Hypoglycemia is an adverse side effect of insulin and sulfonylurea treatment for type 2 diabetes. Factors influencing risk of severe hypoglycemia (requiring external assistance) include duration of diabetes, insulin treatment, renal impairment, age, comorbidities, and impaired awareness of hypoglycemia. Sleep-disordered breathing with associated daytime somnolence is reported in up to 75% of people with type 2 diabetes and is linked to a range of cardiovascular and metabolic morbidities. We hypothesized that sleep disorder and increased daytime sleepiness would be associated with increased frequency of severe hypoglycemia in people with diabetes.

RESULTS—Subjects who scored highly on the Epworth Sleepiness Scale were significantly more likely to have suffered from severe hypoglycemia. This was a significant predictor of severe hypoglycemia in regression analysis including the variables age, sex, duration of diabetes, HbA1c, BMI, and treatment type.

CONCLUSIONS—Daytime sleepiness may be a novel risk factor for hypoglycemia.

OBJECTIVE—Sleep-disordered breathing and sleepiness cause metabolic, cognitive, and behavioral disturbance. Sleep-disordered breathing is common in type 2 diabetes, a condition which requires adherence to complex dietary, behavioral, and drug treatment regimens. Hypoglycemia is an important side effect of treatment, causing physical and psychological harm and limiting ability to achieve optimal glycemic control. We hypothesized that sleep disorder might increase the risk of hypoglycemia through effects on self-management and glucose regulation.

RESEARCH DESIGN AND METHODS—People with type 2 diabetes (n = 898) completed questionnaires to assess sleep-disordered breathing, daytime sleepiness, and occurrence of severe hypoglycemia.

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Corresponding author: Rebecca M. Reynolds, r.reynolds@ed.ac.uk.

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Association Between Excessive Daytime Sleepiness and Severe Hypoglycemia in People With Type 2 Diabetes

The Edinburgh Type 2 Diabetes Study

BERIT INKSTER, MBCHB
RENATA L. RIHA, MD
LIESBETH VAN LOOK, MBCHB
RACHEL WILLIAMSON, MD
STELA McLACHLAN, PHD
BRIAN M. FRIER, MD
MARK W.J. STRACHAN, MD
JACKIE F. PRICE, MD
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previous severe hypoglycemia. High-risk Berlin scores and Epworth scales were positively associated with each other (P < 0.001).

Regression analysis confirmed the ESS as a significant independent predictor of severe hypoglycemia (Table 1). When the regression analysis was performed using Berlin sleepiness category, the Wald statistic was not significant (P = 0.129). Stepwise regression of these variables (including Berlin sleepiness category) confirmed ESS, sex, diabetes duration, and treatment type as independent predictors of severe hypoglycemia. Berlin sleepiness category, age, BMI, and then HbA1c were removed from the model sequentially (Nagelkerke $R^2$ for model = 0.117).

**CONCLUSIONS**—In this large cohort of elderly people with type 2 diabetes, those with increased daytime sleepiness, as measured by two different scoring systems, were more likely to have experienced severe hypoglycemia. This was not observed for other measures of sleep-disordered breathing assessed by the Berlin scale. Sleepiness is a nonspecific symptom caused by a range of underlying causes and should be differentiated from sleep-disordered breathing and sleep deficiency. The data presented here suggest that sleepiness as a symptom, rather than sleep-disordered breathing per se, may be a risk factor for hypoglycemia.

Severe hypoglycemia is more likely to occur during sleep (mainly at night), and hypoglycemia is often prolonged and unrecognized at this time (10–12). These episodes are likely to cause sleep disruption (13) with resulting daytime somnolence, which may be the mechanism of the association. Conversely, daytime sleepiness may reduce awareness and recognition of hypoglycemia (14), therefore increasing risk of severe hypoglycemia because of failure to self-treat at an early stage. Sleepiness may also influence hypoglycemia risk through its effects on behavior and cognition. Sleepiness causes cognitive slowing, reduced attention, increased automatic behavior, and increased errors (for example, medical errors made by interns and motor vehicle crashes) (6,15). This may lead to poorer self-management and increased medication errors in patients.

