



# Association of British Clinical Diabetologists Autumn Meeting 2010 Abstracts

Top three selected abstracts as chosen by the ABCD committee. All abstracts presented at the meeting were considered to be of a high standard and can be viewed in full online at [www.practicaldiabetesinternational.com](http://www.practicaldiabetesinternational.com).

## A baseline audit of the management of adult inpatient hypoglycaemia

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**Background.** Hypoglycaemia can be defined as a blood glucose of <4mmol/L. Prompt and effective management of hypoglycaemia is essential in order to optimise glycaemic control. Locally, there are concerns that inpatient hypoglycaemia is not being managed appropriately.

**Aim.** To undertake a baseline audit on the management of adult inpatient hypoglycaemia.

**Method.** The bedside monitoring charts of patients on all inpatient wards were reviewed. Patients who had experienced a blood glucose of <4mmol/L in the previous 48 hours were included. Data were collected by retrospective review of medical/nursing notes and medication charts.

### Results:

- 125 patients undergoing blood glucose monitoring were identified and 36 had experienced a hypoglycaemic event in the previous 48 hours.
- 52% of blood glucose results <4mmol/L were treated inappropriately (14% received a long-acting carbohydrate; 38% were not treated at all).
- 39% of patients were treated until blood glucose returned to >4mmol/L.
- 8% of patients had the blood glucose result re-checked after 15 minutes ( $\pm$  4 minutes) of an initial measurement of <4mmol/L.
- 85.7% of patients did not receive a long-acting carbohydrate once the hypoglycaemic event was resolved.
- 3.8% of patients on subcutaneous insulin had their next dose inappropriately omitted.

**Conclusion.** The results confirm local concerns of inappropriate management of inpatient hypoglycaemia. An improvement initiative will be implemented immediately and will involve:

- Developing a new treatment algorithm.
- Roll-out of 'Hypo Boxes' on inpatient wards.
- Nurse education programme.
- Pre-printing hypoglycaemia treatment options on insulin charts.

A re-audit will be undertaken to evaluate impact on inpatient hypoglycaemia management.

## Limitations of glycosylated haemoglobin (HbA<sub>1c</sub>) in diabetes screening

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**Aims.** To examine methods for the identification of previously undetected dysglycaemia (diabetes mellitus [DM] and impaired glucose control [IGC, comprising impaired fasting glycaemia and impaired glucose tolerance]) in patients investigated for possible acute coronary syndrome. Specifically, we wished to examine whether the recently advocated use of HbA<sub>1c</sub> would enhance detection rates for diabetes in these patients.

**Methods.** Patients (n=200) investigated for possible acute coronary syndrome and not previously known to have diabetes were

recruited and anthropometric data collected. Oral glucose tolerance tests (OGTT), random and fasting plasma glucose (RPG & FPG) concentrations, glycosylated haemoglobin (HbA<sub>1c</sub>), fasting lipids, high sensitivity C-reactive protein and Homeostatic Modular Assessment-Insulin Resistance (HOMA-IR) were obtained during admission. Test accuracy was assessed by the degree of misclassification (both under- and over-diagnosis) of patients into normal glycaemic control (NGT), IGC and DM based on OGTT data using WHO criteria. A predictive index (PI) was generated using stepwise ordinal regression models (incorporating FPG, HbA<sub>1c</sub>, HDL-C, triglycerides, age and gender).

**Results.** The prevalence of DM and IGC was 21% and 33%, respectively. HbA<sub>1c</sub> alone had the highest misclassification rate at 55.6% (19.2% under- and 36.4% over-diagnosed). FPG was marginally better, misclassifying 44.4% (mostly under-diagnosis; 41.4%). The PI had the lowest misclassification rate (35.9%; with 22.7% under- and 13.1% over-diagnosed).

**Conclusions.** Our data confirm the high prevalence of dysglycaemia in this cohort. The recently advocated HbA<sub>1c</sub> has significant limitations if used in diabetes screening. Our approach using a predictive index to combine tests data offers potential for improved performance.

