CASE

# Prolonged hypoglycemia due to sulfonylurea in an elderly woman.

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***Abstract:*** Overuse of antidiabetic medications is the most common cause of hypoglycemia in diabetic subjects. Here, we report a case of hypoglycemia associated with sulfonylurea administration. An 83-year-old female patient was admitted to the emergency department with complaints of loss of consciousness and fainting. The patient's blood glucose level was of 33 mg/dL, and she received emergency treatment with an intravenous 10% dextrose solution. In conclusion, sulfonylureas in combination with antidiabetic therapy increase the risk of hypoglycemic events in elderly patients with renal failure. Therefore, we suggest that physicians should closely monitor these patients for hypoglycemia and, preferably, use drugs that have less hypoglycemia side effects.
***Keywords:*** hypoglycemia; sulfonylurea; diabetes mellitus.

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## INTRODUCTION

Hypoglycemia is a life-threatening complication associated with the treatment of diabetes mellitus. Hypoglycemia manifests as a variety of symptoms resulting from an absolute or relative decrease in blood glucose, which is characterized by various clinical findings *(Scheen, 2014)*. Symptoms of hypoglycemia can be divided into two categories including adrenergic and neuroglycopenic symptoms. Adrenergic symptoms include tremulousness, palpitations, anxiety, sweating, hunger, and paresthesia. Neuroglycopenic symptoms include confusion, weakness, fatigue, cognitive failure, behavioral changes, seizures, coma, and even death *(Towler et al., 1993).*

Although hypoglycemia is usually observed in elderly patients receiving sulfonylurea, its etiology may include alcohol use, sepsis, insulin use, and oral antidiabetic drugs use. In addition, patients with liver and renal insufficiency have a higher risk of hypoglycemia. We report a case of hypoglycemia associated with sulfonylurea in a patient who responded well to the dextrose infusion.

## CASE REPORT

An 83-year-old female patient was admitted to the emergency department with complaints of loss of consciousness and fainting. The patient's blood glucose level was 33 mg/dL, and she received emergency treatment with the intravenous administration of a 10% dextrose solution. On follow-up, her clinical condition improved and responded well to the dextrose infusion. After 15 minutes, the blood glucose level was 55 mg/dL, and the patient was admitted to the internal medicine clinic.

An obese *(body mass index: 35kg/m$^2$)* elderly woman was admitted to our clinic with prominent tachypnea. Her blood pressure was 130/60 mmHg,

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her heart pulse was arrhythmic *(160 beats per minute)*, her body temperature was 36.7 °C, her respiratory rate was 28 per minute and oxygen saturation was 95%. The patient's jugular vein was bulging. The first and second heart sounds were normal without additional sounds or murmur. Crackles were heard up to the middle zones in both hemithoraces with decreased respiratory sounds in the lower zones of the right hemithorax. Bilateral pretibial edemas *(+++)* were observed in the patient. The remainder of the physical examination was unremarkable.

The patient was monitored for hourly blood glucose levels, which were resistant to treatment and considered low; therefore, dextrose infusion was continued. The hypoglycemia in the patient lasted for approximately 48 hours.

The patient had a 7-year history of chronic renal failure and a 20-year history of type 2 diabetes mellitus and hypertension. Her medications included glimepiride *(2 mg once a day)*, metformin *(1 g once a day)*, pioglitazone *(15 mg once a day)*, perindopril/hydrochlorothiazide *(10/2.5 mg once a day)*. She stated that she had never previously developed any symptoms of hypoglycemia.

The patient did not describe a decrease in appetite, alcohol use, or excessive use of antidiabetic medications. The patient's HbA1c level was 5.5%, indicative of tight glycemic control with possible previously unnoticed hypoglycemia episodes. The serum creatinine level was 1.47, thus the glomerular filtration rate *(GFR)* was calculated as 33%. The cortisol value to discard adrenal insufficiency was 13.3 *(reference range: 3.7–19.4)*.

The patient's hypoglycemia was thought to be due to glimepiride use. After 48 hours, hypoglycemia resolved completely. Intravenous dextrose infusion was discontinued after the 48th hour of admission to the clinic. However, blood glucose was closely monitored as often as eight times a day. Oral antidiabetic drugs were replaced with insulin glargine at 10 IU daily. Her blood glucose was maintained by treatment with long-acting insulin once daily. She was discharged from the hospital fully recovered.

## DISCUSSION

Antidiabetic medications of the sulfonylurea group increase insulin release by inhibiting ATP-dependent potassium channels in pancreatic beta cells. Sulfonylureas generally reduce blood glucose concentration by about 20% and decrease HbA1c levels by 1–2% (*Bressler & Johnson, 1997)*.

Hypoglycemia is the most common side effect of sulfonylurea administration. Furthermore, the excretion of sulfonylureas from the kidney increases the risk of hypoglycemia in patients with chronic kidney disease. The estimated GFR of 33% in the studied patient signifies grade 3 chronic renal failure. Glimepiride should be used cautiously, and the dose should be reduced in patients with renal failure because it may cause long-lasting hypoglycemia *(Charpentier et al., 2000)*.

Leonard et al. *(2018)* compared the risk of hypoglycemia in patients receiving oral antidiabetic drugs as monotherapy either with metformin, sulfonylurea, meglitinide or thiazolidinedione; the results showed that sulfonylureas were associated with the highest rate of hypoglycemia. The studied patient was receiving three different oral antidiabetic agents, one of which was sulfonylurea.

The analysis of hypoglycemia rates in diabetic patients receiving multiple oral antidiabetic drugs has led to the conclusion that hypoglycemia was more common in patients who received multiple oral antidiabetic medications compared to those on monotherapy *(Naser et al., 2018)*. The case presented here involved a combined therapy of three oral antidiabetics.

Farahani *(2018)* compared the hypoglycemia rates of subjects treated with metformin plus a sulfonylurea to those treated with metformin plus an SGLT2 inhibitor. The results of this study showed that hypoglycemia was more common in patients receiving sulfonylurea compared to those receiving SGLT2 inhibitors *(Farahani, 2018)*. An analysis of drug-induced hypoglycemia in diabetic subjects over 80 years of age showed that hypoglycemia was more common in diabetic elderly subjects who were treated aggressively with long-acting sulfonylureas *(Greco & Angileri, 2004)*.

Hypoglycemia was less common in patients receiving short-acting sulfonylureas compared to those diabetics treated with sulfonylureas with long-acting effects *(Stahl & Berger, 1999)*. The patient in the present case was treated with glimepiride, which has long-acting effects.

In conclusion, since sulfonylureas and multiple antidiabetic drug therapy increase the risk of hypoglycemic

events in elderly patients with renal failure, we suggest that physicians should closely monitor these patients for hypoglycemia and, preferably, use drugs that have less hypoglycemia side effects.

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