Comparison of Octreotide and Standard Therapy Versus Standard Therapy Alone for the Treatment of Sulfonylurea-Induced Hypoglycemia

Charles J. Fasano, DO
Gerald O'Malley, DO
Paul Dominici, MD
Elizabeth Aguilera, MD
Daniel R. Latta, BS

From the Department of Emergency Medicine, Albert Einstein Medical Center, Philadelphia, PA.

Study objective: This study is designed to test the hypothesis that the administration of octreotide acetate (Sandostatin; Novartis Pharmaceuticals) in addition to standard therapy will increase serum glucose level measured at serial intervals in patients presenting to the emergency department (ED) with sulfonylurea-induced hypoglycemia compared with standard therapy alone.

Methods: This study was a prospective, double-blind, placebo-controlled trial. All adult patients who presented to the ED with hypoglycemia (serum glucose level ≤60 mg/dL) and were found to be taking a sulfonylurea or a combination of insulin and sulfonylurea were screened for participation in the study. Study participants were randomized to receive standard treatment (1 ampule of 50% dextrose intravenously and carbohydrates orally) and placebo (1 mL of 0.9% normal saline solution subcutaneously) or standard treatment plus 1 dose of octreotide 75 μg subcutaneously. Subsequent treatment interventions were at the discretion of the inpatient internal medicine service.

Results: A total of 40 patients (18 placebo; 22 octreotide) were enrolled. The mean serum glucose measurement at presentation was placebo 35 mg/dL and octreotide 39 mg/dL. The mean glucose values for octreotide patients compared with placebo were consistently higher during the first 8 hours but showed no difference in subsequent hours. Mean glucose differences approached statistical significance from 1 to 3 hours and were significant from 4 to 8 hours after octreotide or placebo administration.

Conclusion: The addition of octreotide to standard therapy in hypoglycemic patients receiving treatment with a sulfonylurea increased serum glucose values for the first 8 hours after administration in our patients. Recurrent hypoglycemic episodes occurred less frequently in patients who received octreotide compared with those who received placebo. [Ann Emerg Med. 2008;51:400-406.]

0196-0644/$-see front matter

doi:10.1016/j.annemergmed.2007.06.493

INTRODUCTION

Background

Hypoglycemia is a common presenting sign in emergency department (ED) patients.[1] Sulfonylureas are a widely prescribed class of oral medications for the treatment of diabetes (Table 1). Sulfonylureas are believed to stimulate insulin release from pancreatic β cells through a complex mechanism culminating in calcium influx and release of stored insulin from secretory granules within the pancreas.[1] A frequent and well-reported adverse reaction of sulfonylurea administration is persistent hypoglycemia, often necessitating hospital admission for serial glucose determinations.[2]

Importance

The American Association of Poison Control Centers reported 4,285 sulfonylurea exposures, resulting in 1,334 adverse outcomes, including 11 deaths, in 2005. Octreotide was reportedly used as an antidote 203 times.[3] The true incidence of sulfonylurea-induced hypoglycemia is higher because poisoning and overdose are frequently underreported. Whereas insulin-

Editor's Capsule Summary

What is already known on this topic

Limited prospective and retrospectively collected data suggest octreotide is effective and simplifies therapy for sulfonylurea-induced hypoglycemia. The duration of action and appropriate dosing interval for octreotide are unknown.

What question this study addressed

This 40-patient randomized controlled trial documented the effect of a single injection of octreotide on the serum glucose concentration in adult emergency department patients with hypoglycemia during therapeutic use of a sulfonylurea medication.

What this study adds to our knowledge

In patients receiving octreotide, serum glucose level was higher than that in controls but waned within 8 hours. The number of recurrent hypoglycemic episodes was lower in the octreotide group but was not abolished.