Sleepiness may alternatively act as a marker of an underlying causative factor such as comorbidity or general frailty. The HbA1c in the people with high ESS scores who had experienced severe hypoglycemia tended to be higher than the rest of the cohort (7.6 vs. 7.2% [60 vs. 55 mmol/mol], P = 0.09). This could represent suboptimal self-management, which may increase the risk of hypoglycemia. Alternatively, glycemic targets in these individuals may have been relaxed to try to prevent further severe hypoglycemia.

The main limitation of the current study is the cross-sectional design that does not allow an examination of the temporal nature of the association. Information was not available about potential confounders such as social class, work and sleep habits, comorbidities, and stress. Alcohol and sedative drug use were not included in the regression model, as use of these substances was very low. The $R^2$ values for the regression models were small, indicating that the variables included were relatively weak predictors of severe hypoglycemia. This may relate to the absence of important predictors in the model; however, it also reflects the infrequent and sporadic occurrence of severe hypoglycemia.

The subjective method of capturing severe hypoglycemia may have led to inaccuracies owing to poor recall of previous events, misinterpretation of the question to include episodes where third-party help was provided but not necessarily required, and events that may not have been due to hypoglycemia, as no evidence of low blood glucose was required. Although information about the number of previous episodes was collected, numbers were too small to allow satisfactory assessment of a dose-response relationship, which would strengthen the plausibility of such an association.

This observation in a large, representative cohort is novel and needs to be replicated. Future research should collect prospective data on hypoglycemia, as well as important confounding factors. If further evidence of sleepiness contributing to risk of severe hypoglycemia were available, sleepiness would be another factor to consider in the clinical assessment of hypoglycemia risk. This is an important consideration for treatment decisions and determining an individual’s HbA1c target. Inclusion of a quick and simple questionnaire to assess sleepiness could be incorporated into routine diabetes management to identify those at risk for hypoglycemia.

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B.I. designed and carried out the analysis and wrote the manuscript. R.L.R. designed the analysis and participated in writing the manuscript. L.V.L., R.W., and S.M. collated and analyzed data and approved the manuscript. B.M.F., M.W.J.S., J.F.P., and R.M.R. are principal investigators of the Edinburgh Type 2 Diabetes Study and participated in the study design, collection and analysis of data, and writing the manuscript. R.M.R. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**References**


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**Table 1—Regression analysis for predictors of severe hypoglycemia**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Wald statistic $^{a}$</th>
<th>Significance $^{b}$</th>
<th>Exp b $^{c}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epworth category</td>
<td>4.939</td>
<td>0.026</td>
<td>0.537</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.731</td>
<td>0.393</td>
<td>1.025</td>
</tr>
<tr>
<td>Sex (1 = male, 2 = female)</td>
<td>6.537</td>
<td>0.011</td>
<td>0.539</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>10.354</td>
<td>0.001</td>
<td>0.947</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>12.894</td>
<td>0.169</td>
<td>0.860</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>1.264</td>
<td>0.261</td>
<td>1.025</td>
</tr>
<tr>
<td>Oral antidiabetes agent</td>
<td>3.805</td>
<td>0.016</td>
<td>1.860</td>
</tr>
<tr>
<td>Insulin use</td>
<td>3.951</td>
<td>0.015</td>
<td>0.487</td>
</tr>
</tbody>
</table>

Nagelkerke $R^2$ = 0.126 for regression model. $^a$Measure of whether b-coefficient is significantly different from zero. $^b$Significance of Wald statistic; if P < 0.05, then predictor is making a significant contribution. $^c$Proportionate change in odds resulting from change in the predictor (if <1, severe hypoglycemia more likely with increase in variable and vice versa).
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