Diabetes Research Review™

Making Education Easy

Issue 113 - 2019

In this issue:

Abbreviations used in this issue:

BMI = body mass index; **BP** = blood pressure; **CGM** = continuous glucose monitoring; **CKD** = chronic kidney disease; **CSII** = continuous subcutaneous insulin infusion; **CV** = cardiovascular; **DKA** = diabetic ketoacidosis; **GFR** = glomerular filtration rate; **GLP** = glucagon-like peptide; **HbA_{1c}** = glycosylated haemoglobin; **RCT** = randomised controlled trial; **SGLT** = sodium glucose cotransporter; **SMBG** = self-monitoring of blood glucose; **T1DM/T2DM** = type 1/2 diabetes mellitus.

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Welcome to issue 113 of Diabetes Research Review.

This issue begins with a BMJ meta-analysis assessing the efficacy and safety of sotagliflozin, a dual SGLT-1/2 inhibitor, in the treatment of T1DM (type 1 diabetes mellitus), followed by research published in JAMA reporting greater reductions in HbA_{1c} levels in patients with uncontrolled T2DM when oral semaglutide was added to their treatment compared with when sitagliptin was added. Other included research reports that CSII with integrated CGM and a suspend-before-low feature was associated with fewer sensor-detected hypoglycaemic and severe hypoglycaemic events in hypoglycaemia-prone adults with T1DM when compared with CSII without real-time CGM. The issue concludes with a randomised crossover trial showing that the accuracy of intermittently viewed CGM sensors is reduced during exercise.

I hope you enjoy this issue, and I invite you to send feedback and comments.

Kind Regards,

Dr Mathis Grossmann

mathis.grossmann@researchreview.com.au

Efficacy and safety of dual SGLT 1/2 inhibitor sotagliflozin in type 1 diabetes

Authors: Musso G et al.

Summary: This meta-analysis of six RCTs (n=3238) comparing sotagliflozin with an active comparator or placebo in adults with T1DM found that sotagliflozin was associated with greater reductions in HbA_{1c} level (weighted mean difference –0.34% [p<0.001]), fasting and 2-hour postprandial plasma glucose levels (–16.98 and –39.2 mg/dL, respectively) and daily total, basal and bolus insulin doses. Sotagliflozin also improved time in range and other CGM parameters, and reduced bodyweight, systolic BP and albumin-creatinine ratio and hypoglycaemia (including severe), but significantly increased the risks of DKA, genital tract infections, diarrhoea and volume depletion events. Compared with a sotagliflozin dosage of 200 mg/day, 400 mg/day was associated with greater improvements in most glycaemic and nonglycaemic outcomes with no increase in adverse events.

Comment: Most people with T1DM do not achieve glycaemic targets, and despite some progress in physiological insulin delivery with devices, risks of hypoglycaemia and weight gain persist. Adjunctive drug treatments have so far not been very successful. In this meta-analysis, sotagliflozin, a dual SGLT-1/2 inhibitor (with theoretical but not clinically proven advantages over an SGLT-2-specific inhibitor), had modest beneficial effects on glycaemic parameters, bodyweight, BP and hypoglycaemia, but was associated with significantly increased risks of DKA, dehydration and genital infections. Meta-analysed RCTs were limited by their short duration, and were not powered for hard clinical outcomes. Design flaws (such as masking HbA_{1c} levels) may have favoured the active intervention. While metabolic benefits of sotagliflozin, if sustained, might improve long-term outcomes (e.g. predicted 20% reduction in microvascular events over 6 years), this is counterbalanced by a real risk of adverse effects in the short term, with 61 of the 1912 subjects (3.1%) assigned to sotagliflozin experiencing DKA, despite careful participant selection and monitoring (number needed to harm ~26). The increased risk of DKA despite close supervision in patients participating in clinical trials raises serious concerns that this risk will be even higher in routine clinical practice. The US FDA, earlier this year, rejected approval for sotagliflozin as an adjunctive treatment for T1DM, and sotagliflozin is not approved in Australia. While sotagliflozin may have benefits in carefully selected, well-educated and appropriately monitored individuals, such as obese and/or insulin-resistant who agree to ketone monitoring, better long-term risk-benefit data are necessary to determine whether sotagliflozin has a place in T1DM management.

