

ABCD Spring Meeting Abstracts

<http://dx.doi.org/10.15277/bjd.2017.145>

The ABCD meeting was held at the Titanic Belfast in May 2017

A challenging case of Fanconi Syndrome in pregnancy: managing the paradox of both gestational diabetes and recurrent hypoglycaemia

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Fanconi Syndrome describes a collection of disorders characterised by generalised dysfunction of renal proximal tubules resulting in increased urinary excretion of amino acids, glucose and solutes. The potential clinical manifestations are wide ranging and include proximal renal tubular acidosis, rickets and chronic kidney disease (CKD). Although glycosuria is a common manifestation, hypoglycaemia is rarely described. We present the case of a 37 year old woman with CKD3b and Fanconi Syndrome due to mitochondrial disease controlled on oral solute replacement who became clinically unstable during the latter stages of pregnancy. She was admitted from 28 weeks gestation due to profoundly low plasma bicarbonate levels, hypokalaemia and acidosis. Continuous intravenous replacement of both potassium and bicarbonate was necessary to prevent the harmful effects of acidosis to the developing foetus. An oral glucose tolerance test demonstrated post-prandial hyperglycaemia consistent with gestational diabetes. She paradoxically suffered from recurrent episodes of significant hypoglycaemia requiring intravenous dextrose infusions. Her glucose, potassium and bicarbonate requirements continued to increase until she was delivered at 34 weeks by elective Caesarean-section. Rapid improvement in biochemical and glycaemic parameters were noted after delivery and she was discharged 4 days post-partum. This case demonstrates that pregnancy can exacerbate the clinical manifestations of Fanconi Syndrome and patients may require specialist inpatient management during the antenatal period. In addition, the increased insulin resistance arising from pregnancy can create the exceedingly rare situation of both fasting hypoglycaemia and post-prandial hyperglycaemia and raises the question of how to best manage such patients through to a safe delivery.

Challenges in the investigation and management of a patient with cyclical Cushing's disease and insulin requiring diabetes

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A 40 year old woman was initially referred in 1999 with weight gain, fatigue, easy bruising and hypertension. A screening 24h urinary free cortisol was raised at 3998 nmol/24h (normal <320). Low and high dose dexamethasone tests (LHDDT) and CT imaging were within normal range and she was lost to follow-up. She subsequently developed rheumatoid arthritis requiring corticosteroids at times, steatohepatitis, Sjogren's syndrome, coeliac disease, atrial fibrillation and osteoporosis. She was diagnosed with diabetes in 2001

and was treated with metformin, gliclazide and liraglutide until 2013 when she was referred to the diabetes clinic and insulin was started. Clinical concern was again raised and the LHDDT was repeated but again was within normal range. Given the level of suspicion and a number of incongruent results a 28 day series of early morning urines for cortisol to creatinine ratio were performed and this demonstrated a clear cyclical pattern with peaks every 4-7 days followed by troughs into the normal range. Dynamic pituitary MRI demonstrated a 1.5mm right sided lesion and inferior petrosal sinus sampling for adrenocorticotrophic hormone gradients supported this and she proceeded to trans-sphenoidal surgery. During elective admissions variability in insulin requirements were noted by as much as 50% reflecting the added difficulty of achieving good glycaemic control in this setting. We have previously reported that routine biochemical screening for Cushing's in the diabetes clinic is not useful but rather clinical evaluation remains key. This case also emphasises the challenges of glycaemic control in the setting of cyclical Cushing's disease.

A retrospective study of cardiovascular risk factors compared to guidelines in a type 2 diabetes clinic

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Aims: Our aim was to investigate whether Irish adults with Type 2 diabetes satisfied the American Diabetes Association (ADA) criteria for BMI, Blood pressure, HbA1c and lipids.

Methods: Retrospective cross-sectional study of patients attending a type 2 diabetes clinic at University College Hospital Galway, Ireland between September 23rd 2015 and September 23rd 2016. We extracted the raw data from the patients' last clinic visit from the Diamond™ electronic diabetes database system; any missing information was reconciled using the hospital lab-enquiry system (PAST™). We used the ADA Clinical Practice Recommendations 2016 to define the thresholds for optimal control in Type 2 Diabetes.

Results: During this period 2058 patients were identified as having attended the clinic with a diagnosis of Type 2 Diabetes. Of this cohort of patients 38.9% were female and 61.1% were male. The mean age was 64.9 ± 12.1 years with an average age of diagnosis 63.2 ± 7 years. While 83% of patients satisfied total cholesterol targets (<5 mmol/l) only 41% satisfied HbA1c target (<53 mmol/mol). Furthermore 66% satisfied systolic BP targets (<140 mmHg), while 95% satisfied diastolic BP targets (<90 mmHg).

Conclusion: In our cohort of patients, glycemic targets in particular do not meet the recommended ADA guidelines and therefore require more focused therapeutic intervention.

Primary hyperparathyroidism in pregnancy: a comparison of management strategies

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Primary hyperparathyroidism uncommonly presents during pregnancy; initially the diagnosis may not be considered due to overlap between the symptoms of hypercalcaemia and "normal pregnancy". There are particular challenges for both diagnosis and treatment: the usual imaging sequence for adenoma localization cannot be used and there is little evidence base to guide decisions on treatment. We present 2 cases, comparing different management strategies.

