Abstracts from the Association of British Clinical Diabetologists (ABCD) meetings

Abstracts from the Autumn 2006 meeting

(P1): The effect of a 'Treat to Target' approach with insulin glargine in patients with persistent poor glycaemic control on traditional treatment with twice daily insulin mixtures

REJ Ryder, J Cutler, ML Call and AP Mills
City Hospital, Birmingham. E-mail: bob.ryder@zwhh.nhs.uk

Background and aims: In type 2 diabetes a 'Treat to Target' (T2T) approach, with once daily long acting insulin at bedtime and continuing oral hypoglycaemic agents, has been shown to be remarkably effective in clinical trials involving patients with inadequate glycaemic control despite maximum oral hypoglycaemic agents. The aim was to see if a similar T2T approach could be as successful in unselected patients in an inner city area who were already established on traditional twice daily insulin mixtures and yet remained poorly controlled (HbA1c >8% for at least 1 year).

Material and methods: This audit is of 85 such patients (mean [±SD] age 59 [±9] years; 54% female, 46% male; 53% South-Asian, 24% Caucasian, 23% Afro-Caribbean) were offered a T2T protocol involving a self-applied 2IU increase in the dose of insulin glargine every 3 days if the fasting glucose on self-testing was >5.4mmol/L on each of those days. Patients were on the maximum tolerated dose of metformin. If fasting glucose reached the target but HbA1c remained above 7%, a prandial oral glucose regulator was added and, if this failed, patients were offered prandial fast acting insulin analogue with a dose increasing algorithm. Patients reaching 200 units of insulin daily without glycaemic control were offered the addition of a glitazone. There were sufficient data to make an analysis based on 128/132 patients.

Results: A snapshot was taken at a median (range) of 2.2 (0.2–3.4) years into the ongoing rolling programme. Mean (±SD) HbA1c had fallen from 9.92 (±1.34)% to latest value of 8.2 (±1.5)% (p<10^-5). The lowest HbA1c achieved in response to the protocol was at 1.1 (0.2–2.5) years and was ≤6.5% in 16%, ≤7% in 30%, ≤7.5% in 32% and ≤7.9% in 46%. Only 28% failed to show significant improvement in HbA1c. (HbA1c fall ≥1%). In 25% the HbA1c was not significantly better than baseline.

Conclusion: Whilst the figures from this audit are less impressive than those from formal clinical trials, 41% achieved HbA1c ≤7%. This shows that even in the ‘real world’ of unselected patients in an inner city area, a T2T approach involving patient driven insulin dose adjustment can be considerably more effective than traditional methods involving twice daily insulin mixtures and insufficiently frequent dose adjustment by health professionals.

(P2): Application of a ‘Treat to Target’ approach with once daily long acting insulin at bedtime in the ‘real world’ of unselected patients in an inner city area

REJ Ryder, J Cutler, ML Call and AP Mills
City Hospital, Birmingham. E-mail: bob.ryder@zwhh.nhs.uk

Background and aims: In patients with type 2 diabetes and inadequate glycaemic control despite maximum oral hypoglycaemic agents, a ‘Treat to Target’ (T2T) approach, with once daily long acting insulin at bedtime and continuing oral hypoglycaemic agents, has been shown to be remarkably effective in clinical trials. The aim was to see to what extent this approach could be as successful in the ‘real world’ of unselected patients in an inner city area.

Material and methods: This audit is of 132 such patients (mean [±SD] age 57 [±11] years; 60% male, 40% female; 50% South-Asian, 36% Caucasian, 14% Afro-Caribbean) who between 2002 and 2004 were offered a T2T protocol involving a self-applied 2IU increase in the dose of insulin isophane every 3 days if the fasting glucose on self-testing was >5.4mmol/L on each of those days. Patients were on the maximum tolerated dose of metformin. Those experiencing nocturnal or fasting hypoglycaemia were switched to insulin glargine. If fasting glucose reached the target but HbA1c remained above 7%, a prandial oral glucose regulator was added and, if this failed, patients were offered prandial fast acting insulin analogue with a dose increasing algorithm. Patients reaching 200 units of insulin daily without glycaemic control were offered the addition of a glitazone. There were sufficient data to make an analysis based on 128/132 patients.

