DIABETICMedicine

DOI: 10.1111/dme.12002

Short Report: Treatment

Hypoglycaemia is associated with increased length of stay and mortality in people with diabetes who are hospitalized

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Accepted 28 August 2012

Abstract

Aim To study the length of stay and inpatient mortality of patients with diabetes who had an episode of hypoglycaemia in a non critical care setting at University Hospital Birmingham, UK.

Methods Retrospective analysis of routinely available electronic data of 6374 admissions with a recording of either laboratory or point-of-care blood glucose value. Based on the lowest recorded blood glucose values, patients were categorized into a group without hypoglycaemia (> 3.9 mmol/l), a group with mild to moderate hypoglycaemia (2.3–3.9 mmol/l) and a group with severe hypoglycaemic (≤ 2.2 mmol/l). Length of stay and inpatient mortality were compared between the three groups, adjusting for age, gender, ethnicity, deprivation, admission type, use of insulin and modified Charlson co-morbidity score.

Results There were 148 admissions (2.3%) with severe hypoglycaemia (≤ 2.2 mmol/l), 500 admissions (7.8%) with mild to moderate hypoglycaemia (2.2–3.9 mmol/l) and 5726 admissions with no recorded hypoglycaemic episode (> 3.9 mmol/l). After adjustment, length of stay, when compared with those without a recorded hypoglycaemic episode, was 1.51 (95% CI 1.35–1.68) times higher in the group with blood glucose values of 2.3–3.9 mmol/l and 2.33 (95% CI 1.91–2.84) higher in the group with blood glucose values ≤ 2.2 mmol/l. Adjusted odds ratio of inpatient mortality when compared with the group without hypoglycaemia was 1.62 (95% CI 1.16–2.27) in the group with blood glucose values of 2.3–3.9 mmol/l and 2.05 (95% CI 1.24–3.38) in the group with blood glucose values ≤ 2.2 mmol/l.

Conclusion Hypoglycaemia is associated with increased length of stay and inpatient mortality. Whilst causative evidence is lacking, our data are consistent with the need to avoid hypoglycaemia in our current and continued approach for optimal glycaemic control in people with diabetes admitted to hospital.

Diabet. Med. 29, e445–e448 (2012)

Introduction

Hypoglycaemia is common in hospitalized patients with diabetes [1–4]. In critical care, hypoglycaemia is associated with prolonged length of stay and mortality, irrespective of the diabetes status [2,3]. Limited evidence exists on the effect of hypoglycaemia on length of stay and mortality for patients with diabetes in a non-critical care setting. Turchin *et al.* [1]showed that, in an analysis of 4368 admissions with diabetes in one teaching hospital (Boston, USA), hypoglycaemia (blood glucose values < 2.8 mmol/l) was associated with increased length of stay, an 85% increase in the odds of inpatient death and a 65% increase in the odds of death at 1 year. A recent study from New York, USA, reporting on mortality in a mixed population of patients, with and without diabetes, suggested hypoglycaemia is a marker of disease burden and the greater mortality observed can be explained by the association between the hypoglycaemia and co-morbidities [4].

UK data are sparse on the outcome of inpatients with diabetes who have had a hypoglycaemic episode. It is important we know these outcomes to monitor and improve care through implementation of interventions that will reduce hypoglycaemic episodes and adverse outcomes associated with

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them. To address this, we studied the difference in length of stay and inpatient mortality of patients with diabetes who had and did not have an episode of hypoglycaemia in a non-critical care setting at University Hospital Birmingham, a hospital with approximately 1200 beds. The hospital has a purpose-designed computer-based patient information system, the Patient Information and Communication System (PICS), which records laboratory results, electronic observations and medication orders, and a Patient Administration System (PAS), which records discharge diagnostic codes. We therefore had the opportunity to analyse retrospective data available for the years 2007–2010 from blood glucose concentration measurements, both from the bedside and the laboratory of patients identified as having diabetes based on discharge diagnostic codes and prescribed diabetic medication.

