Welcome to issue 94 of Diabetes and Obesity Research Review. This issue begins with research in patients with type 2 diabetes who had undergone bariatric surgery reporting higher rates of insulin cessation following RYGB than after LAGB. A paper from JAMA reports that offspring of mothers who have gestational diabetes diagnosed by 26 weeks’ gestation seem to have a higher risk of developing an ASD (autism spectrum disorder). Two papers focus on type 1 diabetes-associated coeliac disease, one of which reports on a high rate of spontaneous coeliac serology normalisation in children, and the other describes an association between the presence of coeliac disease and the development of microvascular complications. Thank you for the comments, questions and suggestions you have sent – please keep them coming. Best regards,

Associate Professor Jeremy Krebs
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Insulin cessation and diabetes remission after bariatric surgery in adults with insulin-treated type 2 diabetes

Authors: Ardestani A et al.

Summary: This research in adults with insulin-treated type 2 diabetes who underwent RYGB (n=3318) or LAGB (n=1907) compared postsurgical changes in insulin treatment. Compared with LAGB, RYGB was associated with a significantly greater insulin cessation rate at 12 months (62% vs. 34% [p<0.001]), with a regression analysis showing that RYGB was a strong predictor of insulin cessation at both 1 month and 12 months. In a case-matched analysis at 3 months, RYGB continued to be associated with a higher rate of insulin cessation compared with LAGB (p=0.03), and the rate of diabetes remission was greater at all postsurgery timepoints. RYGB predicted insulin therapy cessation early postsurgery independently of bodyweight, whereas insulin cessation was linked to bodyweight loss after LAGB.

Comment: There is growing knowledge around the metabolic effects of bariatric surgery. Most surgical series demonstrate high rates of resolution of type 2 diabetes, although this does vary depending on the criteria adopted to define this. There are also important differences between the commonly performed operations. This paper reports from a very large longitudinal bariatric surgery database, and selects those who had type 2 diabetes requiring insulin preoperatively. It demonstrates that RYGB is more effective than LAGB in getting people off insulin. Of interest is that this is additional to any difference in weight lost between procedures. This implies that there are physiological changes induced by RYGB that have additional metabolic benefits. This hypothesis is not new, and many research teams are trying to discover the mechanism.


Abstract
Patients’ perceptions of injecting insulin and self-monitoring of blood glucose in the presence of others

Authors: Mehmet S et al.

Summary: These researchers questioned 76 randomly selected patients with insulin-treated diabetes on injecting insulin and SMBG. Forty-nine participants reported problems with injecting insulin and performing SMBG when other people were present. Over one-third of respondents reported ‘almost never’ feeling comfortable injecting insulin and undertaking SMBG in public places, and 50% ‘almost never’ injected insulin in the presence of work colleagues. Most respondents reported feeling comfortable injecting insulin and undertaking SMBG in the presence of their partner, children and family.

Comment: SMBG is an essential component of good glycaemic management for those with type 1 diabetes and those with type 2 using insulin therapy. Yet despite patients knowing this, there is often a disconnect between this and what they actually do. Very commonly when we look at paper records or interrogate meters, there are big gaps in the data, frequently in the middle of the day. There are many factors contributing to this, but this paper highlights one of these. Many people with diabetes simply do not feel comfortable testing or injecting in public or in front of work colleagues. The authors suggest a public awareness campaign, which might help. I also think that effective noninvasive glucose monitoring technology would revolutionise patients’ abilities to track and control their diabetes. Where is that glucose watch?


Efficacy of commercial weight-loss programs

Authors: Gudzune KA et al.

Summary: This was an updated systematic review of 45 studies (39 randomised controlled trials) comparing commercial or proprietary weight-loss programmes with no intervention, education or behavioural counselling in overweight and obese adults. The following increases in proportions of participants achieving bodyweight loss were seen: i) 2.6% at 12 months for Weight Watchers programmes versus control/education; ii) 4.9% at 12 months for Jenny Craig programmes versus control/education and counselling; iii) ≥3.8% at 3 months for Nutrisystem programmes versus control/education and counselling; iv) ≥4.0% (short-term) for very-low-calorie programmes versus counselling, but with some evidence of attenuation after 6 months; and v) 0.1–2.9% at 12 months for Atkins programmes versus control/education and counselling; iii) ≥3.8% at 3 months for Nutrisystem programmes versus control/education and counselling; iv) ≥4.0% (short-term) for very-low-calorie programmes versus counselling, but with some evidence of attenuation after 6 months; and v) 0.1–2.9% at 12 months for Atkins diets versus counselling. Other commercial weight-loss programmes evaluated had mixed findings or limited data.