## Safe insulin prescribing and competency-based assessment

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**Introduction.** We recognise that insulin prescribing is sub-optimal by foundation doctors; previous audits have shown significant errors with patient identifiers, incorrect insulin nomenclature, dosing and timing. Competency-based assessment is primarily designed to (i) enhance patient safety and (ii) identify educational needs of trainees including early identification of trainees in difficulty. By collaborating with the foundation programme tutor we hope to improve this.

**Aim.** Can a formative assessment programme with additional use of the e-learning module via NHS Diabetes improve knowledge and result in safe prescribing of insulin and better patient care? (Reference [www.diabetes.nhs.uk/safe\\_use\\_of\\_insulin](http://www.diabetes.nhs.uk/safe_use_of_insulin).)

**Method.** During the shadowing period of new foundation programme doctors we established a series of tutorials based around diabetes care in hospital: insulin types, safe prescribing, peri-operative management, insulin dose adjustment and hypoglycaemia management. Following this, each foundation doctor undertook a formative assessment with feedback and re-assessment. Further self-directed learning via the NHS Diabetes module was made mandatory for all foundation doctors with a deadline date for 30 November 2010.

**Results.** All 40 F1 doctors undertook the assessment process. Baseline results showed 11% of F1 failed, 37% were borderline and 52% passed. Common initial errors included: illegible prescription, incomplete patient identifiers, incorrect/incomplete insulin names, failure to write enough insulin for the following day, and poor management of hypoglycaemia. Re-assessment results: 48% borderline, 52% passed. To date, 70% of F1 doctors have successfully completed the e-learning module.

**Conclusion.** Collaboration with the foundation programme tutor and establishing a competency-based assessment have improved some aspects of insulin prescribing. However, prior to this formative assessment being incorporated into a summative process, there needs to be standardisation and demonstration of validity and reliability at a deanery level.



### Problems with the NICE guideline for exenatide exposed in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit

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**Introduction.** According to NICE, exenatide use:

- Should be restricted to BMI  $\geq 35.0$  kg/m<sup>2</sup> and HbA<sub>1c</sub>  $\geq 7.5\%$  (58 mmol/mol) and patients not on insulin.
- Should only be continued if both HbA<sub>1c</sub> and weight at 6 months have reduced by at least 1% and 3% of initial body weight respectively.

**Methods.** In the ABCD nationwide exenatide audit, 315 contributors from 126 centres submitted data on 6717 patients. Patients with HbA<sub>1c</sub> and weight data at both baseline and 6 months were analysed to compare reality with NICE recommendations. *Analyses:* (1) all such patients; (2) exclude patients with BMI  $< 35$  kg/m<sup>2</sup> unless there would be a professional hazard using insulin, HbA<sub>1c</sub>  $< 7.5\%$  (58 mmol/mol) or on triple oral therapy or on insulin.

**Results.** *Analysis 1:* 1882 patients. Over 6 months mean HbA<sub>1c</sub> and weight fell ( $p < 0.001$ ) by 0.78% from 9.47% to 8.69% and by 6.6 kg from 114.2 to 107.6 kg respectively. 68.2% had HbA<sub>1c</sub> reduction, 89.2% had a weight reduction and 60.1% had a reduction in both. With regard to the NICE criteria for success 67.9% achieved the weight loss criteria, 44.9% achieved the HbA<sub>1c</sub> criteria but only 28.6% achieved both.

*Analysis 2:* 1081 patients. Over 6 months mean HbA<sub>1c</sub> and weight fell ( $p < 0.001$ ) by 0.97% from 9.73% to 8.76% and by 6.7 kg from 117.1 to 110.4 kg respectively. 72.1% had HbA<sub>1c</sub> reduction, 88.6% had a weight reduction and 63.4% had a reduction in both. With regard to the NICE criteria for success 66.9% achieved the weight loss criteria, 51.8% achieved the HbA<sub>1c</sub> criteria but only 32.9% achieved both.

There were many patients who achieved a substantial reduction in HbA<sub>1c</sub> but not weight and *vice versa*.

