

Obesity Abstracts

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Speaker Abstracts

A year in review – what are the highlights?

OU1

Developments in treatments for rare genetic obesities

Tony Goldstone

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The area of genetic causes of syndromic and non-syndromic obesity has a large unmet clinical need to treat underlying hyperphagia. In recent years, improved understanding of underlying mechanisms resulting from the underlying gene(s) defects has revealed potential therapeutic targets, while designation of orphan disease has promoted the interest of biotechnology and pharmaceutical companies for these rare genetic obesities. This talk will review the emerging trial data on the use of Setmelanotide, a melanocortin-4 receptor (MC4R) agonist, to treat genetic obesity due to variants affecting the leptin-pro-opiomelanocortin (POMC)-MC4R pathway, particularly for POMC deficiency, leptin receptor (*LEPR*) mutations, PCSK1 deficiency, Bardet-Biedel syndrome, and chromosome 16p11.2 deletions involving *SH2B1* gene or *SH2B1* variants. Meanwhile for Prader-Willi syndrome (PWS), the commonest cause of syndromic obesity, there has been more limited success from clinical trials. No benefit has been evident using Setmelanotide, Livoletide (desacyl ghrelin analogue), nor GLWL-01 a ghrelin-O-acyltransferase (GOAT) inhibitor, but some efficacy in reducing hyperphagia has been seen with Carbetocin/oxytocin and DCCR controlled-release diazoxide. Several ongoing and upcoming trials in PWS are assessing potential for the GLP-1 analogue Liraglutide, and drugs targeting histamine/monoamine systems and potential downstream targets that are more proximal to the underlying PWS genes such as PCSK1. Meanwhile, the benefits of specialist residential homes for adults with PWS remains life-saving by providing an environment with rigorous control of the access to food with promotion of physical activity. However, their limited geographical availability, delays navigating funding pathways between NHS Continuing Healthcare and social care, and issues around capacity and patient/family reluctance to consider such residential options can produce barriers to their utilisation.

DOI: 10.1530/obabs.3.OU1

OU2

Semaglutide and beyond: An update on pharmacotherapy for obesity

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Obesity pharmacotherapy has had a difficult history, with many challenges, and some effective medicines withdrawn due to safety concerns. More recently, better understanding of the biological mechanisms underlying body weight regulation have led to development of more effective treatments, some of which are now entering clinical use. These include treatments for single gene disorders, such as metreleptin for the rare condition of leptin deficiency, and setmelanotide for pro-opiomelanocortin (POMC) deficiency, leptin receptor mutations and some melanocortin 4 receptor mutations. One of the most promising areas relates to hormones from the GI tract that have physiological roles in satiety, such as glucagon like peptide 1 (GLP1), peptide YY and amylin; the only approved treatment in this class is liraglutide 3mg, given sc daily, which has recently been approved by NICE for a limited group of patients with severe obesity and impaired glucose regulation. More recently we have seen the results of studies with the weekly injectable GLP1 RA semaglutide that results in weight loss of 15% or more and is associated with improvements in cardiovascular risk factors and quality of life; a major cardiovascular outcome trial, SELECT, is underway in people with obesity without diabetes who have a history of cardiovascular disease. Combining different gut hormones may give even greater weight loss. Promising data are emerging with tirzepatide, a GLP-1/GIP receptor agonist, that has shown weight loss in excess of 10% in people with diabetes. The combination of semaglutide with an analogue of the islet hormone amylin (cagrilintide), has shown weight loss of 17% over 20 weeks in a phase 2A trial. Thus in the future we may see medication that results in weight loss sufficient to rival the effects of bariatric surgery.

DOI: 10.1530/obabs.3.OU2

OU3

Standardising care in the identification and management of patients with post bariatric surgery hypoglycaemia

