Octreotide for the treatment of sulfonylurea poisoning

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Abstract

Background: Sulfonylureas are used extensively for treating type-2 diabetes mellitus. Sulfonylurea poisoning can produce sustained and profound hypoglycemia refractory to IV dextrose, particularly in children and the elderly. Objective: To review the use of octreotide, a long-acting somatostatin analog, in the treatment of sulfonylurea-induced hypoglycemia. Methods: A computerized search of U.S. National Academy of Medicine, Embase, PubMed and Toxline databases was undertaken using the keywords "octreotide", "sulfonylurea", "poisoning", "intoxication", "overdose" and "children". Textbooks of Clinical Toxicology and Pharmacology and the articles cited in their bibliographies were also searched. Twenty-four publications (19 articles and five conference abstracts) were identified; no publication was excluded. Pharmacology of octreotide. Octreotide, a synthetic peptide analog of somatostatin, binds to G protein-coupled somatostatin-2 receptors in pancreatic beta-cells, resulting in decreased calcium influx and inhibition of insulin secretion. Octreotide markedly inhibited insulin secretion and decreased the number of hypoglycemic events and supplemental dextrose requirements in animal studies. In humans octreotide markedly inhibited insulin release, increased serum glucose concentration, reduced dextrose requirement, prevented recurrent hypoglycemia and was superior to IV dextrose and diazoxide after administration of sulfonylureas. Efficacy of octreotide in pediatric sulfonylurea poisoning. Fourteen pediatric patients were reported; 13 ingested second-generation sulfonylureas, with time to hypoglycemia of 1.5-16 hours. IV dextrose (10-25%) was administered before and after octreotide therapy. Octreotide was given after failure to correct hypoglycemia with IV dextrose in doses of 0.51-2 µg/kg IV or SC; two also required an IV octreotide infusion. Seven patients (50%) had recurrent hypoglycemia and received IV dextrose and additional octreotide. Efficacy of octreotide in adult sulfonylurea poisoning. Fifty-three patients were reported in prospective controlled (n=22) and retrospective (n=9) studies, case series (n=6) and case reports. Fifty-one ingested second-generation sulfonylureas with time to hypoglycemia of 1-13 hours. All received IV dextrose (10-50%) before and after octreotide treatment. Octreotide 40-100 µg SC or IV was administered followed by additional doses in most patients; three patients also required an IV infusion. Octreotide significantly increased serum glucose concentrations, decreased dextrose requirement and recurrent hypoglycemic events compared with IV dextrose. Recurrent hypoglycemia was recorded in 22-50% of the patients treated with octreotide. Therapeutic recommendations. Based on the published clinical and pharmacokinetic data of sulfonylureas and octreotide, we suggest the following dose regimens: in children, octreotide 1-1.5 µg/kg IV or SC, followed by 2-3 more doses six hours apart. In adults, octreotide 50 µg SC or IV, followed by three 50 µg doses every six hours. During this treatment IV dextrose infusion should be gradually tapered off. Adverse events. Hypertension and apnea were recorded in one pediatric patient 30 minutes after IV octreotide; the relationship to octreotide is unclear. One adult patient with chronic renal failure treated with atenolol developed severe hyperkalemia. Conclusions. Although relatively limited, the available data suggest that octreotide should be considered first-line therapy in both pediatric and adult sulfonylurea poisoning with clinical and laboratory evidence of hypoglycemia. Maintenance doses of octreotide may be required to prevent recurrent hypoglycemia.