Diabetes & Obesity Research Review™

Making Education Easy

Issue 95 – 2015

In this issue:

Abbreviations used in this issue
ACE = angiotensin converting enzyme
ARB = angiotensin receptor blocker
BMI = body mass index
BP = blood pressure
Hb_{A1c} = glycosylated haemoglobin
ICU = intensive care unit
OR = odds ratio
SSB = sugar-sweetened beverage

Welcome to issue 95 of Diabetes and Obesity Research Review.

This winter edition begins with a network meta-analysis that found no survival benefit with any BP-lowering regimen in adults with diabetes and kidney disease. There is also an interesting report on how published study findings have impacted on the adoption of tight glycaemic control in ICU settings. Researchers from Singapore found that smartphone apps (applications) for calculating insulin doses are generally of poor quality and may even provide our patients with potentially dangerous misleading information. We have concluded this issue with research suggesting that increases in bodyweight may not be the sole contributor to increases in Hb_{A1c} levels that often occur when patients with diabetes quit smoking.

Thank you for your comments, questions and suggestions – please keep them coming.

Best regards,

Associate Professor Jeremy Krebs
jeremykrebs@researchreview.co.nz

Comparative efficacy and safety of blood pressure-lowering agents in adults with diabetes and kidney disease

Authors: Palmer SC et al.

Summary: This was a network meta-analysis of 157 studies (n=43,256) comparing BP-lowering agents in adults with kidney disease related to (mostly type 2) diabetes. Compared with placebo, no antihypertensive regimen reduced all-cause mortality or increased hyperkalaemia or acute kidney injury, although combined ARB plus ACE inhibitor regimens ranked lowest for hyperkalaemia or acute kidney injury among all interventions due to borderline increases in estimated risks (respective ORs 2.69 [95% CI 0.97, 7.47] and 2.69 [0.98, 7.38]). In addition, the likelihood of end-stage renal disease was significantly reduced by treatment with both an ARB and an ACE inhibitor (OR 0.62 [95% CI 0.43, 0.90]) and ARB monotherapy (0.77 [0.65, 0.92]).

Comment: The management of BP is as important as the management of glycaemia in people with diabetes in order to minimise the risk of long-term micro- and macrovascular complications. The most appropriate agents to use and the target BP to aim for continue to be debated, and even more so in those with established renal impairment. This study reported a meta-analysis of studies addressing the benefits and risks of BP lowering in this setting. There is no shortage of data! Unfortunately the results are somewhat sobering. No treatment strategy reduced premature mortality. As we might predict, ACE inhibitors and ARBs either alone or in combination were beneficial in reducing progression of renal impairment. This analysis highlights the importance of early aggressive management of diabetes to prevent the development of nephropathy, as once there is established disease, it may be too late to prolong life even if we can slow the renal failure itself.

Reference: Lancet 2015;385(9982):2047–56
Abstract

Intensive diabetes therapy and ocular surgery in type 1 diabetes

Authors: The DCCT/EDIC Research Group

Summary: These authors presented data over median 23-year follow-up on ocular surgical procedures (self-reported) among participants from the DCCT (n=1441)/EDIC (n=1375) study, which compared intensive versus conventional therapy. Compared with conventional therapy, intensive therapy was associated with a significantly lower proportion of participants undergoing ocular surgery (8.9% vs. 13.4% [p<0.001]), with respective risk reductions for diabetes-related and all ocular surgical procedures of 48% and 37% after adjusting for DCCT baseline factors. Intensive therapy was associated with adjusted risk reductions of 48% for cataract extraction (p=0.002) and 45% for vitrectomy, retinal-detachment surgery or both (p=0.01), and 32% lower surgery costs. Additional adjustment for mean Hb_{A1c} levels over the entire follow-up period fully attenuated these beneficial effects of intensive therapy.

Comment: The DCCT trial remains the landmark trial of glucose treatment in type 1 diabetes, and the long-term follow-up in EDIC has continued to give us rich data on the long-term effects of intensive glucose management. From the original trial it was the reduced risk of retinopathy that was the strongest evidence for benefit of intensive treatment, and from which the widely accepted target Hb_{A1c} level of 7% (53 mmol/mol) was derived. Therefore it is interesting to see this study showing the long-term outcomes of those in DCCT with regard to ocular operations. It is pleasing to see that the early benefits extend out to reduced operative procedures over time, though there were still 9% of participants who required intervention. The observation that glycaemic control was the predictor of need for intervention reaffirms the management goal of intensifying glucose control – to an individualised target.