Jonathan Hazlehurst

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Post bariatric surgery care within the NHS is currently for 2 years. Post bariatric surgery hypoglycaemia (PBSH) can occur many years following surgery. The true prevalence of symptomatic PBSH is difficult to establish given variable recording and high median time to first event following surgery. Screening post-operative patients reveals high rates of asymptomatic hypoglycaemia of uncertain significance. The numbers of symptomatic patients fulfilling Whipple's triad is still comparatively high. Diagnostic methods are varied and include provocation testing such as mixed meals as well as blinded continuous glucose monitoring with a symptom and food diary. Alternative pathologies including adrenal insufficiency and insulinoma have been reported as causes of hypoglycaemia in the post-operative period and should not be missed. The characteristic timing in PBSH is of post-prandial hypoglycaemia occurring several hours following a carbohydrate containing meal. The mainstay of treatment is of dietary adjustment both in terms of meal and snack content, frequency and timing. The pharmacological management of PBSH is extremely heterogeneous with a lack of a step-wise considered approach. Pharmacotherapy in the literature includes metformin, acarbose, diazoxide, incretin-based treatment, calcium channel antagonists, somatostatin analogues as well as newer treatments in ongoing trials. In patients who remain symptomatic despite dietary adjustment and a trial of pharmacotherapy other reported treatments include surgical reversal, endoscopic treatment, partial pancreatectomy or the use of jejunal feeding tubes. Given the heterogeneity of diagnosis and management approaches to PBSH we have conducted a large scoping review to inform a simplified guideline aimed at the non-specialist endocrinologist, GP with specialist interest and colleagues within Tier 3. The guideline is currently underway and this presentation will report on the situation so far and allow a platform for consultation as the guidelines develops further prior to its publication later in the year.

DOI: 10.1530/obabs.3.OU3

OU4

The SOPHIA innovative medicines initiative project

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The objective of SOPHIA is to optimise future obesity treatment. This has been challenging because too often, clinicians, payers and patients do not consider obesity a disease. SOPHIA proposes that obesity is in fact a set of complex and chronic diseases that should be taken just as seriously as other heterogeneous chronic conditions. We define diseases of obesity in the context of (a) the risks of complications linked to obesity and (b) the responses the diseases have to various treatments (lifestyle interventions, pharmacotherapy, and surgery). SOPHIA will identify and characterise clinically-meaningful subpopulations of patients with obesity using their operational variables for (a) risk and (b) response. We will use this knowledge to stimulate a new narrative, understanding and vocabulary around obesity as a set of complex and chronic diseases. To achieve this, we will pursue the following specific aims: Create a federated distributed database of the best available patient information, by identifying and harmonising key cohorts. Identify predictors of risks of obesity complications. We will identify subpopulations who are at risk of specific complications (e.g. type 2 diabetes (T2D), type 1 diabetes (T1D), cardiovascular disease (CVD), cancers and osteoarthritis). Identify predictors of response to obesity treatment modalities (lifestyle, pharmacotherapy, surgery). Involve patients. Patients will be actively involved at any 'touch point' where the work of SOPHIA impacts on the patient – including data collection and analysis with the purpose to take into account patient perspective and priorities. Create a shared value analysis (SVA). To achieve impact, SOPHIA must ensure it meets a number of common needs of a broad range of stakeholders who can all impact positively on change for good when it comes to sustainably effective treatments which can be taken up by patients, payers and providers alike, creating value that is at the intersection of (a) better patient care; (b) reduced societal burden; and (c) commercially viable opportunities to treat obesity.

DOI: 10.1530/obabs.3.OU4

An update on pharmaceutical therapy and new treatments

OU5

The future of anti-obesity medication

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Newer anti-obesity medications (AOM) now offer the prospect of double-digit weight loss, and potentially clinical benefits beyond those from weight loss alone (e.g., diabetes remission, cardiovascular protection) all on a background of increasing prevalence and severity of obesity in most countries. Currently the analytical framework for evaluating efficacy has been anthropometric-centric but will need to develop as it has in other chronic disease areas to be more complication and outcome-centric. Treat-to target (which may not, and should perhaps not be BMI related, could become a reality and this will need to consider the prospect of AOM combination therapy. The relevance of current 'stopping rules', based on a failure to achieve a 5% loss at 12 or 16 weeks of treatment, will become meaningless when (nearly) all achieve this. Demonstrating cost-efficacy will remain the challenge to drive reimbursement, and there is still much stigma and bias against treating obesity with AOMs to be overcome.

DOI: 10.1530/obabs.3.OU5

OU6

Abstract unavailable

DOI: 10.1530/obabs.3.OU6

Debate: Intermittent fasting vs low calorie

OU7

Is time restricted eating superior to continuous dietary restraint for weight management?