Reference: BMJ 2019;365:l1328

Abstract

Independent commentary by Dr Mathis Grossmann, MD, PhD, FRACP, who is a physician-scientist trained in both basic biology and in clinical endocrinology/diabetes. He is Professor of Medicine at the Department of Medicine, University of Melbourne, Austin Health, Australia, and a Consultant Endocrinologist at Austin Health. His research focuses on the regulation of cardiometabolic and musculoskeletal health by androgens and oestrogens, at both the clinical and the molecular levels.

Effect of additional oral semaglutide vs sitagliptin on glycated hemoglobin in adults with type 2 diabetes uncontrolled with metformin alone or with sulfonylurea

Authors: Rosenstock J et al., for the PIONEER 3 Investigators

Summary: Adults with T2DM uncontrolled on metformin with or without a sulfonylurea were randomised to receive oral semaglutide 3mg (n=466), semaglutide 3mg increased to 7mg (n=466), semaglutide 3mg increased to 14mg (n=465) or sitagliptin 100mg (n=467) once daily in the PIONEER 3 trial; the premature discontinuation rates in the respective four trial arms were 16.7%, 15.0%, 19.1% and 13.1%. Compared with sitagliptin, participants from the semaglutide 7 and 14 mg/day arms experienced significant reductions in HbA_{1c} level (primary endpoint; respective differences, –0.3% and –0.5% [p<0.001 for both]) and bodyweight (–1.6 and –2.5kg [p<0.001 for both]) by week 26; significant differences for both these endpoints persisted out to week 78 for semaglutide 14 mg/day versus sitagliptin.

Comment: Several injectable GLP-1 receptor agonists have been reported to improve CV disease outcomes, the leading cause of death in people with T2DM. In this 78-week RCT, 1864 adults with T2DM already taking metformin with or without a sulfonylurea were randomised to an oral once-daily tablet of the GLP-1 receptor agonist semaglutide at different doses (3, 7 and 14mg) or to maximum daily dose sitagliptin (100mg). Similar to previous RCTs using injectable GLP-1 receptor agonists, compared with sitagliptin (a relatively weak antiglycaemic drug), oral semaglutide modestly improved HbA_{1c} (–0.3 to –0.5%) and bodyweight (–1.6 to –2.5kg). Semaglutide was most effective at the highest, 14mg, dose. This was counterbalanced by higher rates of gastrointestinal side effects and premature study drug discontinuation, illustrating the balance between effectiveness and tolerability that has challenged GLP-1 receptor agonist development. At the 7mg oral dose, semaglutide had adverse event rates comparable with sitagliptin, a generally well-tolerated drug, but is less effective than standard-dose injectable semaglutide. An obvious advantage of oral semaglutide is that injection can be avoided. Should future studies confirm CV benefits with oral GLP-1 receptor agonists, and depending on costs, such agents could become a valuable future option in the expanding spectrum of drugs for the treatment of T2DM.

Reference: JAMA 2019;321:1466–80
Abstract

Long-term weight loss with metformin or lifestyle intervention in the Diabetes Prevention Program Outcomes Study

Authors: Apolzan JW et al., for the Diabetes Prevention Program Research Group

Summary: Predictors of long-term weight loss were identified by analysing data from the Diabetes Prevention Program Outcomes Study, undertaken after the masked treatment phase of the DPP (Diabetes Prevention Program) RCT had ended, which compared metformin, an intensive lifestyle intervention and placebo in 3234 individuals. Bodyweight loss of ≥5% from baseline in the first year was recorded for 28.5%, 62.6% and 13.4% of the metformin, intensive lifestyle and placebo groups, respectively, and the respective rates of maintained weight loss between years 6 and 15 after the end of masked treatment were 6.2%, 3.7% and 2.8%. Factors that independently predicted long-term weight loss included greater weight loss in the first year (all groups), older age and continued metformin use in the metformin group, older age and absence of either diabetes or a family history of diabetes in the intensive lifestyle group, and higher baseline fasting plasma glucose levels in the placebo group.