Reference: N Engl J Med 2015;372(18):1722–33
Abstract

CONGRATULATIONS TO
Jacqui Adair
who won the iPad mini 3 by taking part in our recent Subscriptions Update promotion. Jacqui is a Clinical Nurse Specialist at Middlemore Hospital in Auckland.

Effect of published scientific evidence on glycemic control in adult intensive care units

Authors: Niven DJ et al.

Summary: Glycaemic control was compared in 353,464 critically ill patients before and after the publication of clinical trials reporting decreased (Leuven I) and subsequently increased (NICE-SUGAR) mortality with tight glycaemic control. Before Leuven I, 17.2% of patients admitted to an ICU had tight glycaemic control, 3.0% had hypoglycaemia and 40.2% had hyperglycaemia, and after Leuven I, relative quarterly changes were seen for these parameters of +1.7%, +2.5% and –0.6%, respectively (p<0.001 for all). No change was seen for the relative proportion of patients with tight glycaemic control or hyperglycaemia after NICE-SUGAR was published, and although the relative proportion with hypoglycaemia decreased initially by 22.4% (p<0.001), there was no further change over time.

Comment: Hyperglycaemia in patients admitted to hospital has been shown to predict poor outcomes in a number of clinical areas irrespective of pre-admission diabetes status. In the ICU setting, this led to clinical trials to test whether tight glycaemic control would improve outcomes. Several early trials, particularly in surgical postoperative ICU patients, did demonstrate benefit. However, later trials have shown that tight glycaemic control, particularly if at the expense of hypoglycaemia, actually increased mortality. This study looked at the effect of these progressive trial results on clinical practice. It is of note that initial evidence of benefit was slow to be adopted and incorporated into daily practice. Perhaps of more concern though is that the subsequent evidence of harm has not translated into abandoning the previous approach. This may indicate an inherent belief by medical teams that tight glycaemic control must be as beneficial in the ICU as it is in ambulatory care. It raises the concern that we may behave in a similar fashion in other situations when evidence reveals that clinical dogma is not correct.

Reference: JAMA Intern Med 2015;175(5):801–9
Abstract

Smartphone apps for calculating insulin dose

Authors: Huckvale K et al.

Summary: This was a systematic assessment of 46 apps for iOS- and Android-based smartphones that use data on planned carbohydrate intake and blood glucose levels to calculate rapid/short-acting insulin doses. A clinical disclaimer was included in 59% of the apps, 30% documented the calculation formula, 91% lacked numeric input validation, 59% allowed a calculation when ≥1 value was missing, 48% used 'ambiguous' terminology, 9% did not use adequate numerical precision and 4% did not store parameters 'faithfully'. A risk of inappropriate recommended output dose was evident in 67% of the apps. Only one app (for iOS) met all the authors' criteria, and there were no significant differences in issue prevalence by payment model or platform.

Comment: Self-management is the buzzword of the moment in chronic disease care, and diabetes is at the forefront of this. Therefore tools to facilitate and enable better self-management are required. With increasing ownership, use and utility of mobile technology, it is logical that this be used as part of the toolkit for self-management. Not surprisingly there has been a growing number of phone apps available for various aspects of diabetes management, including those providing direct advice on insulin dosing. Whilst this may be an excellent way of assisting those with type 1 diabetes particularly, it comes with considerable risk if such advice is not accurate. This study reviewed a wide range of such apps and found a concerning lack of quality control and errors in the advice, often due to lack of very basic process checks within the app. This highlights a very real clinical risk and the need for some regulation of health apps, and a gap in the app market for a high-quality diabetes app.

Reference: BMC Med 2015;13:106
Abstract

Sugar sweetened beverage consumption among adults with gout or type 2 diabetes

Authors: Murphy R et al.

