Glucose variability and risk of hypoglycaemia amongst inpatients with type 2 diabetes and its relationship to drug class exposure

K M Fairhurst[1], SG Cunningham[2], CAR Sainsbury[1], GC Jones[1]

1) Department of Diabetes, Gartnavel General Hospital, Glasgow, Scotland

2) Clinical Technology Centre, Ninewells Hospital, Dundee, Scotland

Introduction

The complexity of Type two Diabetes Mellitus presents a challenge to optimising long-term management. Reducing blood glucose to HbA1C levels closer to the non-diabetic range has been shown to reduce both micro and macro-vascular complications of chronic hyperglycaemia. However this approach may result in predispose patients to a higher risk of hypoglycaemia. Sulphonureas, commonly used as a second line agent, are often a major culprit.(1) Severe hypoglycaemia has been associated with and increased rate of macrovascular events and mortality in people with type 2 diabetes. Research to date has demonstrated that fluctuations between high and low blood sugar have been linked to oxidative stress activation, worsening diabetic complications, and increase in long-term mortality. (2) Here we explore the association between prescribed medication pre-admission and the characteristics identifiable in inpatient CBGs.

Methods

We identified 594923 capillary blood glucose (CBG) readings of inpatients with T2DM, from admissions during which >4 CBG measurements were made. The first admission for each individual within the dataset was taken as the index admission. Median CBG, interquartile range (IQR) and number of hypoglycaemic (<4 mmol/l) episodes/day were calculated for each admission. Encashment of primary care prescriptions for sulphonylurea, metformin or insulin in the 4 months prior to each admission was used to associate drug therapy with inpatient CBG results during the admission. Individuals were classified by prior drug treatment, and were matched with a comparator group by age (+/- 5y) , median CBG (+/- 0.25mmol/l), diabetes duration (+/- 2y) and admission duration (+/- 0.5days).

Outcomes of interest were glycaemic variability (IQR) and hypoglycaemia rate (episodes /day).

Groups compared:
Sulphonylurea plus Metformin VS metformin alone
Insulin plus Metformin VS metformin alone.
Insulin plus Metformin VS Sulphonylurea plus Metformin
Metformin monotherapy VS no prescribed therapy.

Results

24181 first admissions of 24181 unique individuals were identified. IQR and hypoglycaemia rate for each of the comparisons are shown below. IQR values are given as median (IQR). p-values are shown for a t-test between the log(IQR) values for each grouping.

drug class	IQR (mmol/l)	hypo frequency (episodes / day)
Sulphonylurea plus metformin	2.7 (1.8 – 4.1)	0.13
Metformin alone	2.0 (1.3 – 3.0)	0.05
p-value	<0.001	
n matched pairs	3705	
Insulin plus metformin	3.3 (2.3 – 4.5)	0.23
Metformin alone	2.4 (1.6 – 3.6)	0.07
p-value	<0.001	
n matched pairs	557	
Insulin plus metformin	3.2 (2.4 – 4.5)	0.18
Sulphonylurea plus metformin	3.0 (2.0 – 4.4)	0.12
p-value	<0.01	
n matched pairs	625	
metformin alone	1.9 (1.3 – 2.8)	0.04
no therapy	2.0 (1.2 – 3.0)	0.05
p-value	0.4	
n matched pairs	4808	

Summary and Conclusions

- Inpatient glycaemic variability is increased in admissions associated with pre-admission prescription of sulphonylurea or insulin plus metformin, when compared with metformin alone. There is an increased rate of hypoglycaemia when expressed as episodes / day that would be expected with this increase in variability.
- The hypoglycaemia rate associated with sulphonylurea prescription is substantial at around 0.13 / day.
- There is reasonable concordance of variability and hypoglycaemia episode rate between similar drug groups when compared in different analyses.
- The hypoglycaemia episode rate in those patients with Type 2 diabetes who are insulin treated (0.23) is very similar to the observed rate in our dataset for individuals with Type 1 diabetes (0.22)
- There is a background rate of hypoglycaemia of 0.05 episodes / day seen in those patients with pre-admission prescriptions of either metformin or no medication. This presumably relates to insulin use in these patients either in the context of loss of glycaemic control, or significant illness.

Taken together, these data suggest that when matched relatively tightly for age, duration of admission, duration of diabetes and average level of glucose during admission, treatment with suphonylurea and insulin therapy is associated with a significantly higher glucose variability and rate of hypoglycaemia – both of which have been previously associated with adverse long term outcomes.

References

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