Comment: In the face of the obesity epidemic, health providers are struggling to provide effective weight-loss programmes for patients. However, we might well ask whether this is actually our role? Whilst there are some individuals for who rapid weight loss may have health risks, for the large part weight loss achieved by any of the multitude of diets advertised and sold in books and commercial programmes is of health benefit. This systematic review aimed to examine the efficacy of these programmes, and demonstrated this. However, it is important to note that the quality of the trials reported was relatively low, particularly the short duration and high dropout rates. Many weight loss trials demonstrate the need for ongoing contact to maintain weight lost. That may simply mean that individuals need to maintain involvement in the commercial programme of their choice. The big question here is who should pay for this?


Association of maternal diabetes with autism in offspring

Authors: Xiang AH et al.

Summary: The risk of ASDs associated with intrauterine exposure to pre-existing type 2 and gestational diabetes was explored in a retrospective cohort of 322,323 singleton offspring born in the US during 1995–2009. ASDs were diagnosed during follow-up in 115 children born to 6496 mothers with pre-existing type 2 diabetes, 130 and 180 children born to 7456 and 17,579 mothers with gestational diabetes diagnosed at ≤26 and >26 weeks’ gestation, respectively, and 2963 children born to 290,732 mothers with no diabetes during their index pregnancy (respectively adjusted annual incidences of 3.26, 3.02, 1.77 and 1.77 per 1000). Compared with no maternal diabetes, the risk of ASDs in offspring was significantly increased in those born to mothers with pre-existing type 2 diabetes and gestational diabetes diagnosed at ≤26 weeks’ gestation after adjustment for birth year (respective hazard ratios 1.59 [95% CI 1.29, 1.95] and 1.63 [1.35, 1.97]), but only the latter association remained significant after further adjustment for maternal age, parity, education, household income, race/ethnicity, history of comorbidity and offspring gender (1.42 [1.15, 1.74]). Exposure to antidiabetic medications did not increase the risk of ASDs.

Comment: This is likely to be a very emotive issue. The possible association between diabetes and autism is not a new question. In this retrospective cohort study, rates of autism in offspring were compared between women with pre-existing diabetes during pregnancy, those with gestational diabetes, either diagnosed before or after 26 weeks, and those without diabetes. The initial signal that pre-existing diabetes and early-onset gestational diabetes were associated with greater risk of autism was attenuated when adjusted for multiple confounders, to the point that of the three diabetes states, only early-onset gestational diabetes remained significantly associated with autism. Whilst this raises questions, it seems most unusual that only this specific diabetic state, arbitrarily defined from a continuum, is specifically a causal factor. Interesting questions, but I don’t believe we have the answer.

Reference: JAMA 2015;313(14):1425–34

Abstract
Metformin prescription for insured adults with prediabetes from 2010 to 2012

Authors: Moin T et al.

Summary: The use of metformin in prediabetes was investigated in a retrospective cohort of 17,352 adult Americans with the condition from a private insurance database. Metformin was prescribed to 3.7% of the patients during the 3-year study period. After adjustments, metformin was twice as likely to be prescribed to women and obese patients, and 1.5 times as likely to be prescribed to patients with ≥2 comorbidities.

Comment: What to do with prediabetes? In NZ the estimated rate of prediabetes is 25% – only marginally lower than in America. Currently there is no clear pathway for people with prediabetes. Many individual practices and PHOs have some form of lifestyle programme, but there is no systematic national plan. I am often asked about the use of metformin for these patients. Yes there is evidence of reduced progression to diabetes, but equally we are then treating people with the drug we would start for diabetes anyway. It is therefore of great interest to me that in the US, where I would have expected a much greater use of drugs, only 3% of the prediabetic population studied were prescribed metformin. We need better research in this area, but I would be restricting the use to those on the verge of diabetes anyway. This is of course just an opinion in an evidence-free zone.


Gestational diabetes mellitus screening, management and outcomes in the Cook Islands

Authors: Aung YYM et al.