Summary: These NZ researchers questioned 1023 adults with gout and 580 (including 206 receiving haemodialysis) with type 2 diabetes on their consumption of SSBs (sugar-sweetened beverages). Consumption of ≥1 SSB per day was reported by 64%, 47% and 49% of respondents with gout and type 2 diabetes with and without dialysis, respectively, and the respective rates for consumption of ≥4 SSBs per day were 18%, 9% and 9%. A multivariate analysis revealed that respondents who consumed ≥4 SSBs per day were more likely to be male (adjusted OR 1.8 [95% CI 1.1, 2.9]), younger in age (1.6 [1.1, 2.3] for 40 vs. 65 years), current smokers (5.2 [2.7, 10.1]), obese (1.4 [1, 1.9] for BMI 41 vs. 26 kg/m^2) and Māori (1.8 [1.2, 2.8]) or Pacific Islanders (1.6 [1.1, 2.5]). Compared with respondents with diabetes, those with gout were more likely to report heavy SSB consumption (OR 2.4 [95% CI 1.5, 3.9]), and requirement of dialysis did not affect consumption among respondents with diabetes.

Comment: There is accumulating evidence of negative effects of SSBs on contributing to the development of type 2 diabetes, worsening diabetes control and exacerbating gout. This underpins recommendations for reducing or avoiding these beverages. These NZ data show that this advice is not being acted on, with 50% or more of those with diabetes or gout consuming SSBs daily, and almost 20% with gout and 10% with diabetes consuming ≥4 servings a day. Perhaps not surprisingly these individuals also had other characteristics or risk factors for worse diabetes and cardiovascular outcomes. Unfortunately this is another example of poor uptake and adherence with evidence-based guidelines. The question is what can we as health professionals do to improve this? Or do we simply need a very big tax on them!

Reference: PLoS ONE 2015;10(5):e0125543
Abstract

Effects of acute hypoglycemia on working memory and language processing in adults with and without type 1 diabetes

Authors: Allen KV et al.

Summary: The effects of hypoglycaemia on language processing were investigated in 20 adults with type 1 diabetes and 20 healthy volunteers who underwent a hyperinsulinaemic glucose clamp to lower blood glucose level to 2.5 mmol/L for 60 minutes or maintain blood glucose level at 4.5 mmol/L on separate occasions. Language tests included working memory and language (reading span) and grammatical decoding and encoding. Hypoglycaemia was associated with a significant deterioration in reading span ($p<0.001$) and a significant decrease in correct responses ($p=0.005$), with an increased reading time for the first sentence fragment on self-paced reading test ($p=0.039$); an increase in the reading time for the next fragment was greater in the healthy volunteers than the adults with type 1 diabetes ($p=0.03$). Hypoglycaemia had no significant effect on the number of sentence comprehension errors or the time taken to answer questions, but did significantly negatively affect subject-verb agreement ($p=0.011$).

Comment: We all know how much people with diabetes hate episodes of hypoglycaemia, and this often drives them to run their blood glucose levels higher than ideal. This study examined the effect of hypoglycaemia on aspects of language and memory during periods of highly controlled hypoglycaemia, and demonstrated expected impairments. This effect was simply related to the hypoglycaemia and independent of whether the individual had type 1 diabetes or not, confirming this as a physiological effect rather than a diabetes-related effect. It suggests that any verbal or written instructions given to people when hypoglycaemic need to be very simple and specific to be effective.

Reference: Diabetes Care 2015;38(6):1108–15
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. **FOR FULL BIO CLICK HERE.**

Gender-based differences in glycaemic control and hypoglycaemia prevalence in patients with type 2 diabetes

Authors: Kautzky-Willer A et al.

Summary: Patient-level data from six randomised clinical trials were pooled to examine the impact of gender on glycaemic control and hypoglycaemia in previously insulin-naïve men (n=1349) and women (n=1251) with inadequately controlled type 2 diabetes who received insulin glargine or NPH (neutral protamine Hagedorn) insulin for 24–36 weeks. Hb_{A1c} levels significantly decreased in both sexes, but the reduction in men was greater than in women (–1.36% vs. –1.22% [p=0.002]), and significantly fewer women achieved the target Hb_{A1c} level of <7% (53 mmol/mol [p<0.001]), despite a significantly higher insulin dose (0.47 vs. 0.42 U/kg [p<0.001]). Women also had significantly higher incidences of severe hypoglycaemia (3.28% vs. 1.85%; OR 1.80 [95% CI 1.08, 3.00]) and severe nocturnal hypoglycaemia (2.24% vs. 0.59%; 3.80 [1.72, 8.42]).