How this might change clinical practice

Octreotide improves control of hypoglycemia. Multiple doses or continuous infusion is likely needed to prolong duration of effect.

dependent diabetic patients are usually discharged home after establishing normal blood glucose levels, hospital admission is recommended for hypoglycemic patients taking oral sulfonylureas because of the long duration of effect, delayed clearance of the drugs and their metabolites, and subsequent high likelihood of recurrent hypoglycemic episodes.[2]

Several case reports and 1 prospective study in healthy volunteers have demonstrated the safety and efficacy of octreotide administration for the treatment of sulfonylurea-induced hypoglycemia.[4-7] Many toxicologists suggest that administration of octreotide be considered in treatment of patients after intentional or unintentional ingestion of a sulfonylurea with recurrent hypoglycemia.[8,9]

To our knowledge, this is the first prospective, placebo-controlled investigation of octreotide in sulfonylurea-induced hypoglycemia. Before this investigation, the use of octreotide for the treatment of sulfonylurea-induced hypoglycemia had never been compared to placebo, nor had it been evaluated prospectively in actual ED patients. Authors have called for prospective, randomized, controlled clinical trials to confirm or disprove any potential benefit of octreotide in this population.[10]

Goals of This Investigation

The primary goal of this study was to compare the effect of octreotide on serial mean serum glucose concentrations in actual hypoglycemic ED patients. A secondary goal of this investigation was to quantify the potential decrease in hypoglycemic episodes among those patients who received octreotide compared to placebo.

Table 1. Sulfonylureas or combination products approved by the US Food and Drug administration.

Generic	Trade	Generation
Tolbutamide	Orinase	First
Tolazamide	Tolinase	First
Chlorpropamide	Diabinese	First
Acetohexamide	Dymelor	First
Glyburide	Micronase, Diabeta, Glynase	Second
Glipizide	Glucotrol/Glucotrol XL	Second
Glimepiride	Amaryl	Third
Glyburide/metformin	Glucovance	Combination
Glipizide/metformin	Metaglip	Combination
Glimepiride/rosiglitazone	Avandaryl	Combination

MATERIALS AND METHODS

Study Design

The study was a prospective, randomized, double-blind, placebo-controlled trial. The study was approved by the institutional review board at our institution.

Setting

The study was conducted at an urban, community teaching hospital with 74,000 ED visits annually. Trained physician research assistants familiar with the protocol, research methodology, and the informed consent process staff the ED 24 hours per day.

Selection of Participants

All adult (>18 years old) nonpregnant patients presenting to the ED with hypoglycemia (serum glucose <60 mg/dL) diagnosed at home by family members, emergency medical services (EMS) providers, or ED personnel were identified by the emergency physician and research staff and screened for inclusion. All patients whose medications included an oral sulfonylurea, a sulfonylurea combination product, or a combination of insulin and a sulfonylurea were invited to participate (Table 1). Hypoglycemic patients whose glucose-control medications involved only insulin or a nonsulfonylurea oral agent or who were not taking any diabetes medication were excluded. Patients were screened for enrollment 24 hours per day, 7 days per week from July 1, 2005, to December 31, 2006.

After patients received standard ED therapy for hypoglycemia, 1 ampule (50 mL) of 50% dextrose was administered intravenously and oral carbohydrates were provided. Informed consent was obtained from patients after they returned to baseline mental status or from their families or surrogates.

Nonparticipation in the study did not preclude the patient from receiving octreotide at the discretion of the treating physicians.

Randomization was performed before the start of the study by pharmacy personnel using a table created with a

randomization generator (available at http://www.randomization.com). The randomization table was kept by the pharmacy for the duration of the study.

Interventions

Study patients were randomized to one of 2 treatment arms:

1. 1 ampule (50 mL) of 50% dextrose intravenously and carbohydrates orally plus placebo (1 mL of 0.9% normal saline solution subcutaneously)
2. 1 ampule (50 mL) of 50% dextrose intravenously and carbohydrates orally plus octreotide 75 μg (approximately 1 mL) subcutaneously.

Oral carbohydrates consisted of an 8-oz can of Boost Plus (Novartis Medical Nutrition, Minneapolis, MN), a commercially available nutritional supplement containing 360 calories and 45 g of carbohydrates.

All enrolled patients were admitted to the hospital and monitored for recurrent hypoglycemic episodes for a minimum of 24 hours. All patients with recurrent hypoglycemia occurring in the ED were treated with single bolus dose of 50% dextrose intravenously and reevaluated. Once patients left the ED and were admitted to the inpatient medical unit, management decisions and interventions were at the discretion of the inpatient medical service, although all patients were identified as research subjects to the admitting house staff.