Comment: This observational 15-year follow-up study included participants who achieved ≥5% of weight loss during the DPP, a 12-month RCT that compared the efficacy of an intensive lifestyle intervention, metformin, and placebo in overweight/obese individuals at high risk of diabetes. While those assigned to the intensive lifestyle intervention had the greatest weight loss during the RCT they also regained the most weight at 6 years follow-up. During years 6–15, the percentage who maintained weight loss >5% was lower in the intensive lifestyle intervention group (43%) than in the metformin group (56%). Setting aside limitations inherent in the observational design of the study, and the fact that highly selected individuals were followed, the study demonstrates that a surprisingly high proportion of individuals can maintain weight loss over the long term. This is important because modest weight loss decreases the risk of progression to diabetes. Unfortunately, the study does not clarify whether metformin is better than the intensive lifestyle intervention, given that only 28% of individuals assigned to metformin achieved 5% of weight loss during the RCT and were eligible for follow-up versus 63% of those assigned to the intensive lifestyle intervention. It also remains unknown whether metformin is synergistic to intensive lifestyle interventions. Currently at least 10 trials, including a follow-up of this study, are evaluating the effects of metformin (a cheap and easy to use drug) on CV outcomes and cancer risk. Outcomes of these trials should further inform the decision-making process of choosing the best intervention(s) for long-term weight loss.

Reference: Ann Intern Med 2019;170:682–90
Abstract

Albuminuria-lowering effect of dapagliflozin alone and in combination with saxagliptin and effect of dapagliflozin and saxagliptin on glycaemic control in patients with type 2 diabetes and chronic kidney disease (DELIGHT)

Authors: Pollock C et al.

Summary: Patients with a known history of T2DM, a urinary albumin-to-creatinine ratio of 30–3500 mg/g, an estimated GFR of 25–75 mL/min/1.73m^2 and an HbA_{1c} level of 53–97 mmol/mol (7.0–11.0%) on stable angiotensin blockade and glucose-lowering treatment for ≥12 weeks were randomised to receive dapagliflozin 10mg (n=145), dapagliflozin 10mg plus saxagliptin 2.5mg (n=155) or placebo (n=148) once daily for 24 weeks. Compared with placebo, both dapagliflozin alone and dapagliflozin-saxagliptin reduced urinary albumin-to-creatinine ratios throughout the study, with differences at week 24 for mean change from baseline of –21.0% (p=0.011) and –38.0% (p<0.0001) for dapagliflozin only and dapagliflozin-saxagliptin, respectively. Dapagliflozin-saxagliptin was also associated with a greater reduction in HbA_{1c} level at week 24 compared with placebo (–0.58% [p<0.0001]). The respective adverse event rates in the dapagliflozin only, dapagliflozin-saxagliptin and placebo arms were 54%, 68% and 55%, with serious adverse event rates of 8%, 8% and 11%. No new drug-related safety signals were detected.