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Current guidelines recommend continuous energy restriction for weight loss along with long-term lifestyle behavioural change as the cornerstones of weight management. Time restricted eating versus continuous energy (calorie) restriction is one of the great debates when it comes to weight management. The most common form of weight loss strategy is continuous dietary (calorie or energy) restriction. Time restricted feeding, which includes intermittent fasting, has specified time limited windows of feeding and fasting. These periods within the 24-hour cycle need not be energy restrictive, and people may follow the regime intermittently. When interpreting current evidence there are several factors to be considered including timing and length of the eating window, if there is predefined or spontaneous energy restriction, and whether the change in eating behaviour causes a change dietary composition as well as body weight. Evidence in humans is currently limited to short-term studies of 12-16weeks, with a variety of eating windows of 4-10hours. Where energy intake is maintained (isocaloric) but the dietary pattern is changed, there is some weight loss (2%) and it is notable that greater weight loss is achieved with a reduced number of meals. With ad libitum intakes there is evidence of some weight loss (2-4%). Metabolic changes related to glucose control, lipids and blood pressure, have some potential but results are not unequivocal, and it is unclear if the outcomes are independent of weight loss. Benefits

Pros	Cons
Tool to use as an option for a person-centred approach	Will not suit everyone due to life-style, environment, cultural and personal preferences
May be easier to "frame" with ad libitum intake during eating period	Eating behaviour may impact outcomes e.g. breaking fast with high energy foods
"Simple" regime to follow	Eating window should be adhered to every day
No recommendations for intake composition	Eating habits within the window may not be ideal for nutritional adequacy
Restricted time eating window has some variation (up to 10hrs)	Even drinks containing energy (kcal) have to be excluded during fasting periods
May support weight lost maintenance after a more restrictive regime	Weight loss over long-term unknown

and challenges to applying time restricted eating in clinical practice are summarised below. Overall, findings suggest that this approach may suit some people, and offer an alternative to continuous energy restriction, but results are not superior.

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OU8

Abstract unavailable

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Keynote: COVID, obesity & diabetes update

OU9

COVID, obesity & diabetes update

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The last 18-months has witnessed the collision of the epidemics of diabetes, obesity and COVID-19. The consistent finding of adverse outcomes, from COVID-19, in individuals with diabetes and/or obesity – even with hyperglycaemia in the non-diabetic range – has focused attention on the metabolic dysfunction that may arise with acute illness and the potential benefit to be gained from glycaemic regulation. Significantly worse outcomes in people with microvascular complications (such as retinopathy or nephropathy) points to endothelial dysfunction as a common mechanism of adverse outcomes. These individuals will be vulnerable to the pro-inflammatory state and microthrombi that ensue with Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2). Trial data have shown that glucocorticoids and anticoagulation address the pro-inflammatory and pro-coagulant pathways. There are emerging trial data targeting other endothelial facets, such as the vasoconstrictive and antioxidant pathways. Another notable feature of the SARS-CoV-2 has been the bidirectionality of response. Unlike the morbidity associated with other infectious agents, such as influenza virus, SARS-CoV-2 itself may promote relative insulin deficiency, ketogenesis and hyperglycaemia in susceptible individuals. The future implications of this are uncertain. In this update, I will highlight how obesity and impaired metabolic health increase complications and mortality in COVID-19 and will summarize the data for metabolic normalisation and mitigation of endothelial cell dysfunction in the acute setting. I will also discuss the consequences of SARS-CoV-2 infection for longer-term metabolic health.

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Plenary: Is there a future for bariatric surgery in the NHS?

OU10

Sarcopenic obesity – how to diagnose and impact on treatment

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Sarcopenic obesity (SO) represents a new challenge due to the parallel increase of obesity and life expectancy. In fact the excess of fat mass and the decrease in muscle mass that characterise SO are frequent during the ageing process due, in particular to gender, degree of adiposity, diseases-related alterations, and age-related hormonal changes. At the moment a universal consensus for its diagnosis does not exist and different procedures, parameters and cut-off points have been proposed in the literature to define it. Moreover SO represents also a difficult challenge with regard to treatment. Reducing fat mass with recovery or at least maintaining lean mass, which would be the logical targets of therapeutic intervention in the SO, are difficult to achieve. Both obesity and sarcopenia are associated with the reduction of muscle strength and the impairment of physical performance and therefore to the onset of disability. Furthermore sarcopenia and obesity are both characterised by metabolic aspects related to insulin resistance and inflammation in particular. SO is more strictly associated to CVD risk factors (e.g. arterial hypertension, carotid artery intima-media thickness, lipid profile, insulin resistance) when compared with either obesity or sarcopenia. However the

studies that investigated the association of SO with known cardiometabolic and/or cardiovascular risk factors, described controversial results depending on the considered population and the criteria used for the definition of SO. There is an unclear evidence on the association between SO and mortality, and data from different studies reach diverse