Methods of Measurement

CBC count, basic metabolic panel (electrolytes, glucose, and renal function) and estimated body mass index were measured in all subjects. Serum creatinine was measured in all subjects for the purpose of calculating creatinine clearance. Bedside glucose determinations were collected hourly for 4 hours and then every 2 hours for 24 hours. In the event that the bedside glucose determination was not collected at the specified interval, data points were assigned to the closest 2-hour interval for the purposes of analysis.

Data Collection and Processing

Nurses and research assistants obtained all bedside glucose measurements with a Roche Inform Glucose Meter. Daily quality control measurements were recorded on all machines in the ED to validate the accuracy of the bedside measurements. The Department of Pathology and Laboratory Medicine performed monthly quality control measurements according to standing protocol on all machines used in the study. Data were collected by trained unblinded emergency medicine research assistants using preprinted data collection sheets.

Outcome Measures and Primary Data Analysis

To assess differences in glucose over time between treatment groups, ANOVA in repeated measures was used. For analysis purposes, glucose determinations were averaged during 3 4-hour intervals, creating 5 time points (baseline, 1 to 3 hours, 4 to 8 hours, 9 to 12 hours, and 13 to 16 hours). Only patients with at least 1 value for each of the averaged time points were included in the final ANOVA. To adjust for multiple pairwise comparisons between treatment groups at each time point, the Tukey-Kramer method was used. Student's *t* test was used to test for differences between treatment groups with regard to number of glucose measurements and baseline glucose concentration. Where applicable, data are presented as mean differences with 95% confidence intervals (CIs). All analyses were performed using SAS statistical software (version 9.1; SAS Institute, Inc., Cary' NC). $P<.05$ was considered statistically significant.

Sensitivity Analyses

Sample size calculation based on 1 previous experiment in healthy volunteers[4] estimated a sample size of 20 subjects in each arm to have 80% power to detect a mean serum glucose difference of 40 mg/dL, with a significance level (α) of 0.05 (2-tailed) (SD=70). No power calculation was performed on the secondary outcome measure of difference in absolute hypoglycemic events between the 2 groups.

RESULTS

Characteristics of Study Subjects

A total of 358 hypoglycemic patients were screened for participation. Two hundred forty-two were excluded because they did not meet inclusion criteria. Of those patients not meeting inclusion criteria, 216 were found not to be taking a sulfonylurea, and an additional 20 had a serum glucose level greater than 60 mg/dL. Three patients were previously enrolled, and an additional 3 patients did not meet inclusion criteria, because the class of oral hypoglycemic medication could not be verified owing to a language barrier. One hundred sixteen patients met inclusion criteria and were offered participation in the study. Seventy-four patients either declined or were unable to provide informed consent because of altered mental status. Forty-two patients agreed to participate. Two patients were enrolled mistakenly and were subsequently removed from the study. The protocol violation was reported to the institutional review board (each patient was taking an oral diabetes medication not in the sulfonylurea class). Both patients received placebo and neither had an adverse outcome. Of the 40 remaining subjects, 22 patients were randomized to receive octreotide and 18 to receive placebo (Figure 1). There were no adverse events reported at 24 and 72 hours.

One subject randomized to receive placebo was treated with a sulfonylurea (glipizide) at approximately 12 hours after enrollment by the internal medicine service because of an increased serum glucose level of 346 mg/dL. The patient subsequently had an episode of hypoglycemia at hour 18. Data points for the first 12 hours after study enrollment are included in the analysis, but data after the administration of glipizide were excluded. This hypoglycemic episode was omitted from the comparison of rates of hypoglycemia between the 2 groups.