Results: A snapshot was taken at a median (range) of 2.2 (0.2–3.4) years into the ongoing rolling programme. Mean (±SD) HbA1c had fallen from 10.3 (±1.6)% to latest value of 8.2 (±1.5)% (p<10^-8). The lowest HbA1c achieved in response to the protocol was at 1.3 (0.2–3) years and was ≤6.5% in 20%, ≤7% in 41%, ≤7.5% in 55% and ≤7.9% in 60%. Only 5% failed to show significant improvement in HbA1c. (HbA1c fall ≥1%). Latest HbA1c at the time of the snapshot was ≤6.5% in 9%, ≤7% in 23%, ≤7.5% in 38% and ≤7.9% in 48%. In only 27% was the HbA1c not significantly better than baseline.

Conclusion: The effect of a ‘Treat to Target’ approach with insulin glargine in patients with persistent poor glycaemic control on traditional treatment with twice daily insulin mixtures.
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(P4): Hyperthyroidism presenting with persistent headache and vomiting

K Ashawesh, R Abdulqawi and D Barton
Princess Royal Hospital, Telford. E-mail: k_ashawesh@yahoo.com

Background: The majority of patients with hyperthyroidism are readily diagnosed clinically. Vomiting, headache and/or abnormal liver function have rarely been described as the main presenting features of hyperthyroidism.

Case: A 58-year-old lady with no significant past medical history was admitted with 3 weeks' history of severe headache and persistent vomiting. Physical examination was unremarkable. Initial investigations including FBC, U/E, CRP and CXR were normal. CT head and CSF pressure and analysis were also normal. She was treated symptomatically and discharged home 8 days post-admission. Two weeks later, she was re-admitted with the same symptoms. CT reported weight loss of 2 kg. Physical examination was unremarkable except for sinus tachycardia of 134 beats/min. Her liver function tests (LFTs) were abnormal: ALP 109, ALT 207, bilirubin 41 and GGT 139. Autoimmune and viral hepatitis screen were normal. Ultrasound abdomen showed no abnormalities. Upper gastrointestinal endoscopy revealed reflux oesophagitis secondary to the vomiting. Barium meal and small bowel studies were negative. She was treated with omeprazole, anti-emetics and analgesia with no improvement. While she was in the hospital, she was noted to have a heat intolerance which, in combination with weight loss and tachycardia, led to consideration of hyperthyroidism. Thyroid function tests confirmed the diagnosis of hyperthyroidism. TSH <0.05 mU/L (0.4–4), FT4 68.8 pmol/L (10–25). Thyroid U/S revealed a small multinodular goitre. On treatment with carbimazole and propranolol, her symptoms resolved completely within 4 days (after 5 weeks of persistent vomiting and headache). On 6 weeks' follow up at the outpatient clinic, she was asymptomatic and biochemically euthyroid on carbimazole 20mg/day with normalisation of her LFTs.

Comment: Hyperthyroidism should be considered in patients with persistent vomiting, headache and/or abnormal LFTs. Awareness of these atypical presentations will assist physicians to make a timely and cost-effective clinical decision.

(P5): Self-poisoning with pet medications

KA Ashawesh, R Abdulqawi and D Barton
Medical Department, Princess Royal Hospital, Telford. E-mail: k_ashawesh@yahoo.com

Introduction: Many pet medications are pharmacologically similar to those prescribed for human use. An intentional overdose with pet medications is uncommon. We describe a case in which a pet's anti-epileptic drug was deliberately used for self-poisoning.

Case: A 55-year-old woman with no significant past medical history and with Grade 1 thyroid eye disease; TSH <0.05 mU/L (0.1–5.3 mU/L); T3 2.60 pmol/L (5.3–6.5 pmol/L); antithyroid peroxidase antibody titre 849U/ml (positive >100U/ml). She received an 18-month course of carbimazole but remained thyrotoxic on cessation of therapy. A total thyroidectomy was performed. Histology showed patchy lymphocytic inflammation and occasional germinal centres, consistent with a diagnosis of Graves’ Disease. She currently feels well on thyroid replacement therapy.

