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Hypoglycaemia in the over 75s: Understanding the predisposing factors in type 2 diabetes (T2DM)

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ABSTRACT

Introduction: Hypoglycaemia has been recognised as a problem in the treatment for type 2 diabetes. Here we describe how levels of HbA1C and treatment with a sulphonylurea or insulin relate to risk of significant hypoglycaemia.

Methods: Incident hypoglycaemia as recorded for the previous 10 years was determined from the GP records for patients with T2DM aged 75 years or more.

Results: The anonymised GP records of 5974 T2DM patients (2934 men and 3040 women) aged 75 years or more were analysed.

Mean age of the men was 81.0 (95% confidence interval (CI) 80.9–81.2) years and of the women was 82.2 (95% CI 82.0–82.4) years.

Hypoglycaemic events of significance were recorded in 4.9% of men and 5.1% of women.

The prevalence of hypoglycaemia was higher in those with a higher concurrent HbA1C. HbA1C for those people with a recorded significant hypoglycaemic attack(s) was 57.9 (95% CI 56.4–59.4) mmol/mol compared to those with no history of hypoglycaemic episodes at 51.6 (95% CI 51.3–52.0) mmol/mol ($p < 0.002$).

Even for those on sulphonylurea and/or insulin treatment, hypoglycaemia prevalence increased with HbA1C: for patients with an HbA1C of <48 mmol/mol, age and gender adjusted hypoglycaemia prevalence was 11.1%, for HbA1C of 48–57 mmol/mol, prevalence 9.9%, for HbA1C 58–67 mmol/mol prevalence, 13.2% and for HbA1C 68 mmol/mol or more, prevalence of hypoglycaemia was 16.1%.

Abbreviations: GP, general practitioner; EMIS, Egton Medical Information Systems; BMI, body mass index; HbA_{1c}, glycated haemoglobin; eGFR, estimated glomerular filtration rate; DM, diabetes mellitus; IHD, ischaemic heart disease; (TIA), transient ischaemic attack; (DPP-4) inhibitor, dipeptidyl peptidase-4 inhibitor; SGL-2 inhibitor, sodium-glucose co-transporter 2 (SGLT2) inihibitor.

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There was a slight fall in HbA1C by age (normalised β −0.069, $p < 0.001$) and no difference by level of social disadvantage.
Treatment with a sulphonylurea or insulin very significantly increased the likelihood of a hypoglycaemic episode: odds ratio (OR) 8.94 (95% CI 6.45–12.42), $p < 0.001$, independent of age, BMI, Townsend index and gender.
Conclusion: Prevalence of hypoglycaemia was greater in those individuals with higher HbA1C and in those on sulphonylurea/insulin treatment.
Our findings suggest that it is variance in blood glucose rather than overall lower blood glucose levels that predisposes older people to hypoglycaemia.

1. Introduction

The importance of achieving optimal glycaemic control to reduce the incidence of diabetes complications is indisputable, but many barriers impede the attainment of this. Among these is hypoglycaemia, which has been recognised as a problem in treatment modalities for type 2 diabetes [1] as in type 1 diabetes [2]. The burden of covert hypoglycaemia associated with type 2 diabetes is likely underestimated, particularly in patients treated with sulphonylureas and with insulin [1].

The initial response to a decline in blood glucose is suppression of endogenous insulin secretion followed by release of counterregulatory hormones, of which glucagon and adrenaline (epinephrine) are the most potent. When blood glucose falls in a non-diabetes adult, the secretion of counterregulatory hormones and the onset of cognitive, physiological, and symptomatic changes occur at reproducible blood glucose thresholds [3,4] within a defined hierarchy [5]. This is not necessarily the case in people with type 2 diabetes [1].

Symptoms of hypoglycaemia occur at arterialised blood glucose concentrations around 2.8–3.2 mmol/l (50–58 mg/dl), hypoglycaemic symptoms are idiosyncratic and age specific [6]. However with increasing age, the symptoms of hypoglycaemia may become less intense [7,8] and the symptom profile is modified [9–11]. Cognitive decline has been associated with incident hypoglycaemia [12].

In older people hypoglycaemia can result in injury, hospitalisation and in some cases has life threatening consequences [13]. Some previous studies have indicated that a lower HbA1C predisposes to hypoglycaemia [13,14]. For example a low HbA1C in patients treated intensively to target with sulphonylureas was associated with increased mortality in the ACCORD study [15]. However the relation is complex and includes treatment modality [16].

In this paper we report the results of a primary care based study utilizing the health care records of patients with type 2 diabetes in Cheshire, UK aged 75 years or more. We describe how levels of HbA1C and treatment with a sulphonylurea or insulin relate to risk of significant hypoglycemia as recorded in the GP record.

2. Patients and methods

All patients were attending GP practices in Central and Eastern Cheshire, UK. Data search was performed with the assistance of EMIS®, the provider of the majority of GP operating systems in this area. All patients included in the initial search were on the GP practice diabetes registers. Permission was sought through the local information governance and ethics committees.

Data was drawn on 25 May, 2016 and includes all patients aged 75 or over on that day attending GP practices which contribute to our pseudonymised database (total population 428,000 people).

The only patients not included were those from 2 practices not using EMIS and one practice for which data sharing permission was not given. All three were relatively small practices (total list size <15,000 people).

HbA1C level closest the (last) episode of hypoglycaemia and latest body mass index (BMI) were determined. Hypoglycaemic events for the previous 10 years and the Townsend index of social disadvantage were determined. Information about medication was similarly obtained.

The Townsend index of deprivation was determined in our study population [17]. The four variables that comprise the Townsend index are 1) unemployment as a percentage of those aged 16 and over who are economically active 2) non-car ownership, as a percentage of all households 3) non-home ownership as a percentage of all households 4) household overcrowding. All four variables are standardised using a Z-score and then summed to obtain a single value. Positive values of the Townsend index are associated with geographic areas with high deprivation. Indices with negative values relate to relative affluence.

2.1. Assays

All assays were performed in the Departments of Biochemistry at Macclesfield and Leighton Hospitals, Cheshire, UK. HbA1C was analysed on the Vitros 5.1 autoanalyser (Johnson and Johnson, Rochester, NY, USA).

2.2. Statistical analysis

The data were analysed using the statistical package Intercooled Stata version 10.1 (Stata Corp, Texas). Anthropometric and metabolic data are expressed as arithmetic means with 95% confidence intervals (CI). Comparison of means was by t-test or analysis of variance (ANOVA). Comparison of proportions used Chi-squared tests. Logarithmic transformation was performed on non-normally distributed variables. For uni-

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