Case 1: 33 year old woman with well controlled type 1 diabetes, presented at 33/40 with fatigue, polyuria and polydipsia. Investigations revealed raised serum calcium 2.78mmol/l (NR 2.05-2.55), inappropriately raised PTH 9.1 pmol/l (1.6-6.9) and elevated urinary calcium 16.5mmol/24 hrs (2.5-7.5), consistent with primary hyperparathyroidism. No parathyroid adenoma was identified on ultrasound; she opted for initial conservative management, with regular monitoring of serum calcium. Following delivery, the baby had transient hypercalcaemia, not requiring intervention. Postnatally, sestamibi localised the culprit adenoma, and she underwent successful parathyroidectomy.

Case 2: 32 yr old woman with morbid obesity (BMI 50) presented with hyperemesis gravidarum at 17/40. She was found to have marked hypercalcaemia (cCa 3.3), inappropriately elevated PTH (10.4pmol/l) and elevated urinary calcium (16.3mmol/24hrs). She was admitted for IV rehydration. Ultrasound localised a right inferior adenoma. Given her calcium >3mmol/l and extreme symptoms, surgical treatment was preferred; she had successful parathyroidectomy in the 2nd trimester. Perioperative frozen section confirmed parathyroid tissue; postoperatively, calcium fell to 2.35mmol/l and has remained in the normal range. Due to hypertension and proteinuria developing at 36/40, she was delivered by LSCS of a healthy infant.

The impact of personalized care plans in delivering diabetes care to patients with complex needs in the community: Our experience in managing 12 patients in Llanelli, West Wales

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Background: Diabetes patients currently live longer than ever, but some suffer from disabling conditions associated with aging such as stroke. There are also patients with disabilities whose diabetes care is complex that always requires an MDT approach.

Aim: We present 12 unique cases who had their diabetes care plans specifically designed. We explain the challenges in managing each patient and the impact of care plans on the patients, their carers as well hospital admission rate. Findings: All 12 patients have complex conditions which include: terminal cancer, post-stroke with significant morbidity, frailty, severe needle phobia with complex social issues, psychiatric disorder, blindness, cerebral palsy with learning disability, and permanent disability from brain insult. The age range is from 24 to 84 years old. Ten patients have T1DM vs two with T2DM. They are all on insulin. Eight patients live in their own home, three in nursing institutions and one currently in hospital recovering from a massive stroke. All patients who are managed in the community receive support from family members, carers and district

nurses. The care plans provide guidelines on management of hyperglycaemia, hypoglycaemia, ketosis, and emergency contacts. Eight patients were found to have less number of hospital admissions following the introduction of care plans.

Conclusion: Patients with complex conditions require personalized care plans to deliver diabetes care safely in the community. The community diabetes nurses play important roles in bridging the expertise between primary and secondary care. We have shown the impact of care plans in reducing hospital admission rates.

Keep calm and check the BM – how often do doctors look at blood sugars? A study on inpatients with diabetes in a tertiary hospital

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Diabetes mellitus is posing a strain in general medicine, with an estimation that as many as 1 in 6 patients are diabetic. The National Diabetes Inpatient Audit highlighted profound concerns regarding failings in inpatient diabetes care, including medication errors, severe hypoglycaemic episodes and lack of specialist input. Despite these, there is a paucity of literature on how often doctors review capillary blood sugar level (BM). This quality improvement project sought to evaluate the frequency of BM documentation during ward rounds and any associated hypo- and hyperglycaemic episodes. 54 ward round entries and BM charts of insulin-treated patients were reviewed on two diabetes wards. 37% of reviews had their BMs documented. Of note, "bad BM day" (i.e. BM level <4mmol/L or more than one BM level >11mmol/L) constituted 68.5% of all inpatient days. 22 entries without BM documentation were of "bad BM days". Junior doctors were educated on the importance of seeking good glycaemic control, with the help of oral presentations and written reminders to review BMs daily. A re-analysis of 48 ward round entries were conducted, showing drastic improvement of 2-fold increase in documentation. 10 episodes of "bad BM days" were responded with immediate intervention. Only 5 "bad BM days" were not recorded. Poor BM documentation may reflect a lack of emphasis placed on glycaemic control, the lack of experience and confidence in interpreting BM and individualising insulin therapy. Education has improved medical practice and patients have benefited from regular and daily BM review.

Hyperosmolar hyperglycaemic syndrome and diabetic ketoacidosis in 2 patients receiving a GLP-1 agonist for type 2 diabetes

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We present 2 patients with serious adverse outcomes after commencing on dulaglutide; Hyperosmolar hyperglycaemia Syndrome (HHS) and Diabetic Ketoacidosis (DKA) raising concerns about the safety of this agent and use of concomitant insulin.