Methods

Data sources

We identified all patients of age 16 years and above who were registered in the Patient Administration System as having been admitted to University Hospital Birmingham during the period of 2007–2010 as either an elective or emergency inpatient admission. Patient Administration System data were linked to the Patient Information and Communication System data and patients with a recorded diagnosis of diabetes in the Patient Administration System, or who did not have a diabetes diagnostic code but were identified in Patient Information and Communication System as having received treatment with anti-diabetic medication, were classed as having diabetes if they did not meet our exclusion criteria. The exclusion criteria were: (1) patients on metformin, but without a discharge diagnostic code of diabetes and with a discharge diagnostic code for polycystic ovarian syndrome; (2) patients who received short- or rapid-acting insulin alone, but without a discharge code of diabetes. The latter criteria was chosen to avoid misclassifying patients as having diabetes when they might have received this treatment for hyperkalaemia or control of blood sugar in seriously ill patients with hyperglycaemia. Only patients with at least one recorded blood glucose concentration were included for the study. All patients who had one or more stay at an intensive care unit (ICU) were excluded from the analysis. Any inconsistent records, where a discharge diagnostic code for hypoglycaemia was present, but blood glucose values did not indicate hypoglycaemia, were excluded from the analysis.

We identified episodes of hypoglycaemia at any point during the admission by interrogating blood glucose concentrations from the Patient Information and Communication System database, recorded either from bedside (point of care) or laboratory. We did not differentiate between laboratory blood glucose values and point-of-care blood glucose values, or consider the type of equipment used to measure glucose values.

Cut-off value for hypoglycaemia

We used the National Health Service (NHS) Diabetes guideline treatment cut-off value (blood glucose values of 3.9 mmol/l or less) to categorize hypoglycaemia [5]. Severe hypoglycaemia is best categorized by the need for third-party assistance in treating the episode. Considering this information is not possible to obtain from the data, a cut-off blood glucose value of 2.2 mmol/l was used to describe severe hypoglycaemia. Therefore, blood glucose concentrations of greater than 3.9 mmol/l were categorized as non hypoglycaemic, 2.3–3.9 mmol/l as mild to moderate hypoglycaemia and 2.2 mmol/l or less as severe hypoglycaemia. Admissions were categorized based on the lowest value of blood glucose recorded during the spell.

We then compared the inpatient mortality and length of stay among these three groups to look for any association. Length of stay was calculated by deducting the admission time from the discharge time to the closest hour.

Statistical analysis

The demographic and morbidity characteristics of the patients with and without an episode of hypoglycaemia are summarized using medians (interquartile range) for continuous data and using proportions for categorical data. To allow for the clustering effect of some of the patients being admitted more than once, a multi-level model, using mixed-effect logistic regression, was used to study the inpatient mortality outcome; and a mixed-effect linear regression model was used to study the effect on length of stay. Because of the skewed length-of-stay data, a log transformation was carried out to normalize the data before multivariate analysis. Covariates controlled in the regression analyses were age (years), gender, ethnicity, social class (based on income deprivation), admission type, modified Charlson co-morbidity score and use of insulin. Modified Charlson co-morbidity score is calculated by deducting the score given for diabetes [1]. Effect size from the multivariate analysis is reported as odds ratio for inpatient mortality and as relative ratio (exponential of the regression coefficient of the log transformed data) for the length of stay. Confidence interval is given at 95% and *P*-values less than 0.05 were deemed significant. Data were analysed using Stata 10 software (StataCorp., College Station, TX, USA), using the generalized estimating equation (GEE) class of models.

Results

There were 25 118 admissions with diabetes between 2007 and 2010. Of these, 6374 met our inclusion criteria (see also Supporting Information, Appendix S1). There were 148 admissions (2.3%) with severe hypoglycaemia (blood glucose ≤ 2.2 mmol/l), 500 admissions (7.8%) with mild to moderate hypoglycaemia (blood glucose 2.2–3.9 mmol/l) and 5726 admissions with no hypoglycaemic episode (blood glucose

> 3.9 mmol/l). Patients with increased severity of hypoglycaemia tended to have an older mean age and were more likely to be admitted as an emergency and be on insulin. Fewer of those who did not have a hypoglycaemia episode had a co-morbidity score of 1 or higher (64%) compared with 73% of those with mild to moderate and 74% of those with severe hypoglycaemia (Table 1).

