Hypothermia is a frequent sign of severe hypoglycaemia in patients with diabetes

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Abstract

Aim. – Hypothermia is a recognized complication of severe hypoglycaemia, but its prevalence and characteristics are poorly studied. For this reason, this study aimed to evaluate hypothermia in severely hypoglycaemic patients.

Methods. – A retrospective chart review was performed including all patients discharged between 2007 and 2010 from the Emergency Department of the Geneva University Hospital with a diagnosis of severe hypoglycaemia.

Results. – Hypothermia was identified in 30 (23.4%) out of 128 patients with severe hypoglycaemia. Its incidence was not affected by age, type of diabetes, season or time of day (day/night). Using linear regression, the lowest recorded temperature was associated with the Glasgow Coma Scale (GCS) score (r² = 13.8%, P < 0.0001) and inversely associated with the leukocyte count (r² = 13.1%, P = 0.001).

Conclusion. – Hypothermia is a frequent sign of severe hypoglycaemia in patients with diabetes. The associations between hypothermia and the GCS score and the leukocyte count suggest that it is a marker of hypoglycaemia severity and/or duration. Hypothermia may represent an important compensatory mechanism in severe hypoglycaemia, reflecting a decrease in energy demand during glucose deprivation.

Keywords: Hypoglycaemia; Hypothermia; Diabetes; Insulin

1. Introduction

Hypothermia, a recognized complication of severe hypoglycaemia, was first described in patients undergoing insulin shock therapy for psychiatric disorders [1]. However, the prevalence and implications of hypothermia as a complication of severe hypoglycaemia are not well understood. In this study, we aimed to evaluate the prevalence and characteristics of hypothermia in severely hypoglycaemic patients.
hypoglycaemia in patients with diabetes have been poorly studied [2]. For this reason, the present retrospective study was conducted to determine the prevalence and characteristics of hypothermia in patients admitted to an emergency ward for severe hypoglycaemia.

2. Patients and methods

All charts of patients discharged between 2007 and 2010 from the Emergency Department of the Geneva University Hospital with a clinical diagnosis of severe hypoglycaemia were retrospectively analyzed. The Geneva University Hospital is an 800-bed primary and tertiary urban teaching hospital, with an emergency department receiving approximately 60,000 annual visits. Ten patients were excluded because of obvious coding errors. The following parameters were recorded from the patients’ ambulance and hospital charts:

- diabetes status and type;
- antidiabetic treatments;
- other medications;
- date and time;
- co-morbidities;
- symptoms;
- precipitating factors (skipped meal, alcohol use);
- recorded capillary glucose values;
- blood pressure;
- body temperature;
- and treatments administered.

On a routine basis, levels of consciousness were assessed using the Glasgow Coma Scale (GCS), which was determined according to three components:

- eyes:
  - 4: opening spontaneously,
  - 3: opening on verbal command,
  - 2: opening on pain,
  - 1: no eye opening;
- verbal:
  - 5: oriented,
  - 4: disoriented,
  - 3: inappropriate words,
  - 2: incomprehensible sounds,
  - 1: no verbal response;
- motor:
  - 6: obeys,
  - 5: localizes pain,
  - 4: withdrawal,
  - 3: abnormal flexion,
  - 2: abnormal extension,
  - 1: no motor response [1].

Body temperature measurements were performed at the tympanic level in both the ambulance and emergency ward. Hypothermia was defined as a body temperature less than 35 °C.

Fig. 1. Scatterplot of the lowest tympanic temperatures according to blood glucose values. The hypothermia and hypoglycaemia thresholds are indicated by the straight horizontal and vertical lines, respectively.

The coefficient of determination ($r^2$) was used to express the proportion of variance of a continuous dependent variable explained by an independent variable via univariate linear regression models. All statistical analyses were performed using Stata Statistical Software, release 11.2 (StataCorp, College Station, TX, USA).