Comment: Secondary outcome analyses have suggested that SGLT-2 inhibitors may slow progression of diabetic CKD. This 24-week RCT randomised 461 patients with T2DM and moderate-to-severe CKD (47% had a baseline estimated GFR <45 mL/min) receiving angiotensin blockade to either dapagliflozin, dapagliflozin plus the dipeptidyl peptidase-4 inhibitor saxagliptin, or placebo. Both dapagliflozin alone and the combination therapy reduced albuminuria (primary endpoint) compared with placebo. While the combination therapy achieved a numerically greater decrease, the study was not powered to determine an additive effect. Only combination therapy reduced HbA_{1c} levels, probably because of the limited glycaemic efficacy of SGLT-2 inhibitors at lower estimated GFR. Adverse events were favourable, suggesting that this combination could be used safely in diabetic patients with CKD. Of note, an increased risk of fractures previously associated with dapagliflozin was not confirmed. Unfortunately, whether albuminuric and glycaemic responsiveness of patients with more severe CKD (estimated GFR <45 mL/min) differs from those >45 mL/min was not reported. Moreover, the study was not designed to evaluate definitive clinical outcomes. Overall, this study adds to the growing body of evidence suggesting renal (and CV) benefits with newer agents, such as SGLT-2 inhibitors and GLP-1 receptor agonists, in patients with T2DM.

Reference: Lancet Diabetes Endocrinol 2019;7:429–41
Abstract

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References: 1. Edridge CL *et al. PLoS ONE* 2015;10(6):e0126427. **2.** Shafiee G *et al. Journal of Diabetes & Metabolic Disorders* 2012;11:17. **3.** Lingvay I. *US Endocrinology* 2011;7(2):95-102. **4.** Ritzel R *et al. Diabetes Obes Metab* 2018; 20(3):541–8.

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SANOFI

Disease progression and treatment response in data-driven subgroups of type 2 diabetes compared with models based on simple clinical features

Authors: Dennis JM et al.

Summary: The clinical utility of a subgroup-based approach for predicting diabetes progression and risk of complications was compared with an alternative strategy of developing models for each outcome using simple patient characteristics. Five clusters were identified among 4351 ADOPT trial participants using a previously reported data-driven cluster analysis by Ahlqvist and colleagues, and differences between clusters regarding glycaemic and renal progression were compared with stratification using age at diagnosis for glycaemic progression and baseline renal function for renal progression. The effectiveness of a strategy of selecting glucose-lowering therapy using clusters was compared with one that combined simple clinical features (sex, BMI, age at diagnosis, baseline HbA_{1c} level) in an independent cohort of 4447 patients. The clusters identified in the trial data were similar to those previously reported. Although clusters showed differences in glycaemic progression, a model that used only age at diagnosis was able to explain similar variability for progression. There were differences in CKD incidences among clusters, but estimated GFR at baseline was a better predictor of time to CKD. The clusters also differed with respect to glycaemic response; thiazolidinediones were particularly beneficial in patients from the severe insulin-resistant diabetes cluster, whereas sulfonylureas were better for those in the mild age-related diabetes cluster. However, simple clinical features were found to be better than clusters for selecting individual patients' therapies.

Comment: Successful implementation of personalised or precision medicine requires the identification of characteristics that robustly predict risk of disease progression (for example development of diabetic complications) and response to treatment among individual patients. A previous study identified five distinct diabetic clusters with different underlying disease mechanisms and complication risks, but did not address whether cluster stratification predicted response to therapy. In this secondary analysis of patients enrolled in two large RCTs (ADOPT and RECORD), the authors found similar clusters as in the original Swedish cohort. However, the clusters did not outperform routine clinically available parameters (such as baseline age, sex, BMI, HbA_{1c} level and estimated GFR) in the prediction of disease progression, nor did they help to personalise therapy. Thus, using prediction models incorporating continuous measures of simple clinical characteristics appears to have better clinical utility than models based on defined subgroups, which assume that individuals are homogenous with each subgroup. However, the overall variation explained by available clinical features was relatively low. Further studies should incorporate additional baseline variables (such as lifestyle factors, concomitant medications, biomarkers) into prediction models, and prospectively monitor whether early changes in these variables in response to initial therapy predict long-term outcomes. While precision medicine in T2DM is not ready for primetime, clinicians can be reassured that routine clinical parameters remain useful in guiding treatment of patients with T2DM.