Median length of stay (days) in the group with blood glucose values > 3.9 mmol/l was 5.9 (interquartile range 2.1–12.9), 11.0 (interquartile range 4.7–21.1) in the group with values of 2.3–3.9 mmol/l and 17.0 (interquartile range 8–37.2) in the group with blood glucose ≤ 2.2 mmol/l. The adjusted length of stay was increased by 1.51 (95% CI 1.35–1.68) times in the group with blood glucose of 2.3–3.9 mmol/l and 2.33 (95% CI 1.91–2.84) times in the group with blood glucose values ≤ 2.2 mmol/l group when compared with those without a hypoglycaemic episode (blood glucose > 3.9 mmol/l) (Fig. 1). The associations were highly significant ($P < 0.001$).

Inpatient mortality was 5% in the group with blood glucose values > 3.9 mmol/l, 10% in the group with blood glucose values of 2.3–3.9 mmol/l and 15% in the group with blood glucose values ≤ 2.2 mmol/l. The adjusted odds ratio was 1.62 (95% CI 1.16–2.27) in the group with blood glucose values of 2.3–3.9 mmol/l and 2.05 (95% CI 1.24–3.38) in the group with blood glucose ≤ 2.2 mmol/l in comparison with the non hypoglycaemic group (Fig. 1). Both again were statistically significant ($P \leq 0.005$).

In multivariable (adjusted) analysis, increasing age, emergency admission, insulin use and higher co-morbidity score were independently associated with both increasing length of stay and inpatient mortality (see also Supporting Information, Appendix S2).

Discussion

We report that hypoglycaemia in people with diabetes admitted to hospital associates with increased length of stay and inpatient mortality. Length of stay was 51% greater in those having mild to moderate hypoglycaemia and 133% greater in those having severe hypoglycaemia. The odds of inpatient mortality increased by 62% in those with mild to moderate hypoglycaemia and by 105% in those with severe hypoglycaemia.

Table 1 Characteristics and outcomes of the admissions based on presence and severity of hypoglycaemia

Patient characteristics	No hypoglycaemia > 3.9 mmol/l (*n* = 5726)	Mild to moderate 2.3–3.9 mmol/l (*n* = 500)	Severe hypoglycaemia ≤ 2.2 mmol/l (*n* = 148)
Age median (interquartile range) years	66 (54–76)	68 (55–76)	72 (58–79)
Gender, *n* (%)			
Male	3303 (57.7)	278 (55.6)	85 (57.4)
Female	2423 (42.3)	222 (44.4)	63 (42.6)
Ethnicity, *n* (%)			
White	3904 (68.2)	338 (67.6)	108 (73.0)
Asian	1099 (19.2)	99 (19.8)	26 (17.6)
Black	362 (6.3)	39 (7.8)	8 (5.4)
Other	361(6.3)	24 (4.8)	6 (4.1)
Social class*, *n* (%)			
Least deprived 1	295 (5.3)	25 (5.1)	6(4.2)
2	484 (8.7)	45 (9.3)	13 (9.0)
3	936 (16.8)	86 (17.7)	31 (21.5)
4	1201 (21.6)	95 (19.5)	36 (25.0)
Most deprived 5	2647 (47.6)	235 (48.4)	58 (40.3)
Type of admission, *n* (%)			
Elective	934 (16.3)	56 (11.2)	7 (4.7)
Emergency	4792 (83.7)	444 (88.8)	141(95.3)
Modified Charlson co-morbidity score, *n* (%)			
0	2045 (35.7)	133 (26.6)	39 (26.4)
1	1188 (20.7)	86 (17.2)	29 (19.6)
2 or more	2493 (43.5)	281 (56.2)	80 (54.1)
Insulin use, *n* (%)			
Yes	342 (60.1)	357 (71.4)	119 (80.4)
No	2284 (39.9)	143 (28.6)	29 (19.6)
Outcomes			
Inpatient death, *n* (%)			
Yes	298 (5.2)	49 (9.8)	22 (14.9)
No	5428 (94.8)	451 (90.2)	126 (85.1)
Length-of-stay median (interquartile range) days	5.9 (2.1–12.9)	11.0 (4.7–21.1)	17.0 (8.0–37.2)

*Social class based on income deprivation score. Adds up to 6193 instead of 6374 because of missing postcode values.

