Effect of finerenone on albuminuria in patients with diabetic nephropathy

Authors: Bakris GL et al., for the Mineralocorticoid Receptor Antagonist Tolerability Study – Diabetic Nephropathy (ARTS-DN) Study Group

Summary: ACE (angiotensin-converting enzyme) inhibitor or ARB (angiotensin-receptor blocker) recipients with diabetes and high or very high albuminuria were randomised to receive finerenone 1.25mg (n=96), 2.5mg (n=92), 5mg (n=100), 7.5mg (n=97), 10mg (n=98), 15mg (n=125) or 25mg (n=119) or placebo (n=94) once daily for 90 days. Finerenone at doses of 7.5mg, 10mg, 15mg and 20mg was associated with 90-day reductions in placebo-corrected urinary albumin-creatinine ratio relative to baseline (primary outcome) of 0.79, 0.76, 0.67 and 0.62, respectively (p≤0.004). The respective rates of hyperkalaemia leading to discontinuation in the finerenone 7.5mg, 15mg and 20mg arms were 2.1%, 3.2% and 1.7%; there were no occurrences in the 10mg (or the placebo) arm. There were no differences between the finerenone arms and the placebo arms for estimated glomerular filtration rate reduction of ≥30%, adverse events or serious adverse events.

Comment: The development of microalbuminuria in people with diabetes is an important event, and is a marker not only of risk of more advanced kidney disease, but also of macrovascular disease. Inhibition of the renin-angiotensin system has been the mainstay of therapy with ACE inhibitors or ARBs. However, we often have patients who continue to have progressive albuminuria on these agents, or cannot tolerate them. This study explored the efficacy of a mineralocorticoid blocker, finerenone, in reducing albuminuria in this setting. The positive results across a range of doses are encouraging. What are now needed are studies to test whether finerenone will prevent the decline in renal function and/or reduce cardiovascular risk in longer term trials. These are in fact underway, and many NZ sites will be shortly recruiting for these studies.

Reference: JAMA 2015;314(9):884–94

Abstract
US Community Preventive Services Task Force
recommendations for combined diet and physical activity
promotion programmes for preventing diabetes

Summary: This summary encompasses three papers published in the Sept 15, 2015 issue of Ann Intern Med. The US Community Preventive Services Task Force commissioned an evidence review to evaluate benefits and harms in programmes designed to promote and support individuals to improve their diets, exercise and bodyweight. Thirty studies of diet and physical activity promotion programmes versus usual care, thirteen of more intensive versus less intensive programmes and thirteen of single programmes were included in the systematic review. Compared with usual care, programmes promoting diet and physical activity reduced the incidence of type 2 diabetes (16 studies; risk ratio 0.59 [95% CI 0.52, 0.66]), decreased bodyweight by 2.2% (24 studies), reduced fasting blood glucose level by 0.12 mmol/L (2.2 mg/dL; 17 studies) and improved other cardiometabolic risk factors. Greater effectiveness was seen with more intensive programmes. There were only limited data on clinical events.

The task force also supervised a systematic review of 28 studies on the economic efficiency of these programmes in clinical trial, primary care and primary care-referable settings. The median cost per participant was US$653, but was lower for group-based programmes and those implemented in community or primary care settings than the DPP (Diabetes Prevention Program) trial and the DPP Outcomes Study ($417–424 vs. $5881). Sixteen of 22 studies assessing incremental cost-effectiveness ratios reported a median of $13,761 per QALY (quality-adjusted life-year) saved, with group-based programmes being more cost effective than those with individual sessions ($1819 vs. $15,846 per QALY). No studies reported cost-benefit data.

Based on their review findings, the task force recommends that healthcare systems, communities and other implementers use combined diet and physical activity promotion programmes for individuals at increased risk of type 2 diabetes, also noting the cost effectiveness of such programmes.