The mean age of study participants in the octreotide and placebo groups was 66 years and 70 years, respectively. Men composed 32% of the octreotide subjects and 61% of the

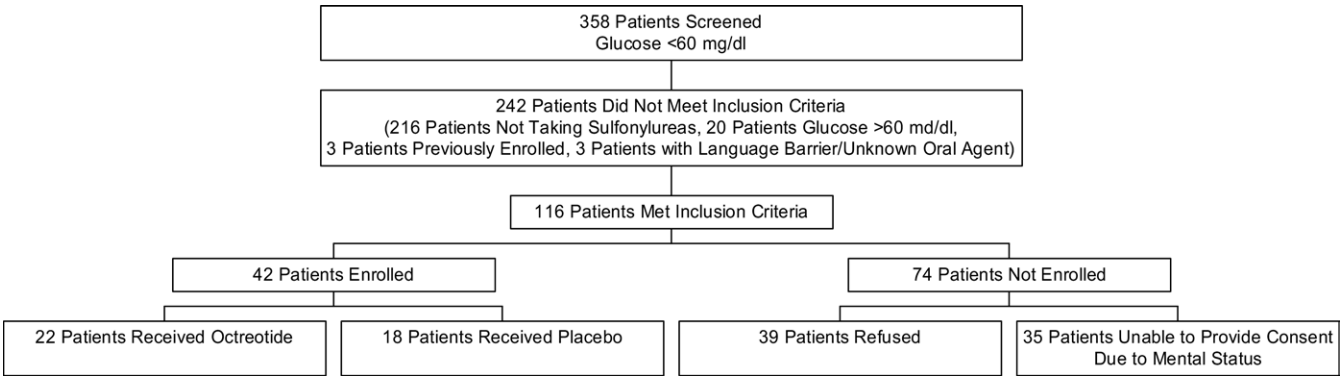

Figure 1. Disposition of patients screened for hypoglycemia.

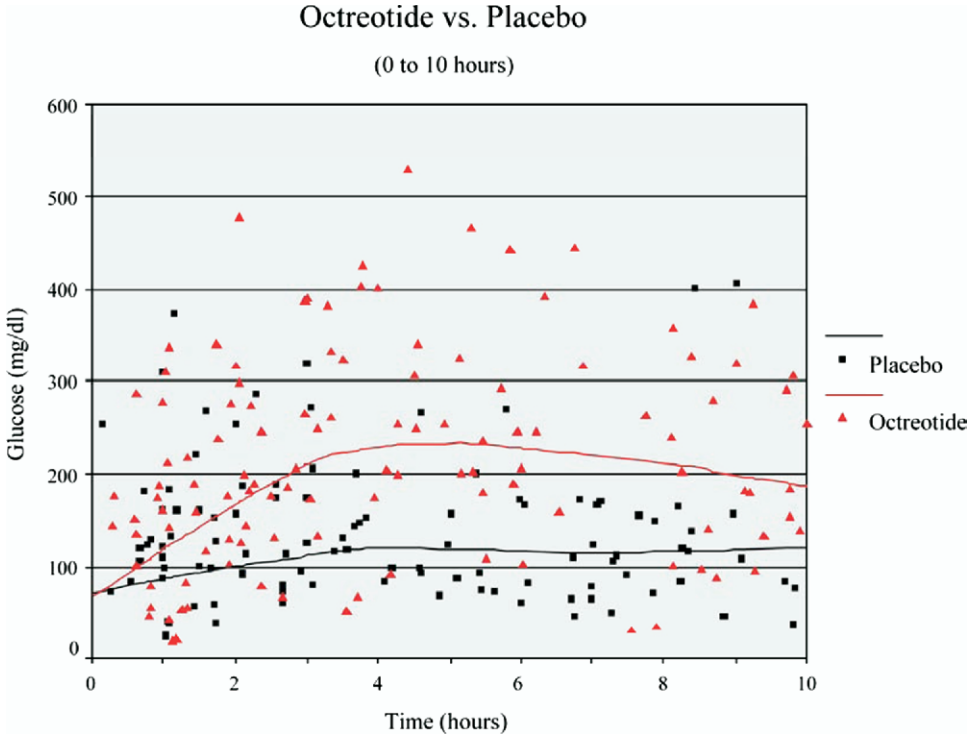

Figure 2. Serum glucose octreotide versus placebo.

placebo group. Blacks accounted for 96% of the octreotide and 78% of the placebo group. The mean baseline glucose level for the octreotide arm was 39 mg/dL; placebo, 35 mg/dL.