Summary: Current practices for gestational diabetes screening in Cook Island women were reported using data from antenatal care attendees during 2009–2012. Screening involved a nonfasting 50g glucose challenge at 24–28 weeks’ gestation, which if positive (1-hour glucose level ≥7.8 mmol/L) was followed by a 75g oral glucose tolerance test. Gestational diabetes was diagnosed if fasting glucose level was ≥5.2 mmol/L or 2-hour glucose level ≥8.0 mmol/L, and pregnancy impaired glucose tolerance was diagnosed on a positive screen and negative diagnostic test. The screening programme uptake had increased from 49.0% to 99.6% at the end of the study period. Among women who underwent a glucose challenge (n=646), 18% had a positive result and 13.8% had an oral glucose tolerance test. Pregnancy impaired glucose tolerance was diagnosed in 13.8% of these women, and gestational diabetes in 13.9%. Women with gestational diabetes and normal glucose tolerance had respective bodyweight gains of 6kg and 10kg and caesarean section rates of 25% and 11%; baby birthweights did not differ significantly. Among 59 women with gestational diabetes who underwent a postnatal glucose tolerance test at their 6-week check, diabetes was confirmed in 35.6%.

Comment: I have included a number of studies in recent issues of Diabetes Research Review highlighting the controversy around gestational diabetes. This study gives this a new perspective. Women in the Cook Islands are at high risk of diabetes, due to family history and high rates of obesity. However, previously there were low rates of uptake of screening for gestational diabetes. After initiating a more systematic screening programme, this increased to almost 100%, and with the exception of more caesarean sections, pregnancy outcomes became similar to women without gestational diabetes. This highlights that the greatest benefits probably come from better implementation of current guidelines and diagnostic criteria than lowering thresholds and overburdening women and the healthcare system.


Abstract

Independent commentary by Associate Professor Jeremy Krebs, an endocrinologist with a particular interest in obesity and diabetes. He is an Associate Professor with the University of Otago, and Director of the Clinical Research Diploma at Victoria University. As well as clinical and teaching activities, Assoc Prof Krebs maintains active research interests in the area of obesity and diabetes, with a focus on nutritional aspects, bariatric surgery and diabetes service delivery.

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High rate of spontaneous normalization of celiac serology in a cohort of 446 children with type 1 diabetes

Authors: Castellana S et al.

Summary: The prevalence of spontaneous normalization of anti-tTG (antitissue transglutaminase) levels and predictors of this were prospectively investigated in 446 children screened for coeliac disease at onset of type 1 diabetes and specified intervals thereafter. Among children who became positive for coeliac serology (n=65), 58% had a persistently elevated anti-tTG titre, 41% had a fluctuating anti-tTG titre and 28% became negative. Positive coeliac disease autoimmunity and overt coeliac disease occurred at prevalences of 14.3% and 8.5%, respectively, values that are 1.5- and 8-times greater than seen in the general paediatric population. The lowest risk of developing coeliac disease was evident in asymptomatic children who were aged >9.1 years at type 1 diabetes onset.

Comment: Coeliac disease is increasing in prevalence. Whether this is a true increase, increased detection or even true coeliac disease is unknown. However, we now commonly screen for it in people with type 1 diabetes, particularly in children, adolescents and young adults. A diagnosis of coeliac disease has a profound impact on a person’s life, particularly when combined with type 1 diabetes. Therefore the findings of this paper are of great interest. Here 40% of children with positive transglutaminase antibodies, but no symptoms, reverted to a negative state after 6 months. They may of course become positive later and/or develop true disease, but this is a large proportion of children for whom dietary restrictions can be avoided. I would be interested to know if there are similar data for adults diagnosed with type 1 diabetes.

Reference: Diabetes Care 2015;38(5):760-6

Abstract

Microvascular complications in childhood-onset type 1 diabetes and celiac disease

Authors: Rohrer TR et al., for the DPV Initiative and the German BMBF Competence Network Diabetes Mellitus

Summary: The risk of developing microvascular complications in type 1 diabetes-associated coeliac disease was investigated in this longitudinal analysis of 56,514 patients aged >10 years with diabetes of <20 years duration from the German-Austrian DPV Database; 812 patients had biopsy-confirmed coeliac disease, 4,769 had a clinical diagnosis or positive antibodies and 50,933 had no coeliac disease. Compared with absence of coeliac disease, its presence was associated with an earlier age at which retinopathy and microalbuminuria were seen in one-quarter of the patients (26.7 vs. 33.7 years and 32.8 vs. 42.4 years, respectively), and coeliac disease increased the risk of both complications (adjusted hazard ratios 1.263 [95% CI 1.078, 1.481] and 1.359 [1.228, 1.504]).

