



Association of British Clinical Diabetologists

ABCD
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Posters

1 NICE guidelines versus clinical practice – GLP-1 receptor agonists in type 2 diabetes: the ABCD nationwide audits

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In conducting two nationwide audits on the use of the GLP-1 receptor agonists (GLP-1RA) exenatide and liraglutide in the UK, we found that deviations from NICE guidelines were common. Using data from both audits which had a combined total of 12,955 patients, we evaluated these treatment decisions as well as critically appraised the NICE guidelines. We found that in their present form, the NICE guidelines for GLP-1RAs essentially prevent their use in patients with more advanced diabetes who still require effective treatment. Also, many patients fail to meet the criteria for continuing GLP-1RA therapy after 6 months. More clinical trials and cost-effectiveness analyses are needed in obese patients with more advanced diabetes; the issue not being the comparative costs of third line diabetes treatment, but that of the comparative costs and effectiveness of patients already on third line therapy who require treatment intensification either by escalating insulin doses or using GLP-1RAs. We would caution clinicians against substituting concurrent diabetes treatment to appear to adhere to guidelines when GLP-1RAs are started due to the risk of glycaemic deterioration. The general requirement by NICE for patients' BMI to be ≥ 35 kg/m² is not strictly evidenced-based, and this strategy to improve cost-effectiveness may be counter-productive if glycaemic improvement is diminished in more obese patients. We propose that patients who achieved significant HbA1c reduction but not weight reduction be allowed to continue GLP-1RA treatment. The criteria of $\geq 1\%$ HbA1c reduction as a requirement for continued GLP-1RA treatment is unfair due to favouring patients with higher HbA1c.

2 **Are patients engaging with web-based resources enabling self-management for diabetes mellitus?**

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Introduction

My Diabetes My Way (MDMY) is an interactive web resource created by NHS Scotland that provides patients with educational content and access to their clinical information. This aim of the service, which was launched in 2010, is to facilitate patient self-management and empowerment. We aimed to determine how many of our patients were aware of and/or using MDMY and explore potential barriers to the use of the service.

Methods

A retrospective cross-sectional study was performed. Consecutive patients with DM attending the North Glasgow Endocrine and Diabetes were invited to complete a questionnaire.

Results

204 patients were recruited into the study (46.6% T1DM, 47.1% T2DM). 2% were users of MDMY, 14.2% were non-users but were aware with the majority (83.8%) unaware of its existence. Patients learned of MDMY from DSN's (21.2%), posters (18.2%) and via the Internet (12.1%). 55% expressed an interest in MDMY with 34.5% believing that participation would help with their diabetes. Reasons for lack of interest included satisfaction with existing level of diabetes knowledge (45.6%), lack of computer access (21.1%) and the perceived complexity of the sign up process (3.4%).

Conclusion

The overwhelming majority of patients had not previously heard of MDMY, with a significant number of patients stating that MDMY could benefit them. Access to a computer remains a significant issue in this cohort from a patient population with many areas of social depravity. Further work is required before MDMY can become a staple of diabetes management in Scotland and be subject to more robust outcome evaluation of perceived efficacy.

3 **How Frequently Are Bedside Glucose Levels Measured in Hospital Inpatients on Glucocorticoid Treatment?**

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Glucocorticoids are widely used in many medical specialities for their anti-inflammatory and immunosuppressive qualities. The majority of glucocorticoid use is in the outpatient setting. Long term glucocorticoid use is associated with several side effects, including the development of hyperglycaemia. Observational data for most medical and surgical conditions requiring hospitalisation suggests that the additional presence of hyperglycaemia or diabetes is associated with poorer outcomes. Despite this association, there are no data on the prevalence of glucocorticoid use in hospitalised inpatients.

We conducted a single centre prevalence study carried out over two consecutive days in January 2014, assessing every adult bed (n=940) in our institution looking at the numbers of patients on glucocorticoids and to see how many had their glucose levels measured.

We found that 120 patients (12.8%) were on glucocorticoids. 99 patients (82.5%) were on prednisolone. The mean daily dose (MDD) for prednisolone was 25.0mg \pm 12.5 (range: 0.5 – 60). 16 patients (13.3%) were receiving dexamethasone, with a MDD of 9.2mg \pm 6.5 (range: 0.5 - 20). Four patients (3.3%) were receiving hydrocortisone, with a MDD of 107.5mg \pm 106.9 (range: 20 – 200). 64 (53.3%) of patients had received their glucocorticoid treatment for longer than 10 days at the time this data was collected.

Of the 120 patients receiving glucocorticoids, only 25 (20.8%) had their blood glucose levels measured during their time as inpatients. Of these, 13 had pre-existing diabetes.

This work has highlighted the continued work that needs to be done to improve the care of hospitalised inpatients.

4 HNF4 alpha mutation - a roller coaster of hyperinsulinism and diabetes

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We present a 10 month old girl with hyperinsulinaemic hypoglycaemia who has screened positive for the HNF4a mutation, which paradoxically predisposes her to maturity onset diabetes of the young (MODY)1. This case highlights the necessity to investigate, in detail, all newborns with persistent hypoglycaemia in order to aid future management.