The 2 cohorts were similar in terms of renal function. The mean estimated creatinine clearance ([[140−age (years)]×weight (kg)]/[72×serum creatine (mg/dL)]×0.85 for women) of the octreotide group was 56 mL/minute (95% CI 38.7 to 72.7 mL/minute; SD 40.73) and 68 mL/minute (95% CI 54.1 to 81.0 mL/minute; SD 29.2) in the placebo group.

Main Results

Glucose values for octreotide patients compared with placebo were consistently higher during the first 8 hours but showed no difference in subsequent hours (drug/time interaction, $P<.0001$; Figure 2). Mean glucose differences (octreotide–placebo) at each time point were as follows: 0 hours 1 mg/dL, 95% CI −59 to 60 mg/dL, $P=1.0$; 1 to 3 hours 56 mg/dL; 95% CI −3 to 115 mg/dL, $P=0.08$; 4 to 8 hours 127 mg/dL, 95% CI 68 to 187 mg/dL, $P<.001$; 9 to 12 hours 16 mg/dL, 95% CI −43 to 76 mg/dL, $P=.99$; 13 to 16 hours −2 mg/dL, 95% CI −61 to 57 mg/dL, $P=1.0$ (Table 2).

There were a total of 22 hypoglycemic episodes (glucose <60 mg/dL). There were 10 solitary hypoglycemic events in 10 of the 22 patients (45%) who received octreotide. No patient who received octreotide had more than 1 hypoglycemic episode. Five of the 10 patients who received octreotide and

Table 2. Mean difference in serum glucose, octreotide versus placebo.

Time After Medication Administration, h	Mean Glucose Difference, Octreotide Versus Placebo, mg/dL	95% CI	*P* Value
0	1	59 to 60	1.0
1–3	56	−3 to 115	.08
4–8	127	68 to 187	<.001
9–12	16	43 to 47	.99
13–16	−2	61 to 52	1.0

subsequently had a hypoglycemic episode experienced the event at the first hourly serum glucose determination after study drug administration (Table 3). There were a total of 13 hypoglycemic events among 6 of the 18 (33%) patients who received placebo. Three patients who received placebo had multiple (2 to 4) hypoglycemic events.

LIMITATIONS

Our inclusion criteria allowed for a wide range of subjects with comorbidity. We did not control for physiologic or pathologic differences among the subjects, and the study was not powered to do subgroup analysis.

No distinction was made between different sulfonylureas (Table 1). It is conceivable that patients ingesting first-generation sulfonylureas with longer elimination half-lives would have a higher potential for recurrent hypoglycemia compared with patients ingesting the second- or third-generation agents.

The informed consent process and patient enrollment were more challenging than expected. Many eligible patients were excluded because of their inability to provide informed consent due to some degree of altered mental status, presumably from hypoglycemia or baseline dementia.

We defined hypoglycemia at a value of 60 mg/dL. No distinction between clinical and numeric hypoglycemia was made in this study. This approach has been criticized in a previous case series investigating the use of octreotide in hypoglycemia.[7] All patients presented to EMS providers or the ED with clinical symptoms consistent with hypoglycemia (Table 3).

We maintained a high degree of compliance and consistence with bedside glucose measurements during the initial 4- to 8-hour period in the ED but had variable success once the patients were monitored on the medical wards. Similarly, there was no standardized protocol for the infusion of dextrose-containing intravenous fluids once the patient left the ED, perhaps leading to unforeseen variability in subsequent serum glucose levels.

No quantitative sulfonylurea drug levels, insulin levels, or c-peptide levels were obtained, largely because of the significant added cost of such tests and our desire to replicate actual scenarios encountered by practicing emergency physicians. Serum levels of drug might clarify the degree to which the hypoglycemia was a result of the sulfonylurea as opposed to some other cause.

Thirty patients (75%) were unwilling to ingest their initial oral carbohydrate load with Boost Plus and preferred a standard hospital food tray (average of 600 total calories).