Comment: This is an interesting study comparing gender differences in the response to insulin initiation in those with poorly controlled type 2 diabetes. The data were extracted from six trials and pooled for this analysis. Hence the studies were never specifically designed to test for gender differences, and although the baseline characteristics of Hb_{A1c} level, age and diabetes duration were similar, there may be other selection biases at play. Furthermore, although there are statistically significant gender differences in reduction in Hb_{A1c} level and insulin doses, in reality these are of very little clinical significance. What may be of more relevance is the observation that women appeared more prone to hypoglycaemia. This may have importance when deciding on individual Hb_{A1c} targets.

Reference: Diabetes Obes Metab 2015;17(6):533–40
Abstract

Stable intergenerational associations of childhood overweight during the development of the obesity epidemic

Authors: Ajslev TA et al.

Summary: Changes in intergenerational resemblances in overweight children across the development of the obesity epidemic were explored in groups of 7-year-old Danish children born during 1952–1989 to parents who were and were not overweight at ages 7 and 13 years; BMI records obtained from the Copenhagen School Health Records Register provided available data for 17,926–42,184 parent-child pairs. Parent-child overweight associations were stable across child BMI groups born to parents who were and were not overweight during childhood, with a slight upward trend in the likelihood for children to be overweight across time if they were born to two parents who were overweight at age 13 years, but not at age 7 years.

Comment: The old debate of 'nature versus nurture' re-emerges with a twist. This novel study assessed the relationship between children's and parents' bodyweights at the same age across a series of cohorts over 40 years. As expected, parental obesity as a child was associated with obesity in their children at the same age. This suggests a genetic determinant, although parenting style and similar environmental setup cannot be excluded. Notably the highest rates of children's obesity were seen when both parents were obese as children. The nature of this relationship was consistent across cohorts, although the prevalence of the children's obesity did increase slightly with time. This might suggest an environmental change as the driver, but this relative increase is well short of the rise in the rate of obesity we have observed across the population. There remains much to learn about the intergenerational trends and influences of obesity.

Reference: Obesity 2015;23(6):1279–87
Abstract

What happens to thyroid function in long-term type 1 diabetes?

Authors: Brooks AP et al.

Summary: The Winchester cohort study of thyroid function in type 1 diabetes was a cross-sectional analysis of 655 patients of a wide age range and diabetes duration ≤50 years. Treated clinical hypothyroidism was the most common form of thyroid dysfunction affecting 7.6% and 22% of males and females, respectively. Two males and two females experienced over-active thyroid episodes. The respective prevalences of treated clinical hypothyroidism had increased in males and females from 1 in 10 and 1 in 6 for 10–29.9 years of diabetes duration to 1 in 6 and 1 in 3 for >30 years' duration.

Comment: The coexistence of more than one autoimmune condition is well recognised. Autoimmune thyroid disease is a common condition in its own right, with very clear gender differences in incidence. This study reported on the prevalence of co-existing type 1 diabetes and thyroid disease in individuals with up to 50 years of diabetes. As expected, hypothyroidism was more common than hyperthyroidism, and women had much higher rates than men. The observation that almost a quarter of women developed thyroid dysfunction strongly supports the guideline for annual monitoring of thyroid function in those with type 1 diabetes. It would be interesting to see the same data for coeliac disease.

Reference: Practical Diabetes 2015;32(4):129–33
Abstract

The association between smoking cessation and glycaemic control in patients with type 2 diabetes

Authors: Lycett D et al.

Summary: The retrospective UK THIN (The Health Improvement Network) primary-care database cohort study examined the impact of quitting smoking on type 2 diabetes control in 10,692 smokers with the disease. Patients who quit smoking and remained abstinent for ≥1 year (n=3131) had a significant nonbodyweight change-mediated 2.34 mmol/mol (0.21%) increase in Hb_{A1c} level during their first year of not smoking, followed by a decline to levels at 3 years that were comparable with those of continual smokers.

Comment: Smoking is an important risk factor for cardiovascular disease and has an additive effect with diabetes. Therefore smoking cessation is regarded as a very important intervention in those who have diabetes and are smokers. This study showed a negative effect of enabling this to happen, with glycaemic control deteriorating by a clinically meaningful degree. The obvious explanation is the weight gain often seen with stopping smoking. However, once adjusted for this, the effect persisted suggesting an independent effect. Although the deterioration appears to resolve after a few years, this may still be relevant in overall risk for micro- and macrovascular complications. However, I suspect the benefits of stopping smoking will still outweigh any negative effect.

Reference: Lancet Diabetes Endocrinol 2015;3(6):423–30
Abstract

CLICK HERE to read previous issues of Diabetes & Obesity Research Review