Reference: Lancet Diabetes Endocrinol 2019;7:442–51
Abstract

Efficacy and safety of suspend-before-low insulin pump technology in hypoglycaemia-prone adults with type 1 diabetes (SMILE)

Authors: Bosi E et al., for the SMILE Study Group

Summary: Patients aged 24–75 years with T1DM for ≥10 years at high risk of hypoglycaemia were randomised to receive open-label CSII with the MiniMed 640G pump with either the suspend-before-low feature enabled (n=76) or SMBG (n=77) for 6 months. Compared with the SMBG group, participants with the suspend-before-low feature enabled had experienced a significantly lower mean number of hypoglycaemic events each week by month 6 (1.1 vs. 4.1 [p<0.0001]) with a significantly lower number of severe events overall (3 vs. 18 [p=0.0036]). The respective overall hypoglycaemia rates in the suspend-before-low feature-enabled and SMBG groups were 5% and 13%, and the hyperglycaemia rate was 9% in both groups. There were no serious adverse device effects or DKA episodes recorded.

Comment: In this open-label 6-month RCT in 153 adults (mean age 48 years) with T1DM and high risk of hypoglycaemia treated with CSII, those assigned to a pump with CGM and a suspend-before-low feature had a 3% absolute reduction in hypoglycaemic events (≤3.1 mmol/L) and fewer severe hypoglycaemic events (3 vs. 18) per week, compared with controls assigned to a pump without CGM. Glycaemic control between groups at study end did not differ (HbA_{1c} level −0.16% in the intervention group vs. −0.25 in controls). SMILE is the fourth study reporting that CGM reduces hypoglycaemia compared with SMBG in hypoglycaemia-prone people with T1DM, without compromising glycaemic control. Effects were consistent among trials irrespective of insulin delivery methods (pump versus multiple daily injections) or CGM-based technologies, or patient age. These studies, while showing clinical benefit, have been conducted in selected populations, under RCT conditions, and are relatively short term. Long-term effects in 'real-world' settings require further validation. Moreover, whether structured self-management education programmes can augment these CGM benefits, and elucidation of underlying mechanisms deserves further study. Such evidence could further reduce hypoglycaemia, which despite mitigation with CGM-based technology, remains an important barrier to achieving optimal glycaemic control in patients with T1DM.

Reference: Lancet Diabetes Endocrinol 2019;7:462–72
Abstract

Durability of a primary care-led weight-management intervention for remission of type 2 diabetes

Authors: Lean MEJ et al.

Summary: Two-year results were reported for the open-label, cluster-randomised DiRECT trial, which assessed the durability of a primary care-led weight management intervention for remission of T2DM. Patients aged 20–65 years with T2DM and BMI 27–45 kg/m^2 (n=149) were randomised to an intervention group or guideline-based best-practice care (controls). The intervention consisted of withdrawal of antidiabetic and antihypertensive medications, total diet replacement (825–853 kcal/day for 12–20 weeks), stepped food reintroduction (2–8 weeks) and structured support for weight loss maintenance. Compared with controls, greater proportions of intervention participants had achieved weight loss of ≥15kg (11% vs. 2%; adjusted odds ratio 7.49 [95% CI 2.05–27.32]) and diabetes remission (36% vs. 3%; 25.82 [8.25–80.84]) at 24 months. A *post hoc* analysis revealed that among participants who maintained ≥10kg weight loss, the remission rate was 64%.