Conclusions

while in some studies SO seems not to confer any greater risk than sarcopenia alone in other studies the combination of (abdominal) obesity and sarcopenia was associated with the highest risk of mortality. The aims of this presentation are to critically appraise the evidence on approaches to diagnose SO and implications for risk prediction and treatment.

DOI: 10.1530/obabs.3.OU10

OU11

New developments in appetite research

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Obesity and related co-morbidities are major global public health issues, and thus the focus of significant research effort. Recent research using cutting edge techniques including optogenetics and chemogenetics has made major new discoveries regarding the systems that control food intake. We are beginning to understand that peripheral hormonal and neural systems that communicate macronutrient ingestion and wider nutritional state to the centres in the brain that regulate appetite, and to tease out the specific brain circuits which are responsible for specific aspects of feeding behaviour and energy homeostasis. This talk will overview recent developments in the field and explore their implications for future clinical therapies.

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OU12

Abstract unavailable

DOI: 10.1530/obabs.3.OU12

Case Discussions

Case Discussions 1

CD1.1

Weight loss maintenance through a multidisciplinary healthy weight clinic in Australia

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Background

Multidisciplinary care is well recognised as being effective for weight and chronic disease management, and in weight loss maintenance. However, in the Australian context, there are inadequate obesity services. In recognising this health service gap, this led to the establishment of the privately funded university hospital-based weight management clinic – the 'Healthy Weight Clinic' to increase access to multidisciplinary services. The effectiveness of the clinic in supporting patients to achieve clinically significant weight loss (at least 5–10% weight reduction) and weight loss maintenance was evaluated.

Methods

A retrospective chart review was conducted to determine weight outcomes from patients who attended an initial consultation March 2017 – March 2019, with follow up data until June 2020 extracted. Patients received one-on-one multidisciplinary care, including endocrinological input for medical and co-morbidity identification and management, lifestyle behavioural counselling from a dietitian and exercise physiologist, with adjunctive pharmacotherapy used in 81.4% patients.

Results

172 patients received more than one follow-up consultation for lifestyle modification, and mean final weight change was -6.2 kg (range -42.0 kg to 10.4 kg; SD 7.4). This equated to a mean percentage weight change of -5.8% (range -41.6% to 10.7%; SD 6.9). Weight loss of $\geq 5\%$ of initial body weight was observed in 49.4% of patients ($n=85/172$) and 27.3% ($n=47/172$) achieved between 5 and 9.9% weight loss. At 12 months, mean weight change was -9.2 kg (SD 7.5), -9.7 kg (SD 5.8) at 24 months and -12.6 kg (SD 25.5) at 36 months. Twenty percent of patients ($n=35/172$) maintained $\geq 5\%$ of initial body weight loss for at least one year. Weight regain from baseline occurred in 10.5% of patients ($n=18/172$).

Conclusions

When receiving support in a structured dedicated holistic obesity service, patients can achieve clinically meaningful weight loss and maintain this loss. One in five patients could maintain this weight loss, which was potentially confounded by COVID-19 period influences on lifestyle habits. Atlantis, E. et al. Clinical Obesity Services in Public Hospitals in Australia: a position statement based on expert consensus. *Clinical Obesity* 8, 203-210, doi:10.1111/cob.12249 (2018). Wing R, Hill J. Successful weight loss maintenance. *Ann Rev Nutr* 21, 323-341, doi:10.1146/annurev.nutr.21.1.323 (2001).

