

Diabetes journals



Hypoglycaemia, CVD risk and mortality: A reminder of some Latin, ethical principles and patient safety

Vinod Patel

Principal Teaching Fellow, Warwick Medical School, University of Warwick and Honorary Consultant in Diabetes and Endocrinology, George Eliot Hospital NHS Trust, Nuneaton

Whenever we think about the complications of diabetes, we focus on the direct effect of diabetes and its various pathophysiological processes resulting in cardiovascular disease (CVD), diabetic retinopathy, diabetic nephropathy and neuropathy. However, it is hypoglycaemia, which is a side effect of the actual treatment of diabetes, that people with the condition absolutely hate and will avoid, even at the expense of developing complications.

In the paper by Khunti et al, summarised alongside, there is very clear evidence showing that hypoglycaemia is not only an inconvenience but is significantly associated with an increased risk of CVD events in people with type 2 diabetes. The authors also reported an increased risk of CVD events in people with type 1 diabetes, but this did not reach significance. However, significant increases in mortality in people with type 1 and type 2 diabetes were observed (hazard ratios, 2.47 and 2.48 respectively). This was among people without pre-existing CVD; for people with pre-existing CVD, there was also an increase in mortality risk (hazard ratio for people with type 1 diabetes and type 2 diabetes were 1.98 and 1.74 respectively).

In the diabetes world, we have been excited by drugs that have the potential to improve glycaemic control and cause less hypoglycaemia than sulphonylureas or insulins. These treatments act via the glucagon-like peptide-1/insulin axis and target beta-cells, which trigger increased insulin output, reduced glucagon synthesis, reduced hepatic gluconeogenesis, increased satiety and reduced stomach emptying, and, most important of all to patients, less hypoglycaemia and increased weight loss (when the injectable incretins are used).

To inform our own practice and to teach our students, we use the very elegant summaries of biomedical ethical practice by Beauchamp and Childress (2001). The foundation of this is

“to abstain from doing harm” (first do no harm – *primum non nocere*). All four *prima facie* ethical and moral principles are shown below. They must all be considered when making clinical decisions. They are all relevant in all cases where we decide which treatments to use for our patients to improve glycaemia control.

- Autonomy: the patient has the right to refuse or choose their treatment. (*Voluntas aegroti suprema lex.*)
- Beneficence: a practitioner should act in the best interest of the patient. (*Salus aegroti suprema lex.*)
- Non-maleficence: first, do no harm. (*Primum non nocere.*)
- Justice: distribution of scarce health resources, and the decision of who gets what treatment (fairness and equality). (*Iustitia.*)

With the justified focus on patient safety post-“the Berwick report” (2013), we have to remember that hypoglycaemia has been reported to increase mortality (McCoy et al, 2012) and CVD events (Desouza et al, 2010). Luckily for us, research from a similar cohort as in the Khunti et al paper strongly suggests that tight glycaemic control targets are not needed. The optimal outcomes in terms of mortality, were seen in participants with HbA_{1c} 7.25–7.75% (56–61 mmol/mol), total cholesterol 3.5–4.5 mmol/L, systolic blood pressure 135–145 mmHg and diastolic blood pressure 82.5–87.5 mmHg (Kontopantelis et al, 2015 [summarised on page 75]). A strong case was made for treating to target ranges for these risk factors, rather than target levels.

Treatments based on avoiding hypoglycaemia will be expensive. However, careful individualised care, taking into account all the biomedical ethics principles, should result in clinical benefits that are important for both patients and the local health economy, which has to optimise cost-efficiencies. ■

Diabetes Care

Link between hypoglycaemia, CV events and all-cause mortality

Readability ////
 Applicability to practice ////
 WOW! Factor ////

1 The authors sought to determine the link between hypoglycaemia, the risk of cardiovascular (CV) events and all-cause mortality in a nationally representative UK cohort using data from the Clinical Practice Research Datalink database. Those selected for the cohort were all insulin-treated people with diabetes aged ≥30 years. There were 3260 people with T1D and 10 422 people with T2D.

2 The data reported all hypoglycaemic events; episodes reported in general practice and severe episodes that required hospital admission.

3 Among people with T1D who experienced hypoglycaemia, there was a significant increase in CV events if there had been no prior incidence of CV disease (CVD; hazard ratio, 1.61 [95% confidence interval, 1.17–2.22]). This increase in risk was not observed for those who had a history of CVD.

4 In people with T2D, CV risk was significantly increased regardless of whether there was prior history of CVD.

5 In addition, there was a statistically significant increase in all-cause mortality associated with hypoglycaemia among people with T1D and T2D with or without prior history of CVD.

6 Therefore, the authors conclude that there should be an effort to lower the risk of hypoglycaemia, especially for those that have experienced a CV event in the past.

Khunti K, Davies M, Majeed A et al (2015) Hypoglycaemia and risk of cardiovascular disease and all-cause mortality in insulin-treated people with type 1 and type 2 diabetes: a cohort study. *Diabetes Care* 38: 316–22

References on next page

Diabet Med

Gender differences in T1D and T2D: Risk factors and complications

Readability ✓✓✓
 Applicability to practice ✓✓✓
 WOW! Factor ✓✓✓

1 The aim of the study was to examine gender differences between diabetes risk factors and the prevalence of diabetes complications among people with T1D and T2D.

2 The study cohort comprised 15 351 people from Ayrshire and Arran, Scotland, and records were from general practices were analysed.