She was born at 37 weeks by normal delivery, weighing 4.4 kg (98th centile). Anomaly scans were normal, Mum developed pregnancy induced hypertension during the third trimester.

Shortly after delivery she developed severe hypoglycaemia. She required escalating concentrations of dextrose and was transferred to tertiary endocrine centre where she received glucagon, hydrocortisone and dextrose to maintain her sugars. She responded to diazoxide and chlorthiazide with polycal feeds, and was discharged with stable blood sugars.

She had a normal systemic examination. She is the second child to white British non-consanguineous parents who are both well.

Genetic testing demonstrated heterozygous mutation in the HNF4a gene.

Following discharge she has developed gastro oesophageal reflux, presumed cow's milk protein allergy and a persistently raised ALT with hepatomegaly, which is under investigation.

HNF4a mutations cause macrosomia and diazoxide-sensitive hyperinsulinaemic hypoglycaemia during the neonatal period. The sugars may normalise², but the individual is subsequently at risk of developing MODY. They can also develop Fanconi-like renal syndrome and vitamin-D deficient rickets².

Once the mutation is identified the family should be offered screening to identify existing MODY1 and inform future pregnancies.

1. McGlacken-Byrne SM et al. (2014) Diabetic Medicine
2. Stanescu DE et al. (2012) Journal of Clinical Endocrinology and Metabolism

5 What impact would changing the diagnostic criteria for gestational diabetes have on our service?

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Introduction and Rationale

Various criteria exist for diagnosing Gestational Diabetes Mellitus (GDM). No consensus exists on which Oral Glucose Tolerance Test (OGTT) thresholds to use. The Dudley Group NHS Foundation Trust (DGOH) uses fasting or 2-hour plasma glucose levels of 6.0 or 7.8mmol/L respectively to diagnose GDM. There is a positive correlation between maternal hyperglycaemia and perinatal morbidity, including high birth weight, neonatal hypoglycaemia, neonatal hypersulinaemia, and

primary caesarean delivery. Changing DGOH's diagnostic criteria could change the number of positive diagnoses, with economic and health implications.

Data Collection

A literature review identified nine GDM diagnostic criteria. OGTT results for all women (127) screened at DGOH over 34 days were collected.

Methods

Complication rates at each glucose interval were calculated from the literature. These were used to predict complication rates (1) for DGOH screened patients and (2) at existing GDM diagnostic criteria.

Results and Analysis

12.7% of screened patients were positive under DGOH's GDM criteria, a higher proportion than if any other published criteria were used. 80% of DGOH patients had fasting glucose levels below 4.8mmol/l, and 80% had 2-hour OGTT levels below 7.0mmol/l.

Complication rates increase with increasing plasma glucose concentration, but there is no single threshold at which all complication rates drastically change.

Discussion and Conclusions

There is no obvious useful diagnostic threshold because:

- (1) There is no single threshold at which all complication rates drastically change.
- (2) Previous research has grouped complication rates into wide glucose ranges.
- (3) Costs of complications vs. positive diagnoses were not considered.

6 Glycosylated haemoglobin (HbA1c) as a diagnostic tool in gestational diabetes mellitus (GDM); Implications of the new 2013 WHO diagnostic criteria

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Background: There is increasing prevalence of type 2 diabetes in women of child-bearing age. Therefore, assessing the glycaemic status during pregnancy is not only essential in identifying dysglycaemia for ante-natal management, but is equally important in identifying those at risk of future development of diabetes. We have previously demonstrated that HbA1c did not have satisfactory efficacy and therefore was unsuitable as a tool to replace the oral glucose tolerance test (OGTT) in the diagnosis of GDM.

Aim: Recently, the World Health Organisation (WHO) produced new guidelines for the diagnosis of GDM. We aimed to:

- 1) Evaluate the concordance between these and the earlier 1999 criteria.
- 2) Assess the role of HbA1c when these criteria are implemented.

Methods: The study cohort included 337 women with confirmed GDM (using OGTT based on the WHO 1999 criteria), together with 281 high risk women with negative antenatal OGTT, managed at the University Hospital of North Staffordshire between January 1999 and March 2007. We calculated the diagnostic accuracy of both FPG and HbA1c against both 1999 and 2013 WHO cut-off values.

Results:

- The application of the WHO 2013 new guidelines did not result in significant difference in the total number of positive vs. negative cases of GDM (277 positive and 277 negative according to WHO 1999 criteria vs. 272 and 282 respectively according to WHO 2013 criteria)

- Out of those who were negative by the 2013 criteria, those who were positive and negative by the 1999 criteria comprised 8.8% and 1.4%; $P = 0.003$). These GDM positive patients will be missed if the 2013 criteria are adopted, which is arguably unacceptable on clinical grounds

- Employing WHO 2013 criteria, the HbA1c cut-off value at or above 48 mmol/mol (6.5%) was 56% aligned to OGTT criteria. However, 43.7% GDM-positive cases (by OGTT WHO 2013 criteria) would be missed by HbA1c alone. Employing the HbA1c cut-off value at or above 42 mmol/mol (6.0%) was 62% aligned to OGTT criteria, with 38.1% misclassified, the majority (36.6%) being GDM-positive cases (by OGTT criteria) who would be missed by HbA1c alone.