DOI: 10.1530/obabs.3.CD1.1

CD1.2

Liraglutide 3.0 mg within a NHS Tier-3/4 weight management service results in similar weight loss compared to regulatory trials – The LIPOSAX first UK real-world evidence study

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Liraglutide 3 mg daily is an approved, prescription injectable GLP-1 receptor agonist, which can reduce weight in patients with obesity, with or without obesity complications. We conducted a 24-week, open-label real-world study involving 62 participants with a BMI >30 kg/m² or >27 kg/m² if they had co-existing dyslipidaemia or hypertension. No patients had type 2 diabetes. Patients received once-daily subcutaneous liraglutide 3.0 mg, alongside NHS Tier-3 lifestyle advice. The reduced calorie diet was based on individual estimated basic metabolic rate. The primary end point was change in body weight. Secondary outcomes included changes in anthropometrics and circulating biomarkers of metabolism

(metabolomics and miRNAs). For miRNA analysis, participants were categorised into responders ($>5\%$ weight loss) and non-responders ($<5\%$ weight loss). Ten miRNAs were analysed (including miR-424, miR-143, miR-222, miR-103 and miR-146b). RNA was isolated using miRNeasy and reverse transcribed into cDNA using miRCURY. Cel-miR-39-3p and Unisp6 spike-ins were used as controls. Their geometric mean was used to normalise miRNA expression by the calculated $2^{-\Delta\Delta Ct}$ values. Final analysis included 49 patients. At baseline, 87.1% of participants were women, patients were aged 38.6 ± 9.8 years (mean \pm SD), weighed 117.5 ± 24.5 kg, had fat-mass of 58.96 ± 15.91 kg and BMI of 41.33 ± 6.9 kg/m². Fasting glucose was 5.3 ± 0.58 mmol/l, and ALT 24.9 ± 12.6 U/l. At week 24, patients lost 12.85 ± 8.4 kg or $9.9 \pm 5.8\%$ body weight ($P < 0.001$) and fat-mass decreased by 11.27 ± 7.88 kg ($P < 0.001$). 55.1% of patients lost 5-10% and 18.4% lost $>10\%$ body weight ($P < 0.001$). Fasting glucose reduced by 0.7 ± 0.7 mmol/l ($P < 0.001$) and ALT by 8.8 ± 12 U/l ($P < 0.005$). Good responders had downregulation of miR-424 ($P < 0.001$) whilst poor responders had upregulation of miR-424 ($P < 0.01$). There were no changes in other miRNAs. The most frequently reported adverse events were mild to moderate nausea and diarrhoea. There were no serious adverse events. In this study, 3.0 mg of liraglutide, as an adjunct to a reduced calorie diet and increased physical activity offered within a UK NHS Tier-3/4 weight management service, was associated with reduced body weight and improved metabolic control similar to what has been reported by regulatory trials.

DOI: 10.1530/obabs.3.CD1.2

Case Discussions 2

CD2.1

Contribution of BMI to ethnic disparities in outcomes following hospitalisation for COVID-19

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Background

Ethnicity and obesity have been recently established as risk factors for adverse coronavirus disease 19 (COVID-19) outcomes. The prevalence of obesity differs across ethnic groups. Thus, previously reported ethnic differences in COVID-19 outcomes may be due to underlying variations in BMI.

Aims

To investigate the association between ethnicity and in-hospital mortality in COVID-19, and the effect of BMI. The secondary aim was to investigate the effect of BMI on the relationship between ethnicity and incidence of pulmonary embolus (PE), admission to the intensive treatment unit (ITU), and length of hospitalisation.

Methods

Retrospective cohort study of 149 patients with confirmed COVID-19 and thoracic CT scans (for evaluation of PE) from Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom. Data on self-reported ethnicity and clinical outcomes were extracted from electronic patient records. The 2018 demographic of the local area was obtained from the Office of National Statistics. Multivariate logistic and linear regression analysis was performed to explore ethnicity as a risk factor for the main outcomes of interest, adjusted for BMI.

Results

Mean (\pm standard deviation) age was 57 ± 16 years; 102 (68%) were male; 59 (40%) were of Black, Asian, and minority ethnic backgrounds; median (interquartile range) of hospitalisation duration was 27 (9–53) days; 31 (21%) died; 97 (65%) were admitted to ITU; and 30 (20%) had a PE. There was a greater percentage of patients of Black ethnicity than the local population (27 vs 20%). BMI was not different across ethnic groups (White vs Black vs Other, 29.3 ± 6.9 vs 29.7 ± 6.8 vs 27.2 ± 5.1 kg/m²; $P=0.438$). After adjustment for BMI, ethnicity was not related to adverse COVID-19 outcomes, including mortality, and presence of PE.

Conclusion

BMI did not modify the effect of ethnicity in predicting adverse COVID-19 outcomes.

