tumour or as a consequence of its treatment. If, however, pituitary imaging is negative then there are a wide variety of alternative causes but no firm consensus as to which should be actively sought. We present two cases of apparent idiopathic hypopituitarism in whom the underlying diagnosis was delayed with potentially serious side effects.

Case Report: A 32 year old male presented with symptoms of hypogonadism. Testosterone (<0.7nmol/L; N 10.5-30 nmol/L) and gonadotrophins were low (FSH <0.5 U/L; LH <0.5 U/L) and prolactin was normal (118mU/L). Thyroid function was normal (fT4 9.7pmol/L; N 7.6-19.7 pmol/L, TSH 1.33mU/L; N 0.45-4.5 mU/L). Insulin tolerance testing established a normal cortisol peak of 1002nmol/L but suboptimal growth hormone response (8.1mU/L) to hypoglycaemia. Pituitary imaging was normal. He presented 5 years later in congestive cardiac failure with an elevated ferritin (6309 ug/L; N 18-325ug/L) and transferrin saturation (100%). Homozygosity for the C282Y mutation confirmed the diagnosis of haemochromatosis.

A 51 year old female presented with non-specific symptoms. Initial testing suggested hypopituitarism with a random

cortisol of <30nmol/L and a low free T₄ (6.9 pmol/L) with normal TSH (2.3 mU/L). Prolactin was 1190mU/L and gonadotrophins were post menopausal (FSH 26.6 U/L, LH 16.8U/L). Insulin tolerance testing confirmed an inadequate cortisol response (<30nmol/L) but a normal GH response (41.3 mU/L) to hypoglycaemia. Pituitary imaging was normal. Four years later, investigation revealed a raised ferritin (389ug/L) and transferrin saturation (74%). She was heterozygous for the C282Y mutation and iron overload was confirmed at liver biopsy.

Haemochromatosis causes pituitary dysfunction by depositing iron in the anterior pituitary. Due to its rarity as a cause of hypopituitarism, it is not always considered by endocrinologists as a potential diagnosis. Imaging is usually normal and patients are often wrongly labelled as having idiopathic hypopituitarism. However, early diagnosis is important as treatment may reverse the pituitary deficit and prevent future sequelae in other organs. We recommend iron studies in all patients who present with hypopituitarism and normal pituitary imaging.

6. Implementing the European Society Of Cardiology Guidelines for evidence based therapy in Heart failure: An audit of Pharmacotherapy at discharge from an Acute Hospital.

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The consistent implementation of guidelines on the use of evidence-based drug therapy in heart failure patients remains a challenge in clinical practice. The purpose of this study was to determine the extent of this problem in a single centre that seeks to adhere to European Society of Cardiology guidelines (2005), to discern its possible causes and to assess whether there is a difference depending on LV systolic function.

281 consecutive patients (150 male, mean age 77 years) admitted between April 2005 and December 2006 were identified from the Mater Hospital Heart Failure database. Of these, 245 patients who had recent echocardiographic data available formed the study population: 154 (63%) had LV systolic dysfunction (LVEF < 40%) (Group LV-S) and 91 had relatively preserved systolic function (Group LV-P).

Results: The groups were similar except for percentage with hypertension (LV-P 80% v LV-S 44%, p<0.001). Mortality was 10.4% in LV-S and 10.9% in LV-P (p NS). Mean serum creatinine was 149µmol/l in LV-S and 135µmol/l in LV-P on admission and 158 µmol/l and 141 µmol/l respectively at discharge.

Review of the clinical records of 24 patients in LV-S not on treatment with ACEi/ARB at discharge revealed that 20 had significantly impaired renal function (mean serum creatinine 264 µmol/l), 2 had profound hypotension with initiation of ACEi, one had severe aortic stenosis and one self-discharged against advice.

The proportion (%) of patients in each group on prognosis modifying medication on admission (A) and at discharge (D) were:

		LV-S	LV-P
ACEi/ARB	A	60	46
	D	83	76
Beta-Blocker	A	55	55
	D	91	94
AA	A	30	24
	D	50	49

ACEi / ARB= Angiotensin converting enzyme inhibitor or Angiotensin Receptor Blocker;

AA = aldosterone antagonist

Conclusions: In this single centre study, use of beta-blockers was very satisfactory. All LV-S patients were on treatment with ACEi/ARB or had a documented contra-indication, usually renal impairment. There appears to be scope for greater use of AA in LV-S. It was also interesting to note the frequent use of AA in heart failure with relatively preserved systolic function.

7. Trends In Lipid Levels In Patients Admitted With Myocardial Infarction To A Regional Cardiology Centre 2000-2006

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Introduction: Hypercholesterolemia is a major risk factor for coronary artery disease. Revised Joint British Society Guidelines 2005 (JBS-2) have recommended tighter lipid targets for both primary and secondary prevention. We reviewed trends in fasting lipid levels of patients admitted with Myocardial Infarction (MI) to our centre and assessed compliance with these guidelines.

Methods: Fasting lipid profiles were analysed on patients admitted with an MI from January 2000 to December 2006 (n=1346). For patients admitted in 2005 lipid profile values were re-evaluated at least 6 months after admission to determine if JBS-2 target lipid values had been achieved.

Results: Average Total Cholesterol decreased from 5.26 mmol/L in 2000 to 4.73 mmol/L in 2006 (p=0.026), LDL Cholesterol from 3.14 mmol/L in 2000 to 2.57 mmol/L in 2006 (p<0.001) and HDL Cholesterol rose from 1.11 mmol/L in 2000 to 1.58 mmol/L in 2002 (p=0.013) but declined to 1.33 mmol/L in 2006 (p=0.423). ST elevation Myocardial Infarction (STEMI) patients had significantly higher Total Cholesterol (5.11 Vs 4.78; p<0.001), LDL (2.97 Vs 2.69; p<0.001) and lower HDL (1.28 Vs 1.39; p=0.399) when compared with those admitted with Non ST-elevation Myocardial Infarction (NSTEMI). In 2005, 69% had achieved Total Cholesterol, 74% LDL and 71% HDL cholesterol targets 6 months after their admission.

Conclusion: Our study reveals reduction in lipid profile values on admission from 2000 to 2006. We also noted that patients admitted with STEMI had a higher Total Cholesterol, LDL and lower HDL than NSTEMI. Current guidelines for primary and secondary prevention of coronary heart disease has led to more fastidious use of anti-lipid medications and has had a significant impact on the reduction of cholesterol.