Comment: There is growing realisation that we MUST do something about the exponential growth in the rates of obesity and type 2 diabetes. Government has finally understood the urgency of this, has embraced the notion that childhood obesity is a critical place to focus efforts, and perhaps that also targeting high-risk individuals with prediabetes is also likely to be a cost-effective strategy. These combined publications are therefore timely. Lifestyle interventions are often criticised as being ineffective and too expensive. There has also been controversy over whether to focus on dietary intake or on physical activity – an argument that is often complicated by political ideation and philosophical stubbornness. These systematic reviews provide further clarity to the debate. It is clear from the current evidence that a combination of both dietary and physical activity elements in a programme is the most effective. It is also clear that delivery of these within a community setting and in groups rather than on an individual basis is more cost effective. We need to embrace this in NZ, and it is pleasing to see that there is growing realisation that simply focusing on education and physical activity is NOT going to be enough.

References:


Authors: Menke A et al.

Summary: These researchers used US NHANES data to estimate recent prevalences and updated trends in total diabetes, diagnosed diabetes and undiagnosed diabetes. In an overall 2011–2012 population of 2781 adults, the respective prevalences for total diabetes, diagnosed diabetes, undiagnosed diabetes and prediabetes were 14.3%, 9.1%, 5.2% and 38.0% according to the HbA1c, fasting plasma glucose or 2-hour plasma glucose level definition, and the unadjusted prevalence of total diabetes was 12.3% according to the HbA1c or fasting plasma glucose level definition, with 25.2% undiagnosed. Non-Hispanic black, non-Hispanic Asian and Hispanic patients exhibited significantly higher age-standardised prevalences of total diabetes (using the HbA1c, fasting plasma glucose or 2-hour plasma glucose level definition) than non-Hispanic white patients, and non-Hispanic Asian and Hispanic patients had significantly higher age-standardised percentages of undiagnosed cases than other ethnicities. Total diabetes according to the HbA1c or fasting plasma glucose level definition increased significantly over time for all age groups, genders, ethnic groups, education levels and poverty income ratio tertiles, with respective age-standardised overall prevalences of 9.8%, 10.8% and 12.4% seen in 1988–1994, 2001–2002 and 2011–2012 (p<0.001 for trend).

Comment: There aren’t really too many surprises in this study, but I have included it for general information and to make us feel good that in NZ we are still a wee way behind the US! Depending on how you look at the data, our prevalence is approximately 8% of the adult population compared with 12–14% in the US. We have similar patterns of differing prevalence by ethnicity, with higher rates in non-Caucasians. The other interesting observation was that the rates of undiagnosed diabetes are now <50% of the total. This indicates that there may be a greater awareness of diabetes, but may also reflect the greater ease of making the diagnosis since the introduction of HbA1c level as a diagnostic option.

Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes

Authors: Mingrone G et al.

Summary: Patients with type 2 diabetes for ≥5 years and body mass index ≥35 kg/m² were randomised to receive medical treatment (n=20), Roux-en-Y gastric bypass (n=20) or biliopancreatic diversion (n=20) in this open-label trial; 88% of participants completed 5 years of follow-up. Five-year diabetes remission was not seen in the medical treatment arm, but was reported for 50% of the surgically treated patients (p=0.007; gastric bypass group 37%; biliopancreatic diversion group 63%). The respective hyperglycaemia relapse rates were 53% and 37% among participants who achieved 2-year remission with gastric bypass and biliopancreatic diversion, respectively. Compared with medically treated participants, a significantly greater proportion of gastric bypass or biliopancreatic diversion arm participants achieved target HbA_1c level of <47.5 mmol/mol (<5.5%); 42% and 68%, respectively, vs. 27% (p=0.457), and they had greater bodyweight loss and significant reductions in plasma lipid levels, cardiovascular risk and medication use. There were five major diabetes complications in the medical treatment arm (including one fatal myocardial infarction) versus one in the surgical arms. Biliopancreatic diversion was associated with some nutritional effects.