DOI: 10.1530/obabs.3.CD2.1

CD2.2

Glycaemic variability assessed by continuous glucose monitoring after Roux-en-Y gastric bypass vs. sleeve gastrectomy

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Background

Roux-en-Y Gastric Bypass (RYGB) and Sleeve Gastrectomy are two widely used bariatric procedures. Longitudinal data have shown similar efficacy in terms of sustained weight loss and diabetes remission in obese patients with type 2 diabetes. Altered glucose dynamics with increased glycaemic variability and the occurrence of hypoglycaemia are common post-bariatric surgery.

Aim

To compare the glycaemic variability and incidence of hypoglycaemia between patients who had undergone RYGB or Sleeve Gastrectomy.

Subjects and Methods

We compared retrospectively seven patients who had undergone RYGB and seven patients who had undergone Sleeve Gastrectomy at 12–60 months post-surgery. Glycaemic variability was assessed by using the Dexcom G6 Continuous Glucose Monitoring system for 7–10 days on each occasion. The CGM metrics

analysed included mean glucose, %CV, CONGA, MAGE and ADDR. The %Time in Range (TIR) and the incidence of hypoglycaemia were also compared between the groups.

Results

There was no significant difference between the weight, HbA1c or mean glucose between the two groups at the time of the study. Despite the fact that the %TIR (3.9 – 10.0 mmol/l) did not differ between the two groups, there was significantly increased glycaemic variability as evidenced by the higher CONGA, MAGE, ADDR and %CV in the RYGB group compared to the Sleeve Gastrectomy ($P < 0.01$). The incidence of hypoglycaemia assessed by %TIR (< 3.9 mmol/l) and %TIR (< 3.0 mmol/l) was also greater in the RYGB group ($P = 0.018$ and $P = 0.019$ respectively).

Conclusions

Despite similar results in terms of weight and glycaemic control as assessed by standard metrics of mean glucose and HbA1c, there is a difference in the glucose profiles as illustrated by the increased glycaemic variability and incidence of hypoglycaemia after RYGB in comparison to Sleeve Gastrectomy. Patients who undergo Sleeve Gastrectomy may be less vulnerable to post-bariatric hypoglycaemia.

DOI: 10.1530/obabs.3.CD2.2

Poster Presentations

P1

Development of severe gastroparesis and gastric food bezoar following administration of glucagon-like peptide 1-receptor agonist (GLP1-RA) therapy

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With the global increase in obesity and diabetes, the use of weight negative therapy, such as the glucagon-like peptide -1 receptor agonists (GLP-1 RA) are increasing. The most common side effects with the GLP-1RA are gastrointestinal symptoms, mainly nausea. Other common adverse effects include headache, injection site reactions, and are usually minor and do not result in cessation of therapy. GLP-1RA are also associated with slowed gastric emptying, by virtue of their mode of action and potentially a gastroparesis (1). Causes of gastric dysmotility include prior gastric surgery (e.g. partial gastrectomy, vagotomy, laparoscopic adjustable gastric banding, and Roux-en-Y gastric bypass). Comorbid medical conditions such as diabetes mellitus are also associated with gastroparesis due to autonomic neuropathy. In diabetics it is therefore worthy to consider pre-existing autonomic dysfunction prior to commencement of GLP-1RA therapy. Gastric bezoars are foreign body masses and are classified according to their composition. Most commonly, patients with gastric bezoars present with nausea and vomiting, epigastric pain, dyspepsia, early satiety, anorexia and weight loss (2). We present a case of a 43 year old non-diabetic woman, with a pre-existing gastric band, who commenced on GLP-1RA therapy for weight loss. Gastroscopy some years after band placement but prior to medical therapy endoscopy was normal. Our patient developed the above GI symptoms and was found to have a gastric bezoar 4 months after initiation of GLP1-RA therapy. A radionuclide study demonstrated severe delay in gastric emptying. removal of the band did not alter the bezoar. Due to the gastric motility slowing effect, patients on GLP-1RAs need to be informed of the risks of impaired gastric emptying. Clinicians need to be particularly aware of at risk populations, namely diabetics and prior bariatric surgical patients. In light of the current GLP-1RA indications, these are the particularly vulnerable populations, and may be more at risk of bezoar formation.