3. Results

Over a 4-year period, 156 patients discharged with a diagnosis of severe hypoglycaemia were identified, of whom 146 had a known diagnosis of diabetes: 67.1% were being treated with insulin; 15.8% by oral hypoglycaemic agents (OHAs); and 16.4% by combined insulin and OHA therapy. Overall, hypothermia was identified in 30 (23.4%) of the 128 patients with severe hypoglycaemia for whom a temperature value was recorded. To better characterize this observation, our analysis then focused on the 122 patients (51 women, 71 men) receiving insulin therapy: 43.4% and 51.4% of these patients were considered to have type 1 and type 2 diabetes, respectively; and 4.9% had diabetes due to pancreatic failure. Loss of consciousness, confusion and seizures were observed in 44.3%, 19.7% and 12.3% of the patients, respectively. An elevated white blood cell (WBC) count (> 12,000 cells/mm$^3$) was observed in 21 (23.3%) of 90 patients with available data. The WBC was weakly, but significantly, associated with the lowest recorded blood glucose value ($r^2 = 5.4\%; P = 0.03$ by linear regression). A high WBC count is most likely the result of a stress response and, thus, is a marker of hypoglycaemia severity.

Hypothermia was observed in 28 (27.2%) of the 103 insulin-treated patients for whom a temperature value was available (Fig. 1). Its incidence was not associated with age, type of diabetes, season or time of day (day vs. night). The temperature range in the patients with hypothermia was 31.8–34.9 °C; however, only two had severe hypothermia, defined as a body temperature less than 32 °C. Hypothermia appeared to be associated with hypoglycaemia severity (Fig. 1). Indeed, it was present in 31.4% of patients for whom the lowest documented blood glucose (BG) value was < 3.5 mmol/L, but in only one of 17
(5.9%) patients whose lowest BG was more than 3.5 mmol/L. By linear regression, the lowest recorded temperature value was associated with the initial GCS score ($r^2 = 13.8\%, P < 0.0001$) and inversely related to the leukocyte count ($r^2 = 13.1\%, P = 0.001$).

4. Discussion

Our present study showed that hypothermia is a frequent sign of severe hypoglycaemia in patients with diabetes. However, the true incidence may have been underestimated in this retrospective survey because of missing values or the delay between initial treatment and the first temperature measurements, among other possible reasons. The associations between hypothermia and the GCS score and leukocyte count suggest that the former is a marker of hypoglycaemia severity and/or duration. Although there were no subsequent temperature values available, the uncomplicated course of the patients, all of whom were rapidly discharged, suggested a transient phenomenon. Thus, hypothermia induced by hypoglycaemia typically appears to be an incidental finding rather than a therapeutic issue in itself. Nevertheless, it still needs to be recognized as such, as it may, at least temporarily, lead to confusion with other causes of hypothermia, such as drugs, endocrine disease and sepsis.

Previous studies have shown that hypothermia arises in experimental and therapeutic insulin-induced hypoglycaemia [2–4]. In animal studies, insulin-induced hypothermia could be mimicked by intravenous and intracerebroventricular administration of 2-deoxyglucose, which inhibits cellular glucose utilization. These observations suggest that hypothermia is a direct consequence of neuroglucopenia, and may be a protective mechanism by decreasing energy demand during glucose deprivation [2]. The neuronal and biochemical pathways involved in this mechanism have not been studied in detail, although a role for nitric oxide has been suggested [5]. Hypothermia would be expected to occur more frequently in older subjects due to defective compensatory mechanisms and the frequent presence of malnutrition [6,7]. However, no association was found between age and the frequency of hypoglycaemia-associated hypothermia in the present study. Also, small previous studies have suggested that accidental hypothermia is more frequent in patients with diabetes [8], a notion that has been neither confirmed nor ruled out by larger studies. Age, cold weather and social isolation are recognized risk factors for accidental hypothermia. It thus appears that hypothermia associated with hypoglycaemia is distinct from accidental hypoglycaemia, as it is typically mild and transient, and not associated with age and seasonality.

In conclusion, hypothermia is frequently seen with severe hypoglycaemia. Although it is rarely a therapeutic issue in itself, it is most likely a marker of hypoglycaemia severity and/or duration. In addition, hypothermia needs to be better identified and further studied as a possible compensatory mechanism in severe hypoglycaemia that decreases energy demand during glucose deprivation.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References