Assessing the thyroid gland with a 123I-scan revealed a cold nodule, suspicious for a cyst. A US-guided fine needle aspiration was performed. The results did not reveal any malignancy.

Case: A 58-year-old lady with no significant past medical history was admitted with 3 weeks' history of severe headache and persistent vomiting. Physical examination was unremarkable. Initial investigations including FBC, U/E, CRP and CXR were normal. CT head and CSF pressure and analysis were also normal. She was treated symptomatically and discharged home 8 days post-admission. Two weeks later, she was re-admitted with the same symptoms. CT reported weight loss of 2 kg. Physical examination was unremarkable except for sinus tachycardia of 134 beats/min. Her liver function tests (LFTs) were abnormal: ALP 109, ALT 207, bilirubin 41 and GGT 139. Autoimmune and viral hepatitis screen were normal. Ultrasound abdomen showed no abnormalities. Upper gastrointestinal endoscopy revealed reflux oesophagitis secondary to the vomiting. Barium meal and small bowel studies were negative. She was treated with omeprazole, anti-emetics and analgesia with no improvement. While she was in the hospital, she was noted to have a heat intolerance which, in combination with weight loss and tachycardia, led to consideration of hyperthyroidism. Thyroid function tests confirmed the diagnosis of hyperthyroidism. TSH <0.05 mU/L (0.4–4), FT4 68.8 pmol/L (10–25). Thyroid U/S revealed a small multinodular goitre. On treatment with carbimazole and propranolol, her symptoms resolved completely within 4 days (after 5 weeks of persistent vomiting and headache). On 6 weeks' follow up at the outpatient clinic, she was asymptomatic and biochemically euthyroid on carbimazole 20mg/day with normalisation of her LFTs.

Comment: Hyperthyroidism should be considered in patients with persistent vomiting, headache and/or abnormal LFTs. Awareness of these atypical presentations will assist physicians to make a timely and cost-effective clinical decision.
tory T cells, as well as a shift from a Th1 to a Th2 immune profile. Emergence of Graves’ Disease is described following Campath-1H therapy in multiple sclerosis, and immune reconstitution in HIV infected individuals. This is, however, the first report of thyrotropic Graves’ Disease complicating ABMT. Physicians should be aware of this possible complication as popularity of ABMT grows.

**(P8): Iopanoic acid – an underutilised treatment for severe thyrotoxicosis in the UK**

DH Gannon and AB Johnson
Southmead Medical Hospital, North Bristol Healthcare Trust. E-mail: gannonanddavis@hotmail.com

Despite being the most potent known 5’-deiodinase inhibitors, all oral cholecystographic agents have been withdrawn from the market in the US. In the UK, iopanoic acid (IA) is currently the only oral cholecystographic agent to remain in clinical use for the treatment of thyrotoxicosis. We report our experience with the use of IA in a series of 10 subjects with thyrotoxicosis.

**Method:** Retrospective case review of 10 consecutive subjects to receive IA at the Southmead Medical Hospital, Bristol. Clinical course and thyroid function tests were analysed.

**Findings:** All patients received a loading dose of 1g, then 500mg BD of IA; mean age of patient 39.6 years (range 18–66); mean duration of use 28.9 days (range 7–68); mean fall in serum FT3, FT4 level after 24 hours from baseline of IA use 46.2%, 5.5%; after 72 hours 63.9%, 7%; after 5 days 70.3%, 34.0%. No side effect from IA use was noted. One patient had relapse of thyrotoxicosis on stopping accompanying thionamide, but improved on restarting thionamide. One patient died from exacerbation of pre-existing cardiac failure despite biochemical amelioration of thyrotoxicosis.

**Conclusions:** IA is a safe and effective adjunct in the treatment of severe thyrotoxicosis. In keeping with published data, the drop in free T3 observed in our small cohort is remarkable, especially when IA is used in combination with a thionamide. We believe it is under-utilised in the UK and fear its future availability is threatened by ever-declining clinical use. IA use should be considered in all patients with severe thyrotoxicosis, especially those awaiting urgent thyrodeectomy.

