

Case Report

Octreotide Treatment for Hypoglycemic Refractory Case Caused by Sulfonylureas with Impaired Renal Function

Terapi Octreotide pada Kasus Refrakter Hipoglikemik yang Disebabkan Oleh Penggunaan Sulfonilurea dengan Gangguan Fungsi Ginjal

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ABSTRACT

Hypoglycemia is an emergency case that is caused by antidiabetic drugs from the sulfonylurea class. Prolonged and refractory hypoglycemia can increase mortality and morbidity. Renal impairment can result in recurrent hypoglycemic symptoms and require special treatment. In this study case, a 47-year-old woman with newly impaired renal function presented in a coma caused by hypoglycemia due to the use of glibenclamide (sulfonylurea drugs) that did not respond to standard hypoglycemic treatment. Treatment of refractory hypoglycemia is a challenge in itself. Octreotide may be considered in cases of refractory hypoglycemia that does not respond to standard glucose treatment, where in this case refractory hypoglycemia is caused by accumulating sulfonylurea because of impaired renal function.

Keywords: *Glibenclamide, octreotide, overdose, refractory hypoglycemia, sulfonylureas*

ABSTRAK

Hipoglikemia merupakan kasus kegawatdaruratan yang dapat disebabkan oleh obat antidiabetes golongan sulfonilurea. Hipoglikemia yang berkepanjangan dan refrakter dapat meningkatkan mortalitas dan morbiditas. Gangguan ginjal dapat mengakibatkan gejala hipoglikemik berulang dan memerlukan perawatan khusus. Studi kasus ini, seorang wanita 47 tahun dengan gangguan fungsi ginjal yang baru diketahui datang dengan kondisi koma yang disebabkan oleh hipoglikemia karena penggunaan glibenklamid (obat sulfonilurea) yang tidak merespon pengobatan hipoglikemik standar. Pengobatan hipoglikemia refrakter merupakan tantangan tersendiri. Terapi oktreotid dapat digunakan sebagai antidote hipoglikemia refrakter pada overdosis sulfonilurea.

Kata Kunci: Gangguan fungsi ginjal, glibenklamid, hipoglikemia refrakter, overdosis, octreotide, sulfonilurea

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INTRODUCTION

Hypoglycemia is an endocrine emergency that is very life-threatening and can cause mortality and morbidity (1,2). Hypoglycemia is a condition that can be easily recognized and treated quickly. Hypoglycemia symptoms include autonomic and neurological symptoms. The most common cause of hypoglycemia in diabetic patients is antihyperglycemic drugs and insulin (1).

Hypoglycemic conditions in patients with chronic kidney disease increase in the sulfonylurea drug administration (3,4). The mechanism of sulfonylureas is to stimulate insulin release from the pancreas. Glibenclamide is a long-acting sulfonylurea, metabolized in the liver and excreted in the kidneys (5). Glibenclamide is not recommended for the treatment of diabetes mellitus in cases of chronic renal failure because it can increase the risk of severe hypoglycemia (6). The use of sulfonylureas can cause recurrent hypoglycemic conditions and the use of octreotide can be considered to overcome this problem (7).

CASE REPORT

A 47-year-old woman came to the Emergency Department of Dr. Saiful Anwar Hospital (RSSA) with chief complaints of an altered mental state for 3 hours before admission. The patient had a gradual decrease of consciousness for 1 week starting with general weakness and worsening 3 hours before arriving in the Emergency Department. The patient didn't have a history of fever, vomiting, and trauma. The patient had hypertension and diabetic mellitus with routine consumed captopril 3x12.5mg and glibenclamide 2x5mg a day.

On physical examination her blood pressure was 201/98 mmHg, heart rate was 90 beats per minute, respiratory rate was 20 times per minute, her temperature was 36°C and saturation was 98% room temperature. Her GCS was 11 and the other neurological status was within normal limits. She had palpebra edema and pale conjunctiva in both eyes. She had pretibial edema on her both legs and tropic change. Her random blood glucose was 20mg/dL (Table 1).

Table 1. Laboratory result

Characteristic	Value
Blood glucose	24mg/dL
Hb	10.5g/dL
Ureum	148.3mg/dL
Creatinine	4.88mg/dL
eGFR	10mL/minute/1.73 m ²

An altered mental state due to hypoglycemia was diagnosed and initial treatment of glucose 50cc D40 was given to her. After 30 minutes of observation GCS was improved to 456 with random blood glucose was 76mg/dL and after 1 hour of initial treatment her blood glucose dropped to 45mg/dL. A second D40 was given and a maintenance D10 to maintain her blood glucose. 30 minutes after being given the second therapy her blood glucose was 52mg/dL and octreotide 100µg was given by

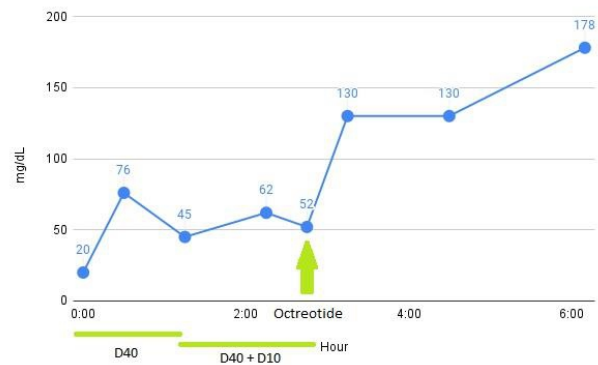


Figure 1. Blood glucose timeline. D40 and D10 = 40 and 10% dextrose.

