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CONTINUOUS OCTREOTIDE INFUSION FOR SULFONYLUREA-INDUCED HYPOGLYCEMIA IN A TODDLER

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□ **Abstract—Background: Ingestion of a sulfonylurea by toddlers can cause profound hypoglycemia and neurologic sequelae. Although mild cases can be managed with dextrose and boluses of octreotide, optimal management of patients with severe hypoglycemia and cerebral injury has not been well established. Objective: Our objective was to report the use of continuous infusion octreotide for tight glucose control after accidental sulfonylurea ingestion with severe neurologic dysfunction. Case Report: A 17-month-old child presented to the emergency department with marked hypoglycemia, cerebral edema, and persistent seizures after ingestion of an unknown amount of glipizide. Hypoglycemia was refractory to i.v. dextrose bolus/infusion and subcutaneous octreotide. Continuous i.v. octreotide was utilized in conjunction with low-volume/high-concentration dextrose infusion as treatment, allowing for tight glucose and fluid management in the setting of cerebral edema. Conclusions: Continuous infusion of octreotide resulted in rapid stabilization of blood glucose levels while maintaining fluid-restriction goals. Our patient demonstrated reversibility of diffuse cerebral edema in this setting with near complete recovery of neurologic function. Octreotide administration by continuous infusion may be preferable to subcutaneous bolus administration for the treatment of severe sulfonylurea-induced hypoglycemia with associated neurologic injury.** © **2013 Elsevier Inc.**

□ **Keywords—glipizide; pediatrics; hypoglycemia; cerebral edema; magnetic resonance imaging**

INTRODUCTION

Sulfonylureas are the most common class of oral hypoglycemic medications prescribed for insulin-resistant diabetes, and function by binding to the sulfonylurea receptor on pancreatic β cells and stimulating insulin release (1). In 2010, the National Poison Center reported a total of 977 pediatric sulfonylurea ingestions (2). Exposures in young children commonly occur after exploratory ingestion (3,4). After ingestion, hypoglycemia develops in approximately 15%–44% of pediatric patients (4–7). Significant hypoglycemia can result from even single-tablet ingestions (3,4,7). Standard treatment for sulfonylurea-induced hypoglycemia includes administration of oral or intermittent i.v. dextrose. Octreotide, which acts downstream from the sulfonylurea receptor to inhibit insulin release, can be used as adjunct therapy to prevent ongoing hypoglycemia (1,3,5,8–11). However, severe hypoglycemia with neurologic sequelae can be refractory to standard therapies, and management of these cases is not well established. Continuous i.v. dextrose infusion can be administered, although it carries a risk of rebound hypoglycemia and may require central access. Continuous octreotide infusion has also been suggested for severe cases, but pediatric experience is limited (3,5,12,13). This report

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presents the management of a toddler with persistent seizures, coma, and diffuse cerebral edema 24 h after ingestion of the sulfonylurea glipizide. Hypoglycemia was refractory to standard management with i.v. dextrose boluses and subcutaneous octreotide. We describe the use of continuous octreotide infusion to achieve euglycemia while maintaining neuroprotective goals, resulting in gradual return of neurologic function.

CASE REPORT

A 17-month-old previously healthy male was found at 10 am on the morning before admission surrounded by 10-mg standard-release glipizide tablets. There were no pills in his mouth and a pill count seemed appropriate, so the family did not seek medical attention. He was asymptomatic at bedtime, but was difficult to arouse when his mother checked on him at 10 am the following morning. By 10:30 am, he was limp and unresponsive with labored breathing, so his mother drove him immediately to the nearest emergency department (ED).

In the ED he was unarousable. He was hypothermic to 93.7°F with moderate tachycardia, but otherwise normal vital signs. Physical examination was notable for easy spontaneous respirations, markedly prolonged capillary refill, and intermittent stiffening of his extremities and neck, concerning for seizures. His examination was otherwise normal. Fluid resuscitation with normal saline and rewarming measures were initiated. Initial laboratory testing revealed blood glucose (BG) of 18 mg/dL, with otherwise normal chemistries, complete blood count, and urinalysis. Blood cultures were obtained and broad-spectrum antibiotics were administered. He received a total of four 0.5 g/kg boluses of IV dextrose, with rapid fluctuations in BG between 212 and 40 mg/dL.

Due to clinical seizures and concern for trauma, a non-contrast head computed tomography (CT) was obtained 15 min after arrival. The CT showed diffuse cerebral edema without herniation or hemorrhage. He continued to have intermittent clinical seizures despite treatment with i.v. boluses of lorazepam, phenobarbital, and fosphenytoin. He was intubated for airway protection and an intraosseus line was placed. Abnormal movements stopped after neuromuscular blockade, but he remained tachycardic, concerning for continued seizures. In the face of ongoing hypoglycemia and persistent seizures, the decision was made to transport him to the pediatric intensive care unit (PICU) at our facility for further care.

He arrived in the PICU 30 h after initial exposure, receiving a continuous infusion of D12 0.9% sodium chloride. BG levels were between 170 and 220 mg/dL. He was tachycardic with dilated, reactive pupils and rhythmic jerking of all extremities. Due to the patient's critical neurologic status and diffuse cerebral edema, neuroprotective management was initiated on arrival. Goals included total fluid infusion rate of 80%−100% maintenance, BG levels 75−110 mg/dL, sodium levels 140−150 mmol/L, normocarbia, and seizure control. Seizures resolved after administration of lorazepam, fosphenytoin, levetiracetam, and midazolam drip. Electroencephalography confirmed resolution of seizures.

BG levels and glucose infusion rates are shown in Figure 1. Despite continuous dextrose infusion, he developed repeated episodes of hypoglycemia. Subcutaneous octreotide (1 μg/kg) was administered 31 h post ingestion with improvement in hypoglycemia. However, after 6 h, BG dropped again to 30 mg/dL. During the following 12 h, he experienced six additional episodes of hypoglycemia, despite two additional 1-μg/kg doses of subcutaneous

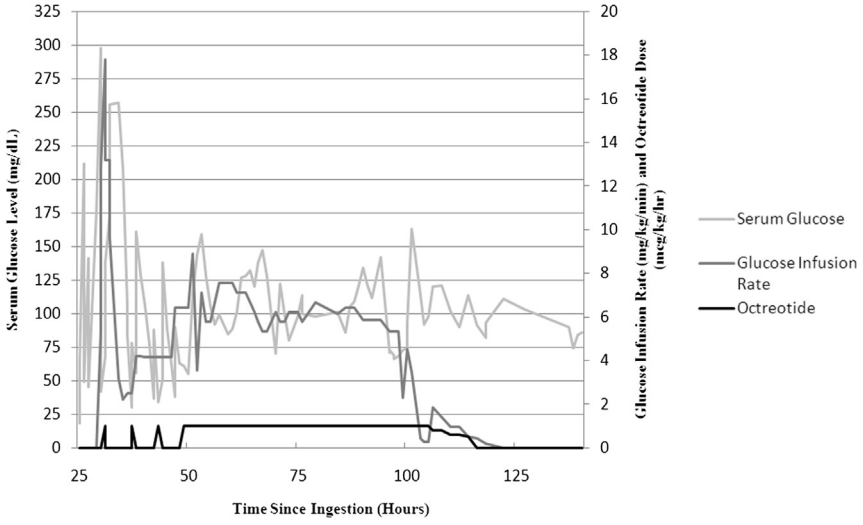

Figure 1. Serum blood glucose, glucose infusion rate, and octreotide dose.