**(P9): Faster resolution of ketosis with higher insulin and glucose concentrations in the management of diabetic ketoacidosis**

MS Hamersley1, R Reddy Gobihal2 and DR Matthews2
1Nuffield Department of Medicine, John Radcliffe Hospital, Oxford; 2OCDM, University of Oxford. E-mail: maggie.hamersley@orh.nhs.uk

**Aim:** To assess the response of ketone concentrations to the treatment of diabetic ketoacidosis (DKA).

**Methods:** A retrospective analysis of the first 24 hours of treatment of 17 patients admitted with DKA. We divided patients into 2 groups (Gp1, Gp2) being those with blood glucose (BG) >10mmol/L (n=10, Gp1) and those with BG <10mmol/L (n=7, Gp2) during the first 16 hours of treatment.

**Results:** The difference in baseline BG and ketones was not statistically significant. During the first 8h, average BGs were 15.8 and 15.9mmol/L, ketones were 4 and 4.4mmol/L, and insulin infusion rates were 4.3 and 3.5 units/L respectively (all NS). In the second 8h BGs were 12.1 and 7.8mmol/L (p<0.001), ketones were 1.4 and 2.7mmol/L (p<0.001), and insulin rates were 3.5 and 1.9 units/L (p<0.001) respectively. In the third 8h, BGs were 10.4 and 8.6mmol/L (p=0.07), ketones were 0.5 and 8mmol/L (p<0.0001), and insulin rates were 2.7 and 2 units/h (p=0.03) respectively. In Gp1 the ketones fell faster than in Gp2 (p<0.001).

**Conclusion:** These data support the hypothesis that the use of higher insulin concentrations in the management of DKA facilitates suppression of ketogenesis. We suggest that ketones should be measured in the management of DKA and that insulin rate should be titrated against both ketone concentration and glucose.

**(P10): Glucagonoma: a rare cause of diabetes**

K Jacob, M Malige, K Dixit and J Valle
Christie Hospital, Manchester. E-mail: koshynita@gmail.com

A 55-year-old lady had presented with pain in her abdomen and dyspeptic symptoms 6 years ago. She was known to have depression, treated by psychiatrists, as well as osteoarthritis, on NSAID. An oesophagogastroduodenoscopy was normal. Ultrasound abdomen was unremarkable except haemangiomata of the right lobe of the liver. She then developed diarrhoea with a history suggestive of steatorrhoea. Clinical examination, blood investigations as well as repeat gastroscopy, barium follow-through and flexible sigmoidoscopy were normal. A diagnosis of irritable bowel syndrome was made. She then developed diet controlled diabetes with some history of weight loss. Two years ago she was admitted with uncontrolled diabetes and started on insulin. An urgent CT scan of her abdomen revealed a heterogenous mass head of pancreas with atrophic body and tail with multiple liver metastases. Subsequent liver biopsy and histopathology confirmed a metastatic neuroendocrine tumour of the pancreas; 24-hour urinary 5HIAA was normal. Fasting gut hormone profile showed an elevated glucagon level of 214±50 confirming glucagonoma. She was started on interferon and interferon as well as Cetuximab to normalise her diabetic control. She had low mood, complained of profound lethargy and worsening arthralgia and myalgia. Interferon was stopped. Subcutaneous octreotide was started, followed later by Sandostatin LAR which helped with reducing the insulin requirement as well as better control of her diabetes. Unfortunately, her scan suggest progressive disease and an MIBG uptake scan followed by possible MIBG treatment is planned.

Glucagonomas are rare tumours and fewer than 250 cases have been described in the literature. In patients with diagnosis of diabetes and irritable bowel syndrome a careful evaluation is necessary to rule out neuroendocrine tumours.

**(P11): Prospective study to determine acute effect of central laser photoagulation on driving ability in patients with diabetic maculopathy**

R Ratnasabapathy1, G Vafidis2, C Kirolos3 and WM Kong3
1Imperial College School of Medicine, University of London; Departments of 2Ophthalmology and 3Diabetes, Central Middlesex Hospital, North West London Hospitals NHS Trust, London. E-mail: uchong@imperial.ac.uk

DVL A guidelines (based on retinal laser data) advise central laser photocoagulation patients not to drive until visual acuity (VA) and visual fields (VF) have been formally tested. The acute effects of central laser photocoagulation for diabetic maculopathy on VA and VF have not been previously examined. There are also no data on the acute effects of tropicamide eye drops on VA on older people with diabetes.