**Conclusion.** On exenatide in real clinical practice:

- Over 60% of patients achieve the ideal of both weight loss and fall in HbA<sub>1c</sub>.
- However, many patients experience a predominant response to only one of weight or HbA<sub>1c</sub> with more minimal response to the other.
- Hence, only about 30% achieve the NICE guideline standard.
- The NICE guideline should change to acknowledge that either significant weight loss or significant HbA<sub>1c</sub> response may represent a beneficial response.

### Initial experiences with liraglutide at a university teaching hospital

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Recently, NICE has recommended liraglutide as an alternative add-on in triple therapy with metformin and either a sulphonylurea or thiazolidinedione in type 2 diabetes mellitus (T2DM) when HbA<sub>1c</sub>  $\geq 7.5\%$  (58 mmol/mol) and BMI  $\geq 35$  kg/m<sup>2</sup>.

We report preliminary experiences using liraglutide in T2DM in a university teaching hospital. Retrospective analysis was undertaken on 97 patients, 62 (48% male, 52% female) being followed up to 3 months. Mean age was 55  $\pm$  14.3 years, and duration of T2DM 10.3  $\pm$  6.9 years.

HbA<sub>1c</sub> improved from 9.41  $\pm$  1.66% to 8.49  $\pm$  1.53%, a reduction of 0.92% ( $p < 0.001$ ), while weight improved from 112.55  $\pm$  20.02 kg to 110.32  $\pm$  20.02 kg, a reduction of 2.23 kg ( $p < 0.05$ ). BMI also improved from 40.18  $\pm$  6.06 kg/m<sup>2</sup> to 38.96  $\pm$  6.93 ( $p < 0.05$ ). Overall, 60% and 35% achieved HbA<sub>1c</sub> reduction  $> 0.5\%$  and  $> 1.0\%$  respectively, maximum reduction being 4.1%. Meanwhile, 34% achieved  $> 3\%$  weight reduction. There were non-significant improvements

in systolic BP and diastolic BP, reductions being 10.73 mmHg and 0.92 mmHg respectively. Similarly, there was a trend toward improved lipid parameters.

Twenty-five patients (40.3%) were on triple therapy of liraglutide with oral hypoglycaemic agents (OHAs), 27 (43.5%) on triple therapy with OHA and insulin, and 10 (16.1%) on dual therapy with insulin. HbA<sub>1c</sub> reductions were 0.99%, 0.89% and 0.50% respectively at 3 months. In contrast, weight reduction was 1.95 kg, 3.11 kg and 2.09 kg. Fifteen patients discontinued liraglutide, 12 on account of gastrointestinal intolerance, and none reported severe hypoglycaemia.

In summary, liraglutide improves glycaemic control and results in weight loss at 3 months, the weight loss being greater in insulin-treated patients.

### Insulin restores selective insulin resistance in type 2 diabetic patients with severe hypertriglyceridaemia

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**Introduction.** Hyperglycaemia is associated with resistance of hepatic transcription factor FoxO1 and adipose tissue lipoprotein lipase to the actions of insulin, resulting in reduced hydrolysis of serum triglycerides. Conversely, recent research has highlighted that hepatic triglyceride production remains sensitive to circulating insulin, perpetuating the detrimental effects of hypertriglyceridaemia. We report the novel use of continuous insulin infusion therapy to restore this selective insulin resistance.

**Methods.** Patients with hyperglycaemia and severe hypertriglyceridaemia (serum triglycerides  $> 15$  mmol/L) treated with continuous insulin infusion were retrospectively evaluated. Demographics, admission details, lipid profiles, glycaemic control, adverse events and lipid lowering therapy were recorded.

**Results.** Fifteen patients were reviewed from 3 ethnic groups. New onset diabetes was diagnosed in 7 cases while mean disease duration measured 60 (2–96) months. Median admission HbA<sub>1c</sub> measured 9.6% (6.1–16.1). Acute pancreatitis was diagnosed in 3 patients. Mean admission serum triglycerides measured 29.12 mmol/L (15.09–48.43). Continuous insulin was infused for an average 48 hours (24–72). Mean serum triglycerides reduced to 16.29 mmol/L (0.79–36.59) following 24 hours. Insulin infusion continued for 72 hours in 7 patients. Mean discharge serum triglycerides measured 6.54 mmol/L (0.79–11.66). Median length of hospitalisation was 4 days (3–15).