Conclusions:

- The application of WHO 2013 criteria did not result in significant difference in the total GDM case load, compared to WHO 1999 criteria.

- HbA1c, using either 48 or 42 mmol/mol (6.5% or 6.0%) cut-off values, risks missing a significant proportion of GDM-positive cases (as diagnosed by WHO 2013 criteria)

7 Latent auto immune diabetes in adults.

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We present a case of LADA to highlight the pitfalls in diagnosis and implications on management.

83yr old lady presented with 2 weeks history of polyuria, polydipsia, sweats, weight loss and being unwell. Preclinic fasting glucose was 17 – 19 mmol/l. Maternal family history of Type 2 diabetes was elicited. Past medical history included Pernicious Anemia. BMI was 24 Kg/m². She was not acidotic. Urine tested 2+ Ketones and 3+ Glucose. Late onset of Type 1 diabetes was suspected, and Insulin was commenced. Antibody results of GAD65 >2000 IU/ml (0-10), IA2 7222 IU/ml (0-10) and ICA (Islet cell antibodies) – borderline positive were in keeping with autoimmune type 1 diabetes.

At diagnosis, patients with LADA are usually non–insulin requiring and clinically indistinguishable from patients with type 2 diabetes, though they tend to be younger and leaner. HBA1C must not be used in this group of patients for making a diagnosis. Immunology helps to make a diagnosis with certainty (esp. GAD). Given the risk of ketoacidosis, insulin should also be considered in such patients, regardless of whether they are thought to have type 1 or type 2, especially those who are catabolic (weight loss or dehydration in the setting of hyperglycemia). The presence of two distinguishing clinical features for diagnosing LADA (age <50, acute osmotic symptoms, BMI <25, personal or family history of auto-immune disease) can detect two-thirds of adults with LADA and has 90% sensitivity. This case highlights the importance of considering a diagnosis of LADA even at an advanced age.

8 How can we recruit more people into clinical research in diabetes? Innovative use of peripatetic health care professionals.

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Aims: To increase recruitment to academic studies and to demonstrate the effectiveness or otherwise of dedicated, travelling researchers.

Methods: A research practitioner and a specialty doctor were each employed part-time for six months by Birmingham and the Black Country Comprehensive Local Research Network(BBC-CLRN) to recruit to two non-commercial portfolio-adopted diabetes studies in hospital trusts across the

West Midlands. Principal Investigators were appointed at each site. Ethics approval and letters of access were obtained. The two BBCCLRN researchers made weekly visits to diabetes clinics in four hospitals, instituted the practical arrangements for research and recruited until the host trusts were ready to take over the studies themselves.

Results: After six months we had recruited to both studies at all four hospitals: a total of 229 patients. Three sites had become self-sufficient in conducting the studies with CLRN support of in-house nurses. Across the CLRN accruals to non-commercial portfolio diabetes studies rose from 23/month in 2011/12 to 49/month in 2012/13 to 125/month in April-July 2013, of which 38% were recruited by this project. The process was facilitated by having a base in an academic unit and the use of simple studies, one a questionnaire, one observational. Obstacles included difficulties gaining access to electronic records, administrative support, clinic space and laboratory facilities.

Conclusions: A short-term investment in peripatetic researchers is an effective way of setting up and increasing recruitment to non-commercial portfolio adopted studies.

9 **A Case of Olanzapine-induced diabetic ketoacidosis**

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We present a case of diabetic ketoacidosis (DKA) occurring in a 38 year old gentleman who was taking olanzapine for schizophrenia. He had no personal or family history of diabetes, body mass index was 42kg/m². He was admitted following a three week history of diarrhoea and vomiting culminating in DKA (pH 7.0, HCO₃ 8.7 mmol/l, blood ketones 6.2mmol/l) with acute kidney injury. The metabolic acidosis was slow to respond to intravenous fluids and a fixed dose insulin regime, resulting in episodes of ventricular tachycardia. He required intubation and ventilation with a sixteen-day stay on intensive care. Initial insulin requirements were high (480 units per day) but fell following the cessation of olanzapine therapy and treatment of his hospital acquired pneumonia, dropping to 120-140 units by day fifteen of admission. By discharge, on day 25, blood glucose levels were well controlled on insulatard 16 units twice a day. Islet cell and anti-glutamate decarboxylase antibodies were both negative.

This case is representative of the tendency for atypical antipsychotics to increase the risk and severity of insulin resistance. Less well recognized is the impact of olanzapine on beta cell function which results in the failure of insulin production to compensate for insulin resistance, leading to a relatively insulin deficient state and subsequent DKA. The potential development of DKA in patients on olanzapine, although rare, is increasingly recognized. DKA is a potentially life threatening condition that may be unexpected in this vulnerable patient group.