Comment: This open-label RCT of 298 adults (mean age 55 years, BMI 34 kg/m^2) with T2DM of <6 years duration showed that of those randomised to a primary care-based structured weight loss programme, 46% were in remission at 1 year, and 36% at 2 years, compared with 4% and 3% of controls receiving best-practice care. Sixty-four percent of participants who maintained a weight loss of >10kg maintained remission, irrespective of group assignment. While there is no universally agreed definition of diabetes remission, the study confirms that weight loss is key to achieving this outcome, and that sustained weight loss with lifestyle leading to diabetes remission is possible, at least in selected patients with short-to-moderate diabetes duration. The study used a fairly resource-intensive approach, including ongoing 30-minute monthly appointments with a nurse or dietician during the second year of the study. While the benefits of weight loss are intuitive, the challenge remains to identify (cost-)effective nonsurgical strategies that work and are feasible for people with diabetes, especially in the prevention of weight regain. This is likely to require a multifaceted approach, including diet, behavioural coaching and pharmacotherapy, adapted to individual needs.

Reference: Lancet Diabetes Endocrinol 2019;7:344–55
Abstract

Semaglutide once weekly as add-on to SGLT-2 inhibitor therapy in type 2 diabetes (SUSTAIN 9)

Authors: Zinman B et al.

Summary: Adults with T2DM with an HbA_{1c} level 53–86 mmol/mol (7.0–10.0%) despite ≥90 days of SGLT-2 inhibitor treatment (n=302) were randomised 1:1 to receive subcutaneous semaglutide 1mg or placebo once weekly for 30 weeks, after a dose-escalation schedule of 4 weeks of semaglutide 0.25mg or placebo and 4 weeks of semaglutide 0.5mg or placebo; 294 participants completed the trial, 267 completed treatment, 216 were receiving metformin and 39 were receiving a sulfonylurea. Compared with placebo, semaglutide recipients had greater reductions in HbA_{1c} level and bodyweight (respective estimated differences, –15.55 mmol/mol and –3.81kg [p<0.0001 for both]). The respective proportions of participants from the semaglutide and placebo groups who experienced adverse events were 69.3% and 60.3%, with respective gastrointestinal event rates of 37.3% and 13.2% and serious adverse event rates of 4.7% and 4.0%. The severe or blood glucose-confirmed hypoglycaemic event rate among semaglutide recipients was 2.7%. Thirteen of the 16 participants who stopped treatment early due to an adverse event were from the semaglutide group. No deaths were recorded.

Comment: This 30-week RCT of 302 patients with non-insulin requiring T2DM (mean age 57 years, BMI 32 kg/m^2, HbA_{1c} level 8.0%) treated with an SGLT-2 inhibitor for ≥90 days (>70% were also on metformin) showed that addition of the GLP-1 receptor agonist to existing SGLT-2 inhibitor therapy reduced HbA_{1c} level by 1.42% and bodyweight by 3.8kg compared with placebo. The findings confirm those of earlier trials combining these two agents, which are not surprising given their complementary mechanisms of action. SGLT-2 inhibitors act on renal glucose excretion by mechanisms independent of insulin secretion and action, while GLP-1 receptor agonists augment glucose-dependent insulin secretion and inhibit glucagon release. One interesting hypothesis, not addressed in this study, is whether the glucagon-suppressing action of GLP-1 receptor agonists could mitigate the SGLT-2 inhibitor-associated increases in hepatic ketone production. If increased ketogenesis providing energy for the failing heart is important for improved CV outcomes with SGLT-2 inhibitors, combination therapy might have negative CV consequences. However, added benefits on bodyweight, BP and lipid profile suggest possible additive CV benefits. Future trials will be required to determine whether the combination of GLP-1 receptor agonists and SGLT-2 inhibitors, the two classes that have individually shown CV benefit in large outcomes trials, can increase this benefit over and above the effects of individual drugs alone.

Reference: Lancet Diabetes Endocrinol 2019;7:356–67
Abstract

Effect of structured self-monitoring of blood glucose, with and without additional TeleCare support, on overall glycaemic control in non-insulin treated type 2 diabetes

Authors: Parsons SN et al.