DISCUSSION

Hypoglycemia can be severe and prolonged and can lead to neurologic impairment, sequelae, and death. Symptoms of hypoglycemia can include dizziness, weakness, headache, confusion, drowsiness, coma, and seizures. Autonomic symptoms may also occur, such as shaking, palpitations, diaphoresis, and nausea (8). This patient has neurologic symptoms in the form of a coma without autonomic symptoms.

Patient has a history of hypertension and diabetes mellitus with regular treatment by buying drugs without a prescription. Patient had no previous history of renal and liver impairment. Treatment of diabetes mellitus using glibenclamide 2x5 mg which is a sulfonylurea drug.

The results of randomized glucose testing of patients with 20mg/dL and neurologic symptoms such as decreased level of consciousness, so the diagnosis of hypoglycemia due to oral antidiabetic drugs can be confirmed. Initial therapy of the patient was given D40 50 cc and the patient experienced clinical improvement with increasing mental state. The results of the patient's re-examination of glucose showed improvement and increased to 76mg/dL after 30 minutes.

Glibenclamide is metabolized in the liver and eliminated in the kidney. Glibenclamide has a long-acting effect (5). Sulfonylureas bind to and inhibit the ATP-sensitive potassium channels (K) in the pancreatic beta cells. As a result, potassium efflux decreases, and the beta-cell membrane depolarizes. Membrane depolarization causes calcium channels to open, leading to calcium influx and increased intracellular calcium, which stimulates insulin secretion from the pancreatic beta cells (9).

On laboratory examination, the patient showed urea 148.3mg/dL, creatinine 4.88mg/dL, and eGFR 10mL/minute/1.73m². According to the classification of the Kidney Disease: Improving Global Outcomes (KDIGO) the patient includes stage 5 chronic renal failure (10).

Due to the excretion of glibenclamide in the kidneys, this drug is contraindicated for the treatment of diabetes mellitus because some metabolites are active and can accumulate in chronic Kidney Disease so which will cause a hypoglycemic effect in the patient (5,9).

After observing vital signs and checking glucose for 1 hour, the patient's blood glucose dropped to 45mg/dL then D40 50cc and maintenance D10 were given to maintain the

patient's blood glucose. Treatment of hypoglycemia is by giving intravenous dextrose at a dose of 0.5 to 1 g/kg using D50W (8). Thirty minutes after administering the second D40 and D10 maintenance, blood glucose was re-examined and the result was 52mg/dL without neurological and autonomic symptoms.

In this case, the patient had refractory hypoglycemia because the patient was taking glibenclamide and had impaired renal function. The patient has refractory hypoglycemia after management standard treatment of hypoglycemia with administration of D40 then followed by administration of D10 as maintenance.

The sulfonylurea overdose was considered and strengthened by the patient's impaired renal function, and the antidote to the sulfonylurea overdose was started. Administration of octreotide 100mg IV is given to the patient to maintain the patient's glucose level.

After the administration of octreotide, the patient's blood glucose level was checked regularly every hour to observe the patient's blood glucose level. After administration of octreotide, the patient's glucose level improved and remained above 70mg/dL. At the 3rd hour, the patient's blood glucose level was 130mg/dL, at the 5th hour the

patient's blood glucose level was 130mg/dL and at the 6th hour the patient's blood glucose level was 178mg/dL.

Octreotide has been used in the treatment of hypoglycemia resulting from sulfonylurea toxicity. Octreotide is a long-acting synthetic somatostatin analog that binds to somatostatin-2 receptors on the pancreatic beta cells, preventing the influx of calcium required for insulin secretion and therefore blocking insulin secretion (8). Administration of octreotide subcutaneously or intravenously at a dose of 50-100µg and can be repeated every 6-12 hours (8,11).

The administration of octreotide in cases of hypoglycemia caused by sulfonylureas has proven to be very beneficial. Some case reports state that giving octreotide can maintain blood glucose levels to prevent a decrease in blood glucose (8,9,11,12).

In cases of impaired renal function, antidiabetic drugs should be considered with extreme caution. Glibenclamide clearance will be prolonged in cases with impaired renal function so that it can cause refractory hypoglycemia. The use of octreotide may be considered in cases of refractory hypoglycemia that do not respond to standard glucose treatment.

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