1. Meier JJ. GLP-1 receptor agonists for individualized treatment of type 2 diabetes mellitus. *Nat Rev Endocrinol*. 2012;8(12):728–742.
2. Khan S et al. Upper gastrointestinal manifestation of bezoars and the etiological factors: a literature review. *Gastroenterology research and practice*. 2019 Jul 15;2019.

DOI: 10.1530/obabs.3.P1

P2

Resistant Hypocalcemia in a patient after Roux-en-Y gastric bypass

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Introduction

It is known that bariatric operations cause nutritional deficiencies especially calcium and vitamin D. Reported hypocalcemia after bariatric surgery ranges from 1% after Roux-en-Y gastric bypass (RYGB) to 25% after bilio-pancreatic diversion-duodenal switch. This is mainly the result of bypassing the preferential sites for calcium and vitamin D absorption. Apart from the bariatric operations, hypocalcemia commonly occurred after total thyroidectomy in 20 percent of patients. Risk of hypocalcemia will increase further after RYGB in history of thyroidectomy, which will make it more difficult to manage.

Case

We are presenting a 49 year-old female with a BMI of 35kg/m² presenting to our clinic for obesity management. She had a previous total thyroidectomy for a compressive goiter 10 years previously, which was complicated by hypoparathyroidism. Which was managed by oral calcium carbonate 1.5 g and alfacalcidol 1mcg bd, with calcium of 2.13 to 2.28 mmol/l. She also had history of connective tissue disease for which she received prednisolone and type 2 diabetes mellitus. She underwent a RYGB in November 2020. Day 1 post-surgery her calcium level was 1.71 mmol/l requiring intravenous replacement in-addition to oral alfacalcidol. She returned 3 months later complaining of paraesthesiae, diarrhoea and a very low calcium of 1.40, phosphate 1.51 mmol/l with parathyroid hormone of 1.2 pmol/l and vitamin D level 79.2 nmol/l. Investigations into her diarrhoea revealed severe bile acid malabsorption for which she was started on colestyramine. She required substantial increases to her alfacalcidol dose (3 mcg bd) before the calcium increased to 1.81 mmol/l.

Conclusion

Our case demonstrates two main factors of post-gastric bypass hypocalcaemia. The main one is malabsorption of oral calcium and vitamin D

which normally takes place in the duodenum and jejunum; bypassing this segment after RYGB and a higher pH contribute to the reduction in absorption. Secondly, severe bile acid malabsorption which presented very soon after her operation, might have further reduced the absorption of vitamin D. To our knowledge our case is the second in the literature presenting RYGB hypocalcemia in a patient with hypoparathyroidism. In such cases higher doses of alfacalcidol seem to be necessary to maintain desired calcium concentrations.

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P3

Gender differences in cardiometabolic abnormalities across different BMI categories

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Background

Not all obese individuals exhibit abnormal cardiometabolic parameters. These are termed as being metabolically healthy obese (MHO). Conversely some normal weight individuals exhibit adverse cardiometabolic parameters and are described as being metabolically unhealthy normal weight (MUHNW). Visceral adiposity is known to be strongly associated with cardiometabolic risk than subcutaneous adiposity. Furthermore, there are gender differences in distribution of fat and in the prevalence of overweight and obesity. This study explored gender differences in the prevalence of adiposity-metabolic health phenotypes (expressed as BMI and presence or absence of certain cardiometabolic parameters) in a nationally representative sample of Maltese subjects. We also investigated gender differences in anthropometric measures and cardiometabolic parameters and in the relationship between BMI categories and metabolic health.

Methods

This was a cross-sectional study. Median age was 41 ± 5 years. Subjects with a BMI < 24.9 kg/m² were normal weight and subjects with BMI ≥ 25 kg/m² were overweight or obese. Metabolic health was defined as presence of ≤ 1 parameters of the metabolic syndrome as per NCEP ATP III criteria and classified into one of the following body composition phenotypes: Metabolically healthy normal weight (MUHNW); metabolically unhealthy normal weight (MUHNW); Metabolically healthy overweight/obese (MHO); metabolically unhealthy obese (MUHO)

Results
A higher percentage of males exhibited the unhealthy metabolic phenotypes (41.3% vs 27.8%). 10.3% of normal weight men and 6.3% of normal weight women were metabolically unhealthy. Despite males having a higher median BMI, there was a lower proportion of males having an abnormally high waist circumference than females. Significant gender differences in biochemical and life-style parameters were noted for each body composition phenotype.