Comment: There have been accumulating data over the last 10 years or so of the benefits of bariatric surgery in those with type 2 diabetes. It has been difficult to compare studies due to the differences between procedures, a variety of definitions of diabetes resolution, and a paucity of randomised trials. However, the overall impression has been one of dramatic benefits and very high rates of diabetes resolution. More recently there have been several well-designed randomised trials comparing bariatric surgery with best medical management, and more rigorous and standardised definitions of diabetes resolution. The present study adds more long-term outcomes to the discussion. Notably, although there are clear benefits of surgery over medical management, the rates of resolution at 5 years are much lower than the 85% previously quoted from earlier studies. It is also notable that diabetes resolution is independent of weight lost. This therefore reopens the debate about the underlying mechanisms of improved glucose metabolism following bariatric surgery.

Reference: Lancet 2015;386(9997):964–73

Fasting until noon triggers increased postprandial hyperglycaemia and impaired insulin response after lunch and dinner in individuals with type 2 diabetes

Authors: Jakubowicz D et al.

Summary: Twenty-two patients with diabetes consumed breakfast, lunch and dinner on one day and lunch and dinner with no breakfast on another day in a randomised crossover design. Compared with the days when breakfast was consumed, days with no breakfast were associated with respective increases in plasma glucose, free fatty acid and glucagon lunchtime under the curve to 180 minutes of 36.8%, 41.1% and 14.8% at lunchtime and 26.6%, 29.6% and 11.5% at dinnertime, whereas the respective values for insulin and intact glucagon-like peptide-1 were 17% and 19% lower at lunchtime and 7.9% and 16.5% lower at dinnertime (p<0.0001). Compared with days when breakfast was consumed, insulin peak was delayed by 30 minutes after lunch and dinner on no breakfast days.

Comment: It has often been said that breakfast is the most important meal of the day. Many people seem to struggle with having breakfast – a concept I can’t understand as I am always starving in the morning! Consequently, I often hear people say that they have a cup of coffee but nothing else until late morning. This study examined what the effect of missing breakfast is on subsequent glucose metabolism later in the day in a group with type 2 diabetes using a crossover design. It clearly demonstrates that after missing breakfast, glucose, free fatty acids and glucagon levels were higher later in the day. These may be useful data to underpin discussions with patients about the importance of making breakfast part of their start to the day.


"LANTUS® (insulin glargine) is now fully funded for Type 2 diabetes patients requiring insulin".

- Once daily Lantus delivers 24-hour peakless efficacy.
- There is no pronounced peak, and less risk of symptomatic and nocturnal hypoglycaemic events than NPH in T2D patients.

For prescribing information, visit www.medsafe.govt.nz
Metformin for the treatment of gestational diabetes

Authors: Kitwitee P et al.

Summary: This updated meta-analysis included eight clinical trials (n=1712) reporting data on metformin and insulin for gestational diabetes mellitus. Differences between metformin and insulin in pooled estimates for fasting plasma glucose, postprandial plasma glucose and HbA1c levels measured at 36–37 weeks’ gestation were very small and statistically nonsignificant, and 14–46% of metformin recipients needed additional insulin. Compared with insulin, metformin was associated with less neonatal hypoglycaemia (relative risk 0.74 [95% CI 0.58, 0.93]) and fewer neonatal intensive-care admissions (0.76 [0.59, 0.97]).

Comment: The role of metformin in the management of gestational diabetes has received attention over the last decade. On occasion contraindicated in pregnancy, primarily because of lack of evidence for safety, metformin has now become an important component of management. The MIG trial based in NZ has provided much of the evidence underpinning this. This study has added to the evidence through a meta-analysis of trials comparing glucose control and neonatal outcomes between metformin and insulin therapy in women with gestational diabetes. Both treatments achieved similar glycaemic control, recognising that some individuals who started on metformin needed to have additional insulin. However, there was a lower risk of neonatal hypoglycaemia and less requirement for neonatal intensive-care admission in those using metformin. Treatments must be individualised, but there is growing support for metformin as the first-line therapy in gestational diabetes, just as it is in type 2 diabetes.


Abstract

Progression of diabetic retinopathy after bariatric surgery

Authors: Murphy R et al.