Comment: …but then you wouldn’t want to miss a diagnosis of coeliac disease either! Following on from the previous study, this study looked at whether coeliac disease is associated with microvascular complications of diabetes. Allowing for the retrospective design, a current diagnosis of coeliac disease was associated with earlier retinopathy and nephropathy in those with longstanding type 1 diabetes. No causal inference can be drawn from this, but the authors recommend regular screening for coeliac disease. However, the real question is whether detection of coeliac disease and treatment with a gluten-free diet will have any impact on an individual’s risk of developing microvascular disease. This would be a difficult study to conduct ethically.


Abstract
Continuous glucose monitoring in people with diabetes

Authors: New JP et al.

Summary: Patients receiving multiple daily insulin injections or continuous subcutaneous insulin infusions for type 1 or type 2 diabetes were randomised to CGM with (n=49) or without (n=48) alarms or SMBG (n=48) in the GLADIS trial. Compared with SMBG, neither the CGM group with nor without alarms differed significantly for time spent outside the glucose level target during days 80–100 (9.7 and 9.9, respectively, vs. 106 h/day [respective p values 0.18 and 0.08]), but time spent in hypoglycaemia was shorter for CGM with alarms (1.0 vs. 1.6 h/day [p=0.030]). Among subcutaneous insulin recipients, the respective CGM with and without alarms groups spent 2.4 and 1.9 h/day less time outside the glucose level target than SMBG (p values 0.0461 and 0.0134). No significant differences in reductions in baseline HbA1c levels were seen among the three groups; however, the proportions of participants with an HbA1c level reduction of ≥6 mmol/mol (≥0.5%) were 18.3% and 16.2% for overweight and 5.7% and 4.7% for obese. Children of Pacific and Maori ethnicity and those from more socioeconomically deprived areas had higher prevalences of overweight and obesity than other children. There were no definite time trends seen over the study period.

Comment: Monitoring of blood glucose levels is an integral component of achieving tight glycaemic control safely without excessive risk of hypoglycaemia. Continuous glucose monitors remove some barriers to monitoring, and additionally can also provide alarms to warn people when they are straying outside of fixed parameters. This study examines whether CGM with or without alarms enables people to remain within target more than self-monitoring with finger prick testing. What stands out to me from this study is how little time any of the participants spent out of target! Although the time has come for more robust measures. The very fact that the media are covering calls for lolly bans in dairies in Auckland indicates a level of public awareness and concern that something needs to be done. We must keep the pressure up. Regulation as part of a broad strategy is required. Bring on the sugar tax. Let’s start somewhere.


Overweight and obesity in 4–5-year-old children in New Zealand

Authors: Rajput N et al.

Summary: These authors reported the results from the first 4 years of the NZ ‘B4School Check’ programme, which included 168,744 BMI measurements representing a coverage rate of 66.5%. The respective mean BMIs for girls and boys were 16.30 and 16.44 kg/m2, with mean BMI z-scores according to the 2006 WHO standards of 0.601 and 0.785. According to WHO 2006 standards, 16.9% and 19.6% of girls and boys were overweight, respectively, and 13.8% and 18.7% were obese; the respective values according to IOTF (International Obesity Task Force) standards were 18.3% and 16.2% for overweight and 5.7% and 4.7% for obese. Children of Pacific and Maori ethnicity and those from more socioeconomically deprived areas had higher prevalences of overweight and obesity than other children. There were no definite time trends seen over the study period.

Comment: One-third of 4- to 5-year-old children in NZ are overweight or obese! Yet we are still getting lip service from the government about the problem. In almost 9 years of the ‘antinanny state’ approach to education and self-responsibility, we have seen no change in the course of obesity in this country either in adults or children. Surely the time has come for more robust measures. The very fact that the media are covering calls for lolly bans in dairies in Auckland indicates a level of public awareness and concern that something needs to be done. We must keep the pressure up. Regulation as part of a broad strategy is required. Bring on the sugar tax. Let’s start somewhere.


Abstract

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