The majority of our study patients (88%) were black, reflecting the demographics of our patient population, and our results may not be applicable to other ethnic groups. Similarly, despite computer randomization there was a disproportionate representation of male patients between the octreotide and placebo groups (32% versus 61%).

DISCUSSION

Octreotide is a somatostatin analog that is known to suppress several hormones, including insulin.[11] Dextrose itself induces insulin secretion, theoretically contributing to rebound hypoglycemia when used to treat low blood sugar.[1,11] Octreotide is thought to lower insulin levels that result from either dextrose or a sulfonylurea medication.[1] We believe our study to be the first prospective, randomized investigation of octreotide in sulfonylurea-induced hypoglycemia.

Several case reports and 1 prospective study in healthy volunteers have demonstrated the safety and efficacy of octreotide administration for the treatment of sulfonylurea-induced hypoglycemia.[4,5,8] Boyle[4] showed that treatment with octreotide reduced the need for exogenous dextrose administration among healthy volunteers who had ingested glipizide compared with individuals treated with dextrose or diazoxide. McLaughlin and McKinney[8] published a retrospective case series of 9 individuals successfully treated with octreotide for recurrent sulfonylurea-induced hypoglycemia, found a marked reduction in the risk of recurrent hypoglycemia, and concluded that octreotide and dextrose should be considered first-line therapy in the aforementioned clinical scenario. Similarly, Bronwyn[5] reported 2 severely ill patients with persistent sulfonylurea-induced hypoglycemia who were successfully treated with an intravenous infusion of octreotide, as evidenced by stabilization of serum glucose and decrease of markedly increased serum insulin and c-peptide levels.

Octreotide is not approved by the US Food and Drug Administration for the treatment of sulfonylurea-associated hypoglycemia, although many toxicologists routinely recommend its use in this clinical scenario.[2,6,9] Common adverse reactions of treatment with octreotide include nausea, abdominal cramps, diarrhea, malabsorption of fats, and flatulence. These effects usually start within hours of the initiation of therapy and usually subside spontaneously in 10 to 14 days, despite continued treatment. Approximately 20% to 30% of patients treated with octreotide for more than 1 month will develop cholesterol gallstones. The mechanism is uncertain but may involve decreased gallbladder emptying caused by complex effects on several hormonal pathways.[11] These adverse effects are likely of minimal consequence to emergency physicians using the drug to treat sulfonylurea-associated hypoglycemia.

An understanding of the pharmacokinetics of octreotide provides insight into the results of our investigation. In healthy volunteers, octreotide is absorbed rapidly and completely after

Table 3. Characteristics of study participants.

Patient Number	Sulfonylurea	Dose, mg	Number of Hypoglycemic Events	Time to Hypoglycemic Event, h	Chief Complaint
Placebo					
4	Glipizide	10	4	2, 10, 13, 15	Diaphoresis
5	Glipizide	10	0		Confusion
8	Glipizide	10	0		Weakness
9	Glyburide	5	0		Unresponsiveness
10	Glipizide	10	0		Decreased responsiveness, lethargy
11	Glipizide	5	0		Decreased mental status
14	Glipizide	5	2	7, 9	Fall, altered mental status, failure to thrive
16	Glyburide	5	1	17	
17	Glimepiride	8	0		Altered mental status
23	Glipizide	Unknown	0		Dizziness, blurred vision
25	Glipizide	10	1	1	Weakness
27	Glipizide	10	3	8, 10, 11	Confusion, disoriented
30	Glimepiride	4	0		Confusion, diaphoresis
32	Glipizide	3	1	1	Altered mental status
33	Glipizide	10	1	1	Slurred speech
37	Glyburide	5	0		Decreased mental status
39	Glimepiride	4	1*	18	Diaphoresis
42	Glipizide	5	0		Weakness, tiredness
Octreotide					
1	Glyburide	5	1	13	Altered mental status
3	Glipizide	Unknown	0	0	Weakness
6	Glipizide	10	1	1	Weakness, dizziness
7	Glipizide	Unknown	0	0	Syncopal event
12	Glipizide	5	0	0	Confusion
13	Glipizide	5	1	12	Blurred vision, lightheadedness, shaking
15	Glipizide	5	0	0	Weakness
18	Glipizide	Unknown	1	8	Altered mental status
19	Glipizide	10	1	1	Weakness
20	Glimepiride	8	0	0	Confusion
22	Glyburide	5	0	0	Altered mental status, hypoglycemia
24	Glipizide	5	0	0	Decreased responsiveness, syncope
26	Glipizide	10	1	1	Hypoglycemia, shaking, weakness
28	Glipizide	2.5	1	1	Fall
29	Glyburide	5	0	0	Dizziness
31	Glyburide	5	1	1	Blurry vision, numbness in hands
34	Glipizide	10	0	0	Confusion
35	Glyburide	3	0	0	Weakness, dizziness
36	Glimepiride	4	0	0	Weakness
38	Glyburide	5	1	3	Syncope
40	Glipizide	5	1	7	Altered mental status
41	Glyburide	5	0	0	Confusion, disoriented