Summary: This was an analysis of retrospective data from 318 NZ patients with type 2 diabetes who had undergone bariatric surgery and had preoperative and ≥1 postoperative retinal screening records. The respective minimal, mild/ moderate and high-grade diabetic retinopathy rates were 18.9%, 8.5% and 4%; 68.6% had no diabetic retinopathy. No change in retinopathy grade was seen at the first postoperative retinal screen in 73% of the patients, while 11% had regressed and 16% had progressed. Significant associations were seen between the probability of having a grade moderate or higher diabetic retinopathy post-surgery and the magnitude of HbA1c level reduction, a shorter postoperative retinal screening duration, more severe preoperative retinal screening grade, male gender and non-Maori/Pacific ethnicity.

Comment: A question I am frequently asked is whether people with diabetes who undergo bariatric surgery and have resolution of their diabetes postoperatively require ongoing retinal surveillance? It is therefore very useful to have the results of this study looking at the changes in retinal status postoperatively in an NZ cohort. Although these data are not exclusively in those with full resolution of diabetes, the observation that 16% of patients had progression of retinopathy postoperatively highlights that ongoing retinal surveillance is required. It is of note that those with worse retinopathy preoperatively and those whose HbA1c level drops the most following surgery were at particular risk. Patients considering undergoing bariatric surgery with a primary aim of ‘curing’ their diabetes must be made aware of these findings, and primary care teams must also know that they need to continue regular retinal photography.


Abstract

Weight-based hypoglycaemia treatment protocol for adults with type 1 diabetes

Authors: McTavish L et al.

Summary: Thirty-one evaluable patients with type 1 diabetes and frequent hypoglycaemic episodes (capillary glucose level <4.0 mmol/L) received glucose tablets 0.2 g/kg, 0.3 g/kg and 15 g in a randomised crossover manner for ≤15 hypoglycaemic episodes. The respective unadjusted mean capillary glucose levels 10 minutes following glucose 0.3 g/kg, 0.2 g/kg and 15g administration were 4.67, 4.29 and 4.37 mmol/L. After adjustment for clusters and baseline, administration of glucose 0.3 g/kg was associated with a significantly higher capillary glucose level at 10 minutes than glucose administration of 15g (difference 0.26 mmol/L [p=0.02]); the difference after 0.2 g/kg administration was not significant. Three hypoglycaemic episodes resulted in capillary glucose levels >8 mmol/L.

Comment: One of the consequences of aiming for tight glycaemic control is an increased frequency of hypoglycaemia. Whilst this is somewhat inevitable, if hypoglycaemia is not well managed it can have a major impact on wellbeing and on overall glycaemic control. If insufficient glucose is taken then patients remain hypoglycaemic, and if excessive glucose is taken then rebound hyperglycaemia is common. This study explored whether using a weight-based glucose treatment had better outcomes than a fixed-dose, employing a crossover design in people with type 1 diabetes. The conclusion was that 0.3 g/kg appears to have an advantage over a fixed dose or a lower ratio (0.2 g/kg). This evidence may be used to underpin patient education on management of hypoglycaemia. It would be interesting to know whether this will also apply to those with type 2 diabetes, and a similar study in that group would be worthwhile.


Abstract

Visual exposure to obesity: experimental effects on attraction toward overweight men and mate choice in females

Authors: Robinson E & Christiansen P

Summary: This research investigated women’s exposure to men of varying bodyweights on their attraction to overweight men. Two separate studies showed that women exposed to obese men had altered visual perceptions of ‘normal’ healthy bodyweights, resulting in greater attraction towards an overweight man. A third study showed that women’s attraction to overweight men increased if they were regularly exposed to men of heavier bodyweight. The fourth study in this research found that women in an online dating study who were exposed to obesity were more likely to select an overweight man to date over a healthy weight man.

Comment: I just threw this study in for interest and water cooler discussion value. What a fascinating concept this is. I wonder if the opposite is also true.


Abstract