Summary: Patients with T2DM for >1 year not receiving insulin therapy, with suboptimal glycaemic control, were randomised to a group using structured SMBG alone with (n=148) or without (n=147) additional monthly 'TeleCare' support or usual care (control group; n=151) in the 12-month SMBG trial; the trial completion rate was 72%. Compared with the control group, the SMBG alone and SMBG with TeleCare groups both experienced significantly greater decreases from baseline in mean HbA_{1c} level at 12 months (11.4 and 12.8, respectively, vs. 3.3 mmol/mol, or 1.1% and 1.2% vs. 0.3% [p≤0.0001]). Predictors of achieving an HbA_{1c} level of ≤53 mmol/mol (≤7.0%) were lower baseline HbA_{1c} level, shorter diabetes duration and higher educational achievement.

Comment: Despite many studies, the question as to whether SMBG provides benefits in patients with T2DM not on insulin therapy remains debated. Recent recommendations relegate SMBG to a safety role rather than an essential part of management. In this 12-month open RCT, 446 patients with non-insulin treated T2DM (mean age 62 years, HbA_{1c} level 8.6%) were randomised to 'usual care', structured SMBG or structured SMBG with additional monthly telehealth support. Dropout was relatively high, almost 30%, and the proportion in 'usual care' using SMBG is not reported. Nevertheless, as expected, if presumably motivated patients (by virtue of agreeing to participate in the trial and remaining in it) are recruited, HbA_{1c} level decreased in all groups, albeit more so in the SMBG and SMBG telehealth groups compared with usual care. Telehealth coaching provided no added benefit. This study confirms clinical experience that if motivated patients with suboptimally controlled T2DM use SMBG to identify glycaemic patterns and take appropriate action when needed, glycaemic control can improve. However, clearly in other patients, SMBG is not a useful exercise, and can negatively affect overall quality of life. Use (or not) of SMBG is best individualised.

Reference: Diabet Med 2019;36:578–90
Abstract

Impact of physical exercise on sensor performance of the FreeStyle Libre intermittently viewed continuous glucose monitoring system in people with type 1 diabetes

Authors: Moser O et al.

Summary: Ten patients with T1DM completed 55-minute cycle ergometer exercise sessions over 5 consecutive days while receiving either their usual or a 75% basal insulin dose, switching to their alternative basal insulin dose for a second exercise period after a 4-week washout period in this randomised crossover trial; the researchers obtained 845 glucose level values during exercise for evaluation of intermittently viewed CGM sensor performance. The median absolute relative difference between reference values and those obtained by the sensor across the glycaemic range overall was 22%, with values of 36.3%, 22.8% and 15.4% during hypoglycaemia, euglycaemia and hyperglycaemia, respectively. Worse sensor performance was seen with usual basal insulin doses than with the reduced basal insulin doses during exercise (median absolute relative difference, 23.7% vs. 20.5% [p<0.001]).

Comment: Intermittently viewed CGM sensors are increasingly used by people with diabetes. These sensors measure interstitial glucose levels with reasonable accuracy, with median absolute relative differences around 10% from reference blood glucose levels under standard conditions. Exercise provides important health benefits, but can increase the risk of glycaemic instability, in particular hypoglycaemia in people with diabetes, and the performance of intermittently viewed CGM sensors is not well described during exercise. In this small crossover study, moderately intensive exercise was associated with diminished accuracy relative to baseline sedentary state. At resting conditions, the median absolute relative difference was 13.7% and this increased to 22% during exercise and was especially marked during hypoglycaemia (36%). Intermittently viewed CGM values tended to overestimate blood glucose levels based on reference values, which were drawn from the earlobes during exercise, which is a limitation of the study. It is possible that exercise-induced changes in subcutaneous blood flow and larger glucose excursions during exercise may have contributed to these findings. Definitive studies assessing intermittently viewed CGM sensor performance under different conditions are needed, but clearly, finger-prick glucose confirmation of intermittently viewed CGM readings are important, and may need to be performed more frequently during exercise.

Reference: Diabet Med 2019;36:606–11
Abstract

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