*Patient received glipizide at hour 12; see Discussion.

subcutaneous injection. Peak concentrations of 5.2 ng/dL (100-μg dose) were reached 0.4 hours after injection.[12] The elimination of octreotide from plasma had an apparent half-life of 1.7 to 1.9 hours. Approximately 32% of the dose is excreted unchanged in the urine. In patients with renal impairment, the elimination of octreotide from plasma was prolonged. In persons with mild renal impairment (creatine clearance 40 to 60 mL/minute), the half-life was 2.4 hours, and in those with moderate and severely decreased renal function (creatine clearance 10 to 39 mL/minute and <10 mL/minute), the half-life increased to approximately 3 hours. Additionally, in patients with cirrhosis or fatty liver disease the half-life of octreotide increased to nearly 3.5 hours.[12]

Octreotide should have minimal effect on serum glucose level 8 to 10 hours after a single subcutaneous injection. In patients with normal renal function, the medication is eliminated quickly. In patients with renal insufficiency and a predicted half-life of 3 hours, only one eighth of the original drug would be available at hour 9. None of our patients had demonstrable renal insufficiency, which most likely explains the lack of octreotide effect after 8 hours.

The indications and ideal dosing regimen of octreotide for sulfonylurea-induced hypoglycemia are not established. Some authors advocate the administration of octreotide after a single hypoglycemic episode and others, only after a second decreased glucose measurement.[2,6,8,9] Route of administration and dosing

intervals also vary widely in the literature.[6] For simplicity, we chose a single subcutaneous injection after 1 hypoglycemic episode.

Our results show no significant difference in mean glucose level among octreotide and placebo after 9 to 12 hours, which may represent either underdosing or inadequate dosing regimen (1 subcutaneous dose as opposed to repeated doses or continuous infusion) (Table 2). Subtherapeutic dosing of octreotide has been mentioned as contributing to treatment failure.[6]

Five of the 10 patients who received octreotide and subsequently had a hypoglycemic episode had the event within the first hour after study drug administration. A possible explanation is that the onset of action of octreotide in actual ED patients is greater than 1 hour.

None of the 40 study participants were believed to have consumed a large amount of sulfonylurea as an attempt at suicide. Case reports have demonstrated improvement in serum glucose level after massive glyburide overdose (500 to 1000 mg).[13,14] Because of the absence of any study participants with suspected intentional sulfonylureas overdose, we can make no comment on the efficacy of octreotide in this subpopulation. Additionally, no children were included in the protocol, although several case reports have illustrated the safety and efficacy of octreotide in children for the treatment of hypoglycemia after the ingestion of sulfonylureas.[15]

Our results suggest that it would be prudent to admit all patients with sulfonylurea-induced hypoglycemia to the hospital for frequent blood glucose determinations. We found that although patients who received a single dose of octreotide were less likely to experience multiple subsequent hypoglycemic episode compared with placebo, such patients are still at risk of further solitary hypoglycemic events.

To our knowledge, this is the first study demonstrating the efficacy of octreotide for the treatment of sulfonylurea-induced hypoglycemia in an actual ED population in a randomized double-blinded protocol. The results from this study show a statistically significant increase in mean glucose level among patients who received octreotide compared with placebo. The effects are most pronounced in the first 4 to 8 hours after the administration of a single 75-μg subcutaneous dose. Recurrent hypoglycemic episodes occurred less frequently in patients who received octreotide compared with those who received placebo. There were no adverse events recorded within the first 72 hours after octreotide administration.