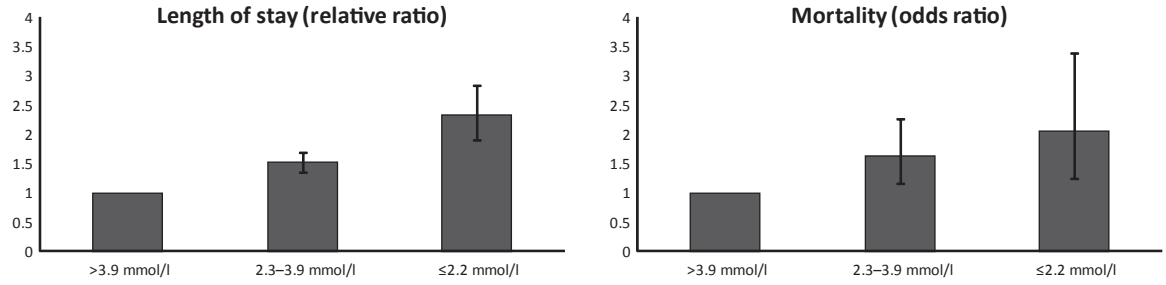

FIGURE 1 Presence and severity of hypoglycaemia vs. inpatient mortality and length of stay* (*adjusted odds ratio for mortality and adjusted relative ratio for length of stay). Relative ratio here is the exponential of regression coefficient obtained from the analysis of log transformed length-of-stay data. Covariates adjusted for are age, gender, ethnicity, social class, admission type, insulin use and Charlsonco-morbidity score. Bars indicate the confidence intervals.

Our findings are consistent with that of Turchin *et al.* who found an 85% increase in inpatient mortality with a hypoglycaemic episode [1]. This consistency persists despite the differing definitions of hypoglycaemia (2.8 mmol/l) compared with our cut off value (3.9 mmol/l). Our findings indicate hypoglycaemia as either being a marker of poor prognosis or that the patients are being at risk of an adverse outcome as a consequence of hypoglycaemia. Increase in length of stay in patients with hypoglycaemia may result from the need to optimize glycaemic control prior to discharge, or may result from the increased chance of having and detecting an episode of hypoglycaemia with a longer inpatient stay.

The limitations of our study were the inconsistent availability of electronic blood glucose values for admissions with diabetes and the retrospective nature of the study. Our definition of severe hypoglycaemia was based on a biochemical cut-off value (blood glucose < 2.2 mmol/l) rather than the accepted categorization based on the need for third-party assistance. By using the Charlson co-morbidity index, we have adjusted for key confounding illnesses, such as liver disease, renal impairment and congestive heart failure, but this does not encompass all possible confounders, such as excessive alcohol intake. However, the data set is large, with over 6000 admissions, and findings are consistent with previous studies that used similar approaches [1,4].

Conclusions

Hypoglycaemia is associated with increased length of stay and inpatient mortality. Whilst causative evidence is lacking, our data are consistent with the need to avoid hypoglycaemia in our current and continued approach for optimal glycaemic control in people with diabetes admitted to hospitals.

Funding sources

None.

Competing interests

Nothing to declare.

Acknowledgement

This study was funded by the National Institute for Health Research (NIHR) through the Collaborations for Leadership in Applied Health Research and Care for Birmingham and Black Country (CLAHRC-BBC) programme. The views expressed in this publication are not necessarily those of the NIHR, the Department of Health, NHS Partner Trusts, University of Birmingham or the CLAHRC-BBC Theme 9 Management/Steering Group.

References

1 Turchin A, Matheny ME, Shubina M, Scanlon JV, Greenwood B, Pendergrass ML. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. *Diabetes Care* 2009; **32**: 1153–1157.
2 Krinsley JS, Schultz MJ, Spronk PE, Harmsen RE, Houckgeest FV, van der Sluijs JP *et al.* Mild hypoglycemia is independently associated with increased mortality in the critically ill. *Critical Care* 2011; **15**: R173.
3 Krinsley JS, Schultz MJ, Spronk PE, van Braam HF, van der Sluijs JP, Melot C. Mild hypoglycemia is strongly associated with increased intensive care unit length of stay. *Ann Intensive Care* 2011; **24**: 49.
4 Boucai L, Southern WN, Zonszein J. Hypoglycemia-associated mortality is not drug-associated but linked to comorbidities. *Am J Med* 2011; **124**: 1028–1035.
5 Joint British Diabetes Society. *The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus*. Newcastle Upon Tyne: Joint British Diabetes Society, 2010.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Flow diagram of admissions included for analysis.

Appendix S2. Adjusted odds ratio for inpatient mortality and adjusted relative ratio for length of stay in patients with diabetes.