3 Among people with T1D, men had significantly lower BMI, total cholesterol, HDL-cholesterol and HbA_{1c} than women. They also had higher blood pressure and non-fasting triglyceride levels, and had a higher prevalence of neuropathy than their female counterparts.

4 Among people with T2D, men again had a significantly lower BMI, total cholesterol and HDL-cholesterol, but they had higher non-fasting triglyceride levels compared to women. Men also had a higher prevalence of ischaemic heart disease, stroke and peripheral vascular disease. Women tended to be older, heavier and had a higher prevalence of hypertension.

5 Treatment-wise, more people with T2D were on lipid-lowering medication than people with T1D.

6 This study gives insight into the differences in complication development and metabolic variables between the genders. There are few gender differences in the management of T1D and T2D, and the findings of this study suggest the differences are in aetiopathophysiology, which does not suggest there is a need to change clinical practice.

Collier A, Ghosh S, Hair M, Waugh N (2015) Gender differences and patterns of cardiovascular risk factors in type 1 and type 2 diabetes: a population-based analysis from a Scottish region. *Diabet Med* **32**: 42–6

Diabet Med

Lipid-lowering medication in primary care

Readability ✓✓✓✓
 Applicability to practice ✓✓✓✓
 WOW! Factor ✓✓✓✓

1 The aim of this study was to investigate the variation in lipid-lowering medication prescription to people with screen-detected T2D, and any associations with practice or participant characteristics and risk of cardiovascular disease (CVD) events and all-cause mortality.

2 An observational cohort analysis was carried out using data from 1533 people aged 40–69 years from the ADDITION-Denmark study.

3 In total, 174 general practices were cluster randomised to receive routine diabetes care or intensive multifactorial target-drive diabetes management.

4 Over a follow-up period of 9431 person-years, there were 118 CVD events, and there was huge variation in the proportion of people receiving lipid-lowering medication between practices (0–100%).

5 The quartile of general practices that was the lowest for prescribing lipid-lowering medications had a significantly higher risk of CVD compared to the highest quartile for prescribing (adjusted odds ratio, 3.4; 95% confidence interval, 1.6–7.3). Similar trends were found for all-cause mortality.

6 More frequent prescription of lipid-lowering treatment appears to be associated with a lower incidence of CVD and all-cause mortality, which highlights the benefits of intensive treatment on people with screen-detected T2D.

Simmons RK, Carlsen AH, Griffin SJ et al (2014) Variation in prescribing of lipid-lowering medication in primary care is associated with incidence of cardiovascular disease and all-cause mortality in people with screen-detected diabetes: findings from the ADDITION-Denmark trial. *Diabet Med* **31**: 1577–85

Diabetologia

Ethnicity, T2D and CVD risk: Pakistani ethnicity at high risk

Readability ✓✓✓✓
 Applicability to practice ✓✓✓✓
 WOW! Factor ✓✓✓✓

1 Data from Scottish Care Information-Diabetes were linked to national morbidity and mortality records for dates between 2005 and 2011 to determine a potential association between cardiovascular disease (CVD) incidence and ethnicity among people with diagnosed T2D.

2 Of 156 991 people with T2D who had coded ethnicity (White: 114 461; Multiple Ethnic: 2554; Indian: 797; other Asian: 319; Pakistani: 2250; Chinese: 387; African-Caribbean: 301), 77.4% had no CVD at baseline. The participants were followed for a mean time of 4.8±2.3 years for the development of fatal and non-fatal CVD.

3 During the follow-up period, 16 265 people developed CVD.

4 The age- and sex-adjusted hazard ratios (HRs) for CVD were 1.31 (95% confidence interval [CI], 1.17–1.47) in Pakistanis ($P<0.001$) and 0.66 (95% CI, 0.47–0.92) in Chinese ($P=0.014$) compared with whites.

5 After adjustment for an area measure of deprivation and other baseline characteristics, the HRs were still statistically significantly different for Pakistani and Chinese people compared to whites.

6 Therefore, in this cohort, of CVD risk, those of Pakistani ethnicity were at increased risk and Chinese people were at decreased risk compared to whites.

7 The authors were unsure of the reasons for these observations but suggest that Pakistani ethnicity is an independent risk factor for CVD among people with T2D.

Maiik MO, Govan L, Petrie JR et al (2015) Ethnicity and risk of cardiovascular disease (CVD): 4.8 year follow-up of patients with type 2 diabetes living in Scotland. *Diabetologia* **58**: 716–25

“More frequent prescription of lipid-lowering treatment appears to be associated with a lower incidence of cardiovascular disease and all-cause mortality.”

References from commentary
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 Berwick D (2013) *A promise to learn – a commitment to act: improving the safety of patients in England*. Department of Health, London
 Desouza CV, Bolli GB, Fonseca V (2010) Hypoglycemia, diabetes, and cardiovascular events. *Diabetes Care* **33**: 1389–94
 Kontopantelis E, Springate D, Reeves D et al (2015) Glucose, blood pressure and cholesterol levels and their relationships to clinical outcomes in type 2 diabetes: a retrospective cohort study. *Diabetologia* **58**: 505–18
 McCoy RG, Van Houten HK, Ziegenfuss JY et al (2012) Increased mortality of patients with diabetes reporting severe hypoglycemia. *Diabetes Care* **35**: 1897–901