Supervising editor: Richard C. Dart, MD, PhD

Author contributions: CJF and GO conceived the study and designed the trial. CJF, PD, EA, and DRL supervised the conduct of the trial and data collection. CJF, PD, EA, and DRL undertook recruitment of patients and managed the data, including quality control. GO, PD, and DRL provided statistical advice on study design and data analysis. CJF drafted the article, and all authors contributed substantially to its revision. CJF takes responsibility for the paper as a whole.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article, that may create any potential conflict of interest. The authors have stated that no such relationships exist. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement.

Publication dates: Received for publication February 9, 2007. Revisions received March 20, 2007; April 23, 2007; and May 21, 2007. Accepted for publication June 8, 2007. Available online August 30, 2007.

Earn CME Credit: Continuing Medical Education for this article is available at: www.ACEP-EMedHome.com.

Presented as preliminary data at the Society for Academic Emergency Medicine annual meeting, May 2006, San Francisco, CA.

Reprints not available from the authors.

Address for correspondence: Charles J. Fasano, DO, Department of Emergency Medicine, Albert Einstein Medical Center, 5501 Old York Road, Philadelphia, PA 19141; 215-456-5994; fax 215-456-8502; E-mail fasanoc@einstein.edu.

REFERENCES

1. Harrigan RA, Nathan MS, Beattie P. Oral agents for the treatment of type 2 diabetes mellitus: pharmacology, toxicity and treatment. *Ann Emerg Med*. 2001;38:68-78.
2. Bosse GM. Antidiabetic and hypoglycemic agents. In: Goldfrank LR, Flomenbaum NE, Lewin NA, et al, eds. *Goldfrank's Toxicologic Emergencies*. 7th ed. New York: McGraw-Hill; 593-603.
3. Lai MW, Klein-Schwartz W, Rodgers GC, et al. 2005 Annual report of the American Association of Poison Control Centers' national poisoning and exposure database. *Clin Toxicol*. 2006;44:803-932.
4. Boyle PJ. Octreotide reverses hyperinsulinemia and prevents hypoglycemia induced by sulfonylurea overdoses. *J Clin Endocrinol Metab*. 1993;76:752-756.
5. Bronwyn AL. Octreotide for the treatment of sulfonylurea-induced hypoglycemia. *Med J Aust*. 2004;180:540-541.
6. McLaughlin SA. Octreotide: an antidote for sulfonylurea-induced hypoglycemia. *Ann Emerg Med*. 2000;36:133-138.
7. Schier JG. Octreotide as antidote for sulfonylurea-induced hypoglycemia [letter]. *Ann Emerg Med*. 2001;37:417.
8. McLaughlin SA, McKinney PE. Octreotide. In: Dart RC, ed. *Medical Toxicology*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 230-232.
9. Howland MA. Antidotes in depth. Octreotide. In: Goldfrank LR, Flomenbaum NE, Lewin NA, et al, eds. *Goldfrank's Toxicologic Emergencies*. 7th ed. McGraw-Hill; 611-613.
10. Lheureux PE, Zahir S, Penaloza A, et al. Bench-to-bedside review: antidotal treatment of sulfonylurea-induced hypoglycemia with octreotide. *Crit Care*. 2005;9:543-549.
11. Lamberts SW, et al. Drug therapy: octreotide. *N Engl J Med*. 1996;334:246-254.
12. Novartis Corporation. Available at: http://www.us.sandostatin.com.
13. Carr R. Octreotide for sulfonylurea-induced hypoglycemia following overdose. *Ann Pharmacother*. 2002;36:1727-1732.
14. Green RS, Palatnick W. Effectiveness of octreotide in a case of refractory sulfonylurea-induced hypoglycemia. *J Emerg Med*. 2003;25:283-287.
15. Tenenbein M. Recent advancements in pediatric toxicology. *Pediatr Clin North Am*. 1999;46:1179-1188, vii.