**Methods:** We prospectively studied 9 patients requiring laser treatment for diabetic maculopathy (laser group) and 10 controls (diabetic people not requiring laser treatment); (all age >50 years, VA >6/12). VA and VF were tested at: t=1 (baseline), t=2 (20min post-1% tropicamide), t=3 (30min post-laser), t=4 (2 hours post-laser).

**Controls** were assessed at time matched intervals. VA was measured using a LogMar chart (a change of 0.02 = 1 letter on the chart). Binocular VF were tested using the Esterman Fields Test according to DVL A criteria.

**Results:** There was no difference in VA between the laser and control groups at baseline. Tropicamide reduced VA (t=2: change LogMar score, mean ± SD; [controls] -0.08±0.09, p<0.001). There was no significant difference from baseline in mean LogMar score at t=3 and 4. VA decreased following laser; (change in VA, laser vs controls, t=3: -0.17±0.12, p<0.02, t=4: -0.13±0.26, p<0.001). Tropicamide did not reduce VF. Controls fulfilled DVL A vision requirements for VA and VF at all timespoints. Two laser patients failed DVL A VA requirements at t=3 and 1 patient at t=4. Only 33% of the laser group returned to their baseline binocular VA compared to 60% of controls.
Conclusion: VA is reduced by tropicamide but remains within DVLA requirements in patients over 50. Central laser treatment significantly decreases VA acuity but not VF for at least 2 hours to DVLA requirements in patients over 50. Central laser treatment significantly decreases VA acuity but not VF for at least 2 hours to

(P12): Re-audit outcome of diabetic foot osteomyelitis in large district general hospital setting
K Nikookam1, T Boochandran1, A Ahonkai1, S Lacey2, K Wise1 and S Jacob1
Departments of 1Diabetes, 2Microbiology, 3Podiatry, and 4Vascular Surgery, King George Hospital (KGH), Barking Havering Redbridge NHS Trust, Ilford. E-mail: khash.nikookam@bhrhospitals.nhs.uk

There are around 1.3 million people in the UK currently diagnosed with diabetes and another million may have diabetes without knowing it. Diabetic patients have over 60% a greater risk of leg amputations and approximately 20–40% develop peripheral vascular disease and neuropathy. It has been argued for long since 1989 (St Vincent Declaration) that the incidence of diabetic osteomyelitis should be reduced by 50% over a 5-year period.

We designed a foot proforma looking at referral source, diagnostic criteria, site of lesion, risk factors, route and duration of antibiotics, outcome and follow up and outcome. We then carried out a retrospective analysis of 30 patients admitted to KGH with osteomyelitis identified by PAS system over a 3-year period (2000–2003).

Results: Most of the patients were in their 40s. Around 70% of patients had type 1 diabetes and were white Caucasian. In all, 50% of patients were admitted from A&E, 33% following a non-urgent department. Around 70% of patients were male and had a previous history of foot ulcers. Around 20% had HbA1c >11%. Investigations and outcome treatment of osteomyelitis vary significantly depending on the admitting team and specialty.

Recommendations: These are: development of a foot care protocol, referral form and dedicated multidisciplinary foot team (diabetologist, vascular surgeon, microbiologist, podiatrist and diabetes nurse specialist); and educating health care professionals and encouraging early referral. Following implementation of the recommendations, we re-audited the service by looking at all diabetic patients admitted with osteomyelitis in the year 2004 at KGH and the outcome showed significant improvement, with amputation of 19% compared to 56%, and fully healed ulcers/osteomyelitis at 56% compared to 17% in the year 2004 vs 2003.

Conclusion: Update of foot management guidelines and protocols, and also further resource and early referral to the multidisciplinary foot team are required.

(P13): The use of glargine insulin in pregnancy
NM O’Mullane, E Thomasson, A Roberts and V Mulik
Tameside Acute Trust, Ashton under Lyne. E-mail: Nicholas.OMullane@tgh.nhs.uk

Aims: A review of the outcomes in pregnant diabetic women taking glargine insulin as part of their therapeutic regimen.

