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COMMENTARY

Clinical conditions during severe hypoglycemia in patients with diabetes

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Introduction

Hypoglycemia has been recognized as a dangerous condition that can lead to convulsions, impaired awareness, and traffic accidents [1]. However, the ACCORD trial [2], in which strict glucose control resulted in increased mortality, triggered further research about the association between hypoglycemia and the risk of death and cardiovascular disease. Thus, many investigations about hypoglycemia have been conducted, and severe hypoglycemia has been recognized as one of the most serious problems in patients with diabetes [3–6]. Severe hypoglycemia is defined as the presence of any hypoglycemic symptoms that cannot be resolved by the patients themselves. Some studies have suggested that diabetes and severe hypoglycemia are associated with increased mortality and cardiovascular disease [3, 4]. Although systemic conditions and complications during severe hypoglycemia have remained unclear, recent studies have revealed the clinical presentation during severe hypoglycemia in patients with type 1 and type 2 diabetes [6–10].

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Disorders of consciousness and hypothermia

Hypoglycemia leads to disorders of consciousness, and lower blood glucose levels are associated with lower Glasgow Coma Scale scores [6]. Hypoglycemia cannot only lower the activity in brain cells but also influence the thermoregulatory center in the hypothalamus. A recent study suggested that hypothermia is not uncommon with hypoglycemia [6, 11]; about 20 % of patients with type 1 or type 2 diabetes exhibited hypothermia (body temperature <35 °C) during severe hypoglycemia [6].

Severe hypertension

Hypoglycemia stimulates the sympathetic nervous system and the secretion of counter-regulatory hormones, such as epinephrine and norepinephrine, which can lead to changes in circulatory dynamics. In patients with type 2 diabetes, most of them actually experience blood pressure elevation and severe hypertension during severe hypoglycemia [6]. However, type 1 diabetic patients did not show the same significant elevation in their blood pressure as type 2 diabetic patients did. One of the possible reasons is that patients with type 1 diabetes typically experience hypoglycemia more frequently than those patients with type 2 diabetes, and these repeated hypoglycemic episodes lead to hypoglycemia-associated autonomic failure, which may blunt the sympathetic system response to hypoglycemia [12].

Hypokalemia

Patients with type 1 and type 2 diabetes present with hypokalemia during severe hypoglycemia [6]. Because the

primary causes of severe hypoglycemia in patients with type 1 and type 2 diabetes are antihyperglycemic agents such as insulin and sulfonylureas, the potassium in the extracellular fluid may be transferred to the intracellular fluid by the relative hyperinsulinemia caused by these agents, as well as by the release of catecholamines that can be induced by severe hypoglycemia. Although hypokalemia due to severe hypoglycemia has hardly appeared as a problem, hypokalemia can lead to deadly arrhythmias, and therefore hypokalemia may be another threat during severe hypoglycemia.

Prolonged QT interval

The association between QT prolongation and hypoglycemia in patients with type 1 diabetes has been previously reported [8, 10, 13]. However, patients with type 2 diabetes may also have QT prolongation during severe hypoglycemia [6]. Although the possible cause for QT prolongation may be hypercatecholaminemia, hypothermia, and hypokalemia due to severe hypoglycemia, further research is required to establish the detailed mechanism of this process. QT prolongation can lead to lethal arrhythmias such as torsade de pointes. In addition, QT prolongation may also be associated with the onset of atrial fibrillation [6, 14].

Cardiovascular events during severe hypoglycemia

Newly diagnosed cardiovascular events during severe hypoglycemia have been found in a small but significant minority of patients with type 2 diabetes [6]. Although the causal relationship is unknown, severe hypoglycemia may lead to cardiovascular events because of a significant cardiac load and its exacerbation in the atherosclerotic lesion [15], platelet agglutination [16], and vascular endothelial impairment [17]. In contrast, the association between severe hypoglycemia and cardiovascular events in patients with type 1 diabetes has been not found [6, 18]. The possible reasons for this finding may be the hypoglycemia-associated autonomic failure and/or the presence of fewer cardiac risk factors in patients with type 1 diabetes.

In summary, type 1 and type 2 diabetic patients with severe hypoglycemia may develop critical conditions such as cardiovascular disease, lethal arrhythmias, and death. More attention is required to study the fact that the complications associated with severe hypoglycemia may develop under conditions of disturbed consciousness.

Conflict of interest The authors have no conflicts of interest to report.

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