**Conclusions.** Administration of continuous insulin achieves normoglycaemia and dramatically corrects severe hypertriglyceridaemia. It is established that insulin stimulates the action of lipoprotein lipase in adipocytes and these findings support this. We speculate that administration of exogenous insulin may also regulate gluconeogenesis and hepatic triglyceride synthesis in hyperinsulinaemic patients, restoring selective insulin resistance.

### 16.6% (1 in 6) patients who continued insulin at the time of exenatide start came off insulin in the Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit

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**Introduction.** ABCD conducted a nationwide audit on exenatide in real life clinical practice, with 315 contributors from 126 centres participating. Exenatide is not licensed for use with insulin, but patients who stop insulin when trialling exenatide often have worsening glycaemic control. We evaluated the likelihood and predictors of coming off insulin if insulin was continued at exenatide start. **Methods.** Patients who continued insulin at exenatide start were identified in the audit. Baseline and latest HbA<sub>1c</sub> and weight were

compared between patients who remained on insulin and patients who continued but subsequently weaned off insulin. Logistic regression was performed to identify characteristics of these groups.

**Results.** From 6717 patients, 1496 patients were on insulin at exenatide start and 1257 patients had their insulin continued. At a median follow up of 26.3 weeks, 1048/1257 patients remained on insulin, while 209/1257 (16.6%) came off insulin. Mean ( $\pm$ SD) baseline characteristics of both groups combined were HbA<sub>1c</sub> 9.50 $\pm$ 1.71%, weight 113.7 $\pm$ 22.6kg, BMI 40.3 $\pm$ 7.5kg/m<sup>2</sup>, age 55.3 $\pm$ 10.3 years, diabetes duration 12.2 $\pm$ 6.4 years, insulin dose 120.3 $\pm$ 98.9 units/day, and 51.2% female. Comparing patients who remained on insulin and those who came off, mean ( $\pm$ SE) HbA<sub>1c</sub> and weight reduction were 0.51 $\pm$ 0.06% vs 0.49 $\pm$ 0.17% ( $p=0.927$ ), and 5.2 $\pm$ 0.3 vs 8.8 $\pm$ 0.7kg ( $p<0.001$ ), respectively. Characteristics that were independently associated with patients coming off insulin were a higher weight loss ( $p<0.001$ ) and lower total daily insulin dose ( $p<0.001$ ).

**Conclusion:**

- 16.6% (1 in 6) patients who continued insulin at the time of exenatide start came off insulin in the ABCD nationwide exenatide audit.
- A lower total daily insulin dose predicted the likelihood of coming off insulin when starting exenatide in obese, insulin-treated patients.

### Obstructive sleep apnoea in patients with type 2 diabetes

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**Objectives.** To find out if obese patients with type 2 diabetes had a significant incidence of obstructive sleep apnoea, and to see how this related to their glycaemic control.

Previous studies have found a positive association between sleep apnoea and type 2 diabetes, and sleep apnoea is associated with poorer cardiovascular outcomes.

We studied patients with a range of glycaemic control, attending a hospital outpatient clinic for those with type 2 diabetes.

**Methods.** Fifty consecutive obese patients (BMI >30), attending our type 2 diabetes outpatient clinic, had an Epworth Score done. Their BMI, HbA<sub>1c</sub> and smoking habits were also recorded.

**Findings.** Three patients had Epworth Scores over 17. Of these, 2 were confirmed as having obstructive sleep apnoea on further testing. Seventeen patients had Epworth Scores over 11.

Obstructive sleep apnoea is associated with obesity, but our small study did not confirm this.

No correlation with Epworth Score was found with poor glycaemic control.

Only 3 out of 50 were smokers, but their mean Epworth Score was 15.33 compared to the mean for the whole group of 8.8.

**Conclusions.** In our small group, 34% had possible significant sleep apnoea.

Sleep apnoea was not linked to glycaemic control or, surprisingly, to degree of obesity, but was linked to smoking.

We should consider using the Epworth sleepiness scale routinely at review of type 2 diabetic patients.