Discussion

Males were more likely to be insulin resistant and to exhibit a metabolically unhealthy profile than females despite exhibiting an abnormal waist circumference less frequently and having similar waist index. This suggests that the currently used cut-off for waist circumference should be revised downwards in men. Normal weight men were more often metabolically unhealthy than normal weight women, thus, BMI cut-offs may also need to be lowered in men. The gender divergence between metabolic risk factors is consistent with gender differences in the pathogenesis of cardiovascular disease.

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P4

Vitamin D Receptor (VDR) polymorphisms & metabolic health status in a Maltese cohort

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Background

Several studies have investigated the association between vitamin D receptor (VDR) variants and the risk of cardiometabolic complications. The pleiotropic action of VDR in extra-skeletal tissues gives physiologic plausibility to the associations between VDR variants and metabolic health, particularly in obese individuals. Whilst multiple conflicting findings have been reported, clinical data has shown that despite an increase in physical activity and nurturing healthier dietary choices, there are individuals who do not benefit from lifestyle changes. This study aims to replicate the association between common VDR variants and obesity risk in a well-characterised Maltese cohort stratified into metabolically

healthy and unhealthy obese phenotypes; a hypothesis that has never been investigated in the Maltese population.

Methods

A cross-sectional case-control study involving 480 working age Maltese adults was conducted. The cohort was stratified into four different body composition phenotypes based on BMI and metabolic syndrome components. Four VDR polymorphisms [FokI (rs2228570), BsmI (rs1544410), ApaI (rs7975232) and TaqI (rs731236)] were genotyped by PCR-RFLP, and the association with metabolic health phenotypes was investigated.

Results

The VDR TaqI C/C genotype was associated with higher odds of obesity, independent of metabolic health status. A higher frequency of the BsmI G/A and TaqI T/C genotypes was observed in the MHO (metabolically healthy obese) subgroup when compared to the MUHO (metabolically unhealthy obese) subgroup. VDR haplotype block 2 was associated with a significantly higher odds of MHO.

Conclusions

Our results suggest that in the high prevalence Maltese population, VDR polymorphisms are associated with obesity and metabolic health status. Future studies should further investigate the overall effect of multiple variants associated with obesity phenotypes and relate genotypes with the longitudinal progression of obesity to assess the dynamic nature of metabolic health.

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P5

Energy expenditure trends in patients following roux-en-y gastric bypass surgery

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Background

Resting energy expenditure (REE) and diet induced thermogenesis (DIT) are known to influence long term maintenance of weight loss following bariatric surgery. Although it is known that fat free mass (FFM) contributes to REE to a greater extent than fat mass (FM), there has been relatively little work looking at the REE:FFM ratio and its overall effect on and relationship to weight loss.

Aim

To assess weight loss, REE and REE:MMT ratio in patients undergoing Roux-en-Y Gastric Bypass (RYGB) up to one year post-operatively.

Methods

20 patients undergoing RYGB were followed up for one year. Weight, REE and FFM were measured at baseline (pre operatively), 1, 3, 6 and 12 months using the Tanita BC-418MA body composition analyser. One way ANOVA was used to compare results at 1, 3, 6 and 12 months to baseline.

Results

There were 16 females and 5 males. Mean age was 48. Overall mean weight (kg) decreased significantly over the course of one year (117.8 kg vs 80.6 kg $P < 0.0001$). Mean REE decreased significantly at all times points compared to baseline (2037 kcal at baseline vs 1583 kcal at 12 months). DIT increased at 3 months compared to baseline and then decreased at one year (229.5 kcal vs 354.7 kcal vs 263.3 kcal respectively) however this difference was not significant. FFM decreased significantly from baseline to 12 months ($P < 0.0001$). REE:FFM ratio decreased significantly at 3 and 6 months compared to baseline ($P = 0.028$), there was no significant difference at 12 months ($P = 0.215$).

Conclusion

Our findings indicate a decrease in weight, REE and FFM over 12 months in RYGB patients. REE:FFM ratio was also significantly decreased at 3 and 6 months. This suggests that the reduction in REE may either be independent of FFM (i.e. another factor is contributing to REE decrease) or the inherent metabolic activity of the FFM in these post-operative patients has decreased. Further studies are required to investigate the relationship of FFM to REE and weight loss.

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