Methods: Glargine insulin was used as the basal insulin with a soluble insulin in 12 pregnancies (11 mothers). Average maternal age 29 years (range 15–35). There were 8 type 1, 1 gestational and 1 type 2 on insulin. The reasons for using or continuing glargine insulin were: 5 mothers were already on glargine at the time of conception, and poor control of diabetes in 7 pregnancies (2 of whom had hypoglycaemic fits). Results: Mean HbA1c at booking was 5.6% (range 5.6–9.6), at delivery was 6.3% (range 5.6–8). The hypoglycaemic fits ceased in the 2 patients. The average gestational age at delivery was 38.5 weeks (range 36–40). Delivery was normal vertex 5, ventouse 2, elective section 1, emergency section 4. Appgar score was 9 or 10 in all babies at 5 minutes. The mean weight of babies (6 girls and 6 boys) was 3464g (range 2250–4507). There were no neonatal abnormalities; 1 baby had significant hypoglycaemia.

Conclusion: The use of glargine insulin in 12 pregnancies was safe to administer, and helped improve the control of the diabetes; in 2 mothers hypoglycaemic fits no longer occurred.

(P14): Audit of glycaemic control from insulin sliding scale regimens with and without the continuation of glargine
NA AlAli, EP Birdalal and JM Roland
Peterborough and Stamford Hospitals NHS Foundation Trust. E-mail: jonathan.roland@php-tcnhs.uk

Aim: To evaluate the glycaemic control obtained on standard insulin sliding scale regimens and on regimens modified for patients whose glargine treatment was continued whilst on the sliding scale.

Method: Retrospective analysis of the case notes of 72 patients (45 standard and 27 modified for glargine) given sliding scale insulin in a district general hospital. Fifty-one of the episodes were surgical, 11 obstetric and 10 medical.

Results: On standard sliding scales, 88% of random blood glucose measurements were in the 4–14mmol/L range with 9% >14mmol/L and 3% <4mmol/L. This compared with 83% 4–11mmol/L, 10% <4mmol/L and 7% >14mmol/L on the glargine-modified regimens. (P=0.04 for increase in hypoglycaemia.) Junior medical staff compliance with and understanding of the glargine-modified regimen was poor and in contravention of local guidelines. Six patients on glargine received intravenous insulin when their glucose was <11mmol/L. Furthermore, 4 (15%) patients on glargine and 3 (11%) on standard regimens received 0.9% saline instead of a dextrose-containing intravenous fluid to accompany the insulin infusion.

Conclusion: The regimens themselves probably lead to inadequate glycaemic control. However, errors in execution of the glargine-modified regimens resulted in an increase in hypoglycaemia. A new chart of the administration of sliding scale insulin for patients in whom glargine was continued was needed and has been developed.

(P15): Case report. Relapsing and remitting insulin requiring diabetes: type 1 or type 2?
C Wing, Chiu See
Royal London Hospital. E-mail: candyl@doctors.org.uk

A 28-year-old Barbadian man presented acutely in 1998 with osmotic symptoms, dehydration and a random plasma glucose of 21mmol/L with ketonuria and arterial pH 7.24. He was treated uneventfully for diabetic ketoacidosis, and was discharged on twice-daily mixed insulin. Anti-islet cell antibodies were negative.

He was troubled by frequent hypoglycaemia, and subsequently stopped his insulin altogether, with no recurrence of his ketoacidosis. He remained well off all hypoglycaemia treatment for 6 years, and a glucose tolerance test as part of an employment medical was normal. He was referred acutely with symptomatic hyperglycaemia in 2004, and ketonuria was present. Insulin was again commenced, but he rapidly stopped this due to recurrent hypoglycaemia. Relapse occurred in 2005, with marked hyperglycaemia and ketonuria, when he was treated with repaglinide, with good glycaemic control achieved.

He is likely to have ‘ketosis prone type 2 diabetes’, also called idiopathic type 1, J-type, type 1½, or type 3 diabetes. The mechanism of this condition is thought to arise from acute glucose toxicity leading to beta-cell dysfunction and insulin deficiency, and it is hypothesised that a predisposition to oxidative stress is a risk factor for this type of diabetes, as evidenced by that fact that these patients often have G6PD deficiency. The epidemiology and pathogenesis of this type of diabetes are discussed.