Case 1 is a 65 year old lady with longstanding diabetes, BMI of 29.8, HbA1c of 94mmol/mol commenced on dulaglutide. She was on insulin which was stopped, but previously been treated liraglutide and insulin, which was stopped due to poor efficacy. She developed vomiting and presented with acute kidney injury and HHS treated, was recommenced on insulin and made a full recovery. There were no other precipitants found for her HHS and her c peptide was low.

Case 2 is a 73 year man, BMI 34.9, HbA1c 90 mmol/mol with long standing poorly controlled type 2 diabetes, stopped insulin and commenced on dulaglutide. He presented with a DKA, no other precipitants found, low c peptide. He was recommenced on insulin and made a full recovery.

Discussion: These cases raise concerns for insulin omission after commencing dulaglutide. There is intrinsic GLP-1 resistance in the community, seem frequently in those with chronic hyperinsulinaemia. There is also a lag time of efficacy wherein patients are vulnerable for hyperglycaemia as well as the possibility of GI side effects in early GLP-1 treatments. Thus there needs to be some research and advice to clinicians as to who is at risk, whether to stop insulin or wean it off to ensure patient safety on these new agents.

Unexpected complications of a GLP-1R agonist in 2 patients with a long history of poorly controlled type 2 diabetes

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Two patients with over 10-year-history of type 2 diabetes poorly controlled on insulin and metformin and with HbA1cs >10%, presented with polyuria, polydipsia, nausea and vomiting three days after starting dulaglutide. Following investigations our first case was diagnosed with a mixed picture of diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS) and the second with DKA. There are currently no reports of GLP-1R agonists associated with DKA or HHS. Our poster presents two such cases.

DKA and HHS remain feared complications of diabetes and one of the aims of diabetes management is to prevent these potentially fatal events by ensuring availability of insulin, reducing its resistance in tissues and impairing glucagon secretion. GLP-1R agonists control blood sugar by employing these mechanisms and potentially reducing the occurrence of DKA and HHS. But what went wrong in our two cases? What we know so far is that GLP-1R agonists exert their effect by binding to GLP-1 receptors (GLP-1Rs) on pancreatic beta-cells but studies have shown that in chronic hyperglycaemia there is down-regulation of GLP-1Rs. This begs the question, are there adequate GLP-1Rs in those patients with years of poorly controlled diabetes? Also, studies have highlighted the role of C-peptide in predicting patients who may fail a switch from insulin to other agents including GLP-1R agonists.

In our poster, we discuss the effects of chronic hyperglycaemia on beta-cells and how the downregulation of GLP-1Rs affects the efficacy of GLP-1R agonists. Through literature review we propose that our patients were likely in the subgroup of people who will respond poorly to a GLP-1R agonist due to their history of chronic hyperglycaemia. DKA and HHS in these cases were likely secondary to a sudden discontinuation of their insulin therapy in association with poor

response to dulaglutide. We recommend that serum C-peptide be checked in patients who have had a long history of poorly controlled diabetes because a low C-peptide may predict patients at risk of complications if their insulin is discontinued acutely when introducing a GLP-1R agonist.

The use of continuous subcutaneous insulin infusion (CSII) in a case of severe insulin insensitivity

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Introduction: This case study is of a patient with severe insulin resistance in a patient with presumed type 2 diabetes who has no clinical features of an insulin resistance syndrome. Her diabetes control was only adequately managed using CSII.

Case History: 45-year-old lady with a normal BMI was referred to our diabetes clinic with poorly controlled diabetes. She was diagnosed with T2DM at the age of 40. Her BMI was 24 kg/m² and BP 135/85. There was no acanthosis or lipoatrophy. She had normal renal function, raised total cholesterol 8.1mmol/L, TC/HDL 9.10, HbA1c 134 mmol/mol, CBGs>20, Ketones 1, VBG: normal PH and bicarbonate. She had a history of hypertension, peripheral neuropathy and microalbuminuria. There was little improvement in response to multiple oral antihyperglycaemic agents (Metformin, Sitagliptin, Gliclazide, Pioglitazone). Basal bolus insulin regime (bd Lantus and tds NovoRapid) was initiated in combination with oral agents. She required >200 units of insulin per day and HbA1c only declined to 128mmol/mol.

An admission to hospital confirmed that diabetes control was poor despite taking all her medication. Her overnight dexamethasone suppression test and 24 hour urinary free cortisol levels were normal. Insulin autoantibodies were negative. To improve insulin absorption, divided doses of U500 insulin with concurrent use of Metformin, Sitagliptin and Dapagliflozin was tried. Her HbA1c was declined to a nadir of 102mmol/mol. She was then referred to King's College Hospital where a diagnosis of type B insulin resistance was made. She was switched to CSII pump therapy using Humulin R U500 insulin. Her HbA1c declined to 6.7% within 3 months and insulin requirements declined. 10 months after her care was returned to a district general hospital, funding for CSII pump therapy was threatened.

Discussion: NICE currently recommends the use of CSII only in patients with type 1 diabetes. This case study demonstrates a dramatic reduction in HbA1c and insulin requirements in a patient with severe insulin resistance and no history of type 1 diabetes. Maintaining funding for CSII therapy in district general hospitals for such patients remains a major challenge, despite the clear benefits that it brings.