Meeting report: EASD Annual Meeting 2020

Stay abreast of the latest news that could impact diabetes nursing. In this issue, we summarise the key presentations from the Annual Meeting of the European Association for the Study of Diabetes.

The European Association for the Study of Diabetes Annual Meeting was held virtually on 21–25 September 2020. Here we summarise the key presentations and publications.

Dapagliflozin improves renal outcomes in people with CKD, irrespective of diabetes status

Results of the DAPA-CKD study of dapagliflozin for the treatment of chronic kidney disease (CKD) were presented at the meeting and simultaneously published in the *New England Journal of Medicine*. The sodium–glucose cotransporter 2 (SGLT2) inhibitor was found to significantly reduce CKD progression and mortality, irrespective of whether participants had type 2 diabetes or not.

A total of 4094 people with CKD (estimated glomerular filtration rate [eGFR] 25–75 mL/min/1.73 m^2 and urinary albumin-to-creatinine ratio 23–565 mg/mmol) were randomised 1:1 to once-daily dapagliflozin 10 mg or placebo, in conjunction with standard care including a renin–angiotensin system blocker. The trial was ended early, after a median follow-up of 2.4 years, owing to clear evidence of efficacy.

The primary outcome (a composite of ≥50% eGFR decline, end-stage renal disease [ESRD] or death from cardiovascular or renal causes) occurred in 9.2% versus 14.5% of the dapagliflozin and placebo groups, respectively (hazard ratio [HR], 0.61; 95% confidence interval [CI], 0.51–0.72). Each component of the primary outcome was significantly reduced in the dapagliflozin group. The benefits were consistent in both people with type 2 diabetes and those without.

All prespecifed secondary outcomes were significantly improved in the dapagliflozin group. Death from any cause occurred in 4.7% versus 6.8% in the two groups (HR, 0.69; 95% CI, 0.53–0.88). The number needed to treat to avoid one primary endpoint was 19.

Adverse and serious adverse event rates were similar in the two groups. Diabetic ketoacidosis (DKA) was not observed in any participant in the dapagliflozin group, and neither DKA nor severe hypoglycaemia was observed in any participants without type 2 diabetes.

Renoprotective effects for an SGLT2 inhibitor were previously shown in the CREDENCE study of canagliflozin. The present findings extend these benefits to people without type 2 diabetes. They also demonstrate that dapagliflozin is both safe and effective when initiated in people with an eGFR as low as 25 mL/min/1.75 m^2.

The full study results are available here.

VERTIS CV: Ertugliflozin renal data published

Cardiovascular outcome results from the VERTIS CV trial of ertugliflozin were published at the ADA conference earlier this year, demonstrating safety but, unlike with other SGLT2 inhibitors, not superiority over placebo. Further renal outcomes were presented at the EASD meeting.

The composite outcome of renal death, ESRD (dialysis or transplant) or doubling of serum creatinine was less frequent in people treated with ertugliflozin 5 mg or 15 mg compared with placebo (HR, 0.81; 95% CI, 0.63–1.04), but the reduction was non-significant both for the composite and for its individual components.

These and the cardiovascular outcomes have raised questions about whether the benefits of SGLT2 inhibitors can truly be seen as class effects. A meta-analysis conducted by the investigators and using a revised renal endpoint (incorporating a ≥40% reduction in eGFR into the composite), in order to compare data across the SGLT2 cardiovascular outcome trials, suggested that the renal benefits were consistent across the class. Similarly, reductions in hospitalisation for heart failure seem to be a class-wide benefit.

The full study results are available here.

Once-weekly insulin icodec: Phase 2 clinical trial

Insulin icodec is a once-weekly basal insulin currently in development by Novo Nordisk. This 26-week, double-blind, phase 2 trial compared the efficacy and safety of weekly icodec versus once-daily insulin glargine U100 in people with type 2 diabetes.

A total of 247 insulin-naïve people with type 2 diabetes were randomised to once-weekly icodec plus once-daily placebo, or to once-daily glargine plus once-weekly placebo. Insulin was started at a dose of 70 units per week (or 10 units per day) and was then adjusted to target glycaemia levels on a weekly basis (which the authors acknowledge may have benefited outcomes in the icodec group).

At 26 weeks' follow-up, mean HbA_{1c} fell from a baseline of around 64 mmol/mol (8.0%) by an estimated 14.5 mmol/mol (1.33%) in the icodec group, versus 12.6 mmol/mol (1.15%) in the glargine

group. The difference narrowly fell short of statistical significance.

The authors conclude that the two agents had a similar glucose-lowering efficacy. Icodec and glargine recipients required a mean daily (or equivalent) insulin dose of 33 and 41 units, respectively; however, the difference in dose did not translate to a difference in weight gain.