### Duration of diabetes and association with effectiveness of sitagliptin

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**Aim.** To determine if duration of diabetes influences response to sitagliptin therapy in our type 2 diabetes patients, a diverse population managed in a secondary care diabetes clinic.

**Methods.** All patients started on sitagliptin from 2008–10 were identified from our database. Data were collected on duration of diabetes, HbA<sub>1c</sub>, weight, and other diabetes medications, at

baseline and at either cessation of sitagliptin treatment or most recent follow up.

**Results.** Sixty-five patients were started on sitagliptin, mean age 58.9 years (SD 12.3, range 31–79 years). Duration of diabetes ranged from 3 months to 31 years, with 10 patients having duration  $\leq$ 5 years and 55 patients >5 years. Mean change in HbA<sub>1c</sub> was -0.5% (SD 1.4%, range -6.3 to +2.2%,  $p=0.003$  using 2-tailed paired t-test). The number of patients achieving HbA<sub>1c</sub> <7.5% (58mmol/mol) was 11 at baseline and 19 after treatment ( $p<0.01$  using McNemar's test). For patients with duration of diabetes  $\leq$ 5 years and >5 years, mean change in HbA<sub>1c</sub> was -1.3% and -0.4% respectively ( $p=0.04$  using 2-tailed unpaired t-test). Five patients were able to cease insulin therapy, though 3 different patients started insulin while on sitagliptin.

**Conclusions.** Sitagliptin use was associated with a significant reduction in HbA<sub>1c</sub>. This effect was most marked in patients with a shorter duration of diabetes, as might be expected from progressive beta-cell failure in type 2 diabetes and the mechanism of action of sitagliptin.

### 'Missed' coeliac disease with fatal consequences in type 1 diabetes mellitus

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Our patient is a 40-year-old male with a 22-year history of type 1 diabetes mellitus. His control had been consistently poor with an HbA<sub>1c</sub> higher than 10% (86mmol/mol) throughout disease duration. He had mild bilateral diabetic retinopathy, and no evidence of peripheral neuropathy or nephropathy. There was no family history of autoimmune disease. He was a C1 driving licence holder (Larger Goods Vehicle: 3.5–7.5 tonnes). The DVLA was aware of his diagnosis of type 1 diabetes, but he was allowed to drive as episodes of hypoglycaemia were rare and good awareness was maintained.

In January 2007 he lost 8kg in weight without explanation, and had a change in his bowel habit. He also found that his insulin requirements were reduced and he had more frequent episodes of hypoglycaemia. He did not seek medical attention.

In May 2007 he was involved in a severe road traffic accident, tragically resulting in the death of the other driver. The patient had no memory of the event and was found to be hypoglycaemic by the paramedics. This resulted in a custodial sentence for the patient and loss of his C1 licence and livelihood.

In August 2007 he was admitted to Hinchingbrooke Hospital for investigation of possible causes of his hypoglycaemia. A synacthen test demonstrated a brisk response, thereby excluding Addison's disease. Thyroid function was normal, as was coeliac serology, with a tissue transglutaminase (IgA) 0.6u/ml (0–6) and serum IgA 2.03g/L (0.8–3.7). He was marginally anaemic with Hb 10.4g/dL, and his HbA<sub>1c</sub> was still raised at 10.4% (90mmol/mol). He was discharged without cause found for his hypoglycaemia.

One month later he was readmitted with breathlessness. He was found to be severely anaemic with an Hb 7.8g/dL, and he was referred for a gastroscopy. This showed hyperplastic gastritis of the stomach with some altered blood present. Biopsies of the duodenum were taken and demonstrated subtotal villous atrophy with patchy increase in intraepithelial lymphocytes and crypt hyperplasia. The findings were consistent with coeliac disease. The patient was referred to a dietician for advice on a gluten-free diet. His haemoglobin normalised with iron supplementation and a DEXA scan excluded osteoporosis.

We conclude that new hypoglycaemia in patients with established type 1 diabetes should receive prompt investigation until a satisfactory explanation has been found. Approximately 5% of patients with coeliac disease have normal coeliac serology. Therefore, if there is a strong clinical suspicion a D2 biopsy should be sought under these circumstances.