Mild hypoglycaemia was significantly more common with icodec (5.09 vs 2.11 events per person-year of exposure; rate ratio, 2.42); however, the incidence of moderate-to-severe hypoglycaemia (blood glucose <3.0 mmol/L or requiring third-party assistance) was similar in the two groups. Adverse events were mostly mild, and none of the serious adverse events were adjudicated to be due to the study drugs.

The full study results are available here.

Increased risk of vascular dementia with type 2 diabetes

In this analysis of the Swedish National Diabetes Register, the incidence of dementia, particularly vascular dementia, was associated with type 2 diabetes, with high HbA_{1c} increasing the risk further.

The authors compared 378 299 people with type 2 diabetes and 1 886 022 matched controls for a median of 6.8 years. Over this time frame, 5.7% of the diabetes cohort versus 5.2% of the controls developed dementia.

Vascular dementia had the strongest association with type 2 diabetes (adjusted HR, 1.36; 95% CI, 1.03–1.49). In particular, those with HbA_{1c} >87 mmol/mol (10.1%) had an almost doubled risk compared with an HbA_{1c} of <52 mmol/mol (6.9%).

The association of type 2 diabetes with non-vascular dementia was more modest but still significant, and people with diabetes in fact had a lower risk of Alzheimer's disease overall; however, the risk of both conditions increased with worsening glycaemic control.

While most of the variance was explained by age, modifiable risk factors related to cardiovascular disease, including HbA_{1c}, blood pressure and BMI, accounted for 40% of the risk for vascular dementia, versus only 20% for non-vascular dementia and 10% for Alzheimer's disease. Thus, addressing these risk factors could go a long way towards reducing the risk of this greatly feared disease.

Intermittent very-low-energy diets: A more achievable option?

The DiRECT study has shown it is possible to place type 2 diabetes into remission using an intensive very-low-calorie diet (VLCD) with meal replacement followed by healthcare professional-supported food reintroduction. However, many found it difficult to forego real food and eating opportunities for 8–20 weeks. The MIDDAS study sought to evaluate whether an intermittent VLCD could be a more achievable option.

In the study, 79 people with type 2 diabetes were randomised to an intermittent or a continuous VLCD regimen. The intermittent regimen comprised a 28-week weight-loss phase, in which participants ate an 800 kcal liquid diet on 2 days per week, with normal eating (portion-controlled Mediterranean diet) on the other 5 days. This was followed by a 24-week maintenance phase (food-based 800 kcal diet on 2 days; normal eating on the other 5 days). Hypoglycaemic medications were stopped on the VLCD days.

Compared with the more intensive continuous VLCD regimen (8 weeks of 7-day liquid diets, followed by 4 weeks of structured food reintroduction and 40 weeks of a portion-controlled Mediterranean diet), retention rates were similar in the two groups (69% vs 75% in the intermittent and continuous groups, respectively). At 12 months, mean weight loss was similar in the two groups (5.4% vs 6.0%), and around 20% of both groups achieved ≥10% weight loss and around 5% achieved ≥15% weight loss. Although just over 40% of participants achieved an HbA_{1c} <48 mmol/mol (6.5%), more medication was required to achieve this with the intermittent VLCD.

This was only a pilot study but it suggests a feasible, if slightly less effective, alternative method to achieve significant weight loss. The intervention also involved high-frequency, multidisciplinary support, and this was delivered using the Oviva app and/or by telephone. The ability to support such an intervention remotely has particular relevance considering the COVID-19 pandemic.

Early-onset type 2 diabetes twice as common in South Asian and African–Caribbean populations

This cross-sectional study of nearly 1.5 million GP records across Northwest London analysed the prevalence of early-onset adult type 2 diabetes (defined as age 18–44 years at onset) in different ethnic groups.

Type 2 diabetes in general was significantly more common in South Asian and African–Caribbean people compared with the white population (rates of 10.1%, 8.3% and 3.4%, respectively). With regard to early-onset diabetes, 30.7%, 25.9% and 15.7% of cases were in South Asian, African–Caribbean and white people, respectively.

The most common age at diagnosis was 55–64 years in white people but only 45–54 years in South Asian and African–Caribbean people.

People with early-onset type 2 diabetes have a greater risk of earlier and more severe diabetes complications and early mortality. The doubled prevalence in non-white ethnicities observed here suggests a need for targeted screening at younger ages and early intensive treatment to improve diabetes control in order to avoid these complications. ■

Acknowledgement: Thanks to Pam Brown, Editor-in-Chief of *Diabetes & Primary Care*, for her collaboration in the writing of these summaries.

Citation: Meeting report: EASD Annual Meeting 2020. *Journal of Diabetes Nursing* **24**: JDN153