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# OCTREOTIDE FOR TREATMENT RECURRENT HYPOGLYCEMIA INDUCED BY SULFONYLUREA: A CASE REPORT AND LITERATURE REVIEW

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**ABSTRAK**

Overdosis dapat menyebabkan hipoglikemia yang tidak responsif terhadap pengobatan dengan dekstrosa saja. Octreotide, meskipun tidak digunakan secara luas, adalah antidot untuk overdosis sulfonilurea. Kami menyajikan laporan kasus seorang pria berusia 62 tahun yang secara keliru mengonsumsi 6 tablet sulfonilurea (Glibenclamide®), mengira itu adalah loperamide untuk diare. Ia mengalami pusing, diaforesis, muntah, dan kehilangan kesadaran. Pemeriksaan fisik menunjukkan GCS 225, tekanan darah 188/79 mmHg, denyut jantung 85 bpm, laju pernapasan 24x/menit, dan saturasi oksigen 99%. Hasil darah menunjukkan RBS 13 mg/dl, CBC normal, analisis gas darah normal, hipokalemia 2,87 mmol/l, dan fungsi ginjal serta hati normal. Pasien diobati dengan bolus Dextrose 40%, Dextrose 10% pemeliharaan, dan hidrokortison 100 mg, tetapi kadar gula darah tetap tidak responsif selama 1 jam meskipun dosis infus glukosa ditingkatkan. Setelah 5 jam tanpa hasil memuaskan, kami memberikan dosis pertama octreotide (50 IU IV), yang menghasilkan interval hipoglikemik selama 2,5 jam. Setelah dosis kedua octreotide 50 IU, hipoglikemia teratasi. Pasien dipindahkan ke bangsal umum dan selamat. Dalam kasus ini, octreotide memperpanjang interval hipoglikemia dan mengurangi kebutuhan akan dekstrosa. Penggunaan octreotide untuk kondisi selain overdosis sulfonilurea tidak disarankan.

**ABSTRACT**

**Octreotide For Treatment Recurrent Hypoglycemia Induced By Sulfonylurea: A Case Report And Literature Review**. Overdose can cause hypoglycemia, which is unresponsive to dextrose treatment alone. Octreotide, though not universally used, is an antidote for sulfonylurea overdose. We present a case report of a 62-year-old male who mistakenly consumed six tablets of sulfonylurea (Glibenclamide®), thinking they were loperamide for diarrhea. He developed dizziness, diaphoresis, vomiting, and unconsciousness. Physical examination revealed a GCS of 225, blood pressure of 188/79 mmHg, heart rate of 85 bpm, respiratory rate of 24/min, and oxygen saturation of 99%. Blood results showed RBS at 13 mg/dl, normal CBC, unremarkable blood gas analysis, hypokalemia at 2.87 mmol/l, and normal RFT and LFT. The patient was treated with bolus Dextrose 40%, maintenance Dextrose 10%, and hydrocortisone 100 mg, but blood sugar remained refractory for 1 hour despite increasing glucose infusion. After 5 hours without satisfactory results, we administered the first dose of octreotide (50 IU IV), resulting in a hypoglycemic interval lasting 2.5 hours. After a second dose of 50 IU octreotide, hypoglycemia was resolved. The patient was moved to the general ward and survived. In this case, octreotide extended the interval of hypoglycemia and reduced the need for dextrose. Using octreotide for conditions other than sulfonylurea overdose is not recommended.

## INTRODUCTION

The standard treatment for hypoglycemia is the administration of dextrose, but it is often insufficient when insulin secretagogues cause hypoglycemia. These drugs are generally prescribed owing to their low cost and tolerability. The most well-known is glimepiride, third-generation sulfonylureas.[1] When first-line agents fail to meet target glycated hemoglobin, the American Diabetes Association (ADA) recommends adding sulfonylurea, considering cost an important factor. It is a long-acting insulin secretagogue with a narrow therapeutic window and can stimulate hypoglycemia.[2]

In the event of an overdose, sulfonylureas can cause hypoglycemia that does not respond to dextrose treatment alone.[3] Administering dextrose can also lead to hyperglycemia, which stimulates insulin release from the pancreas, causing recurrent hypoglycemia. This cycle of re-administering dextrose leads to high dextrose requirements and necessitates frequent blood sugar monitoring. Moreover, several sulfonylurea drugs have long action durations, such as glibenclamide, which has 24 24-hour duration of action.[4] Therefore, a medication that can effectively treat recurrent hypoglycemia induced by sulfonylureas without side effects and is accessible to use is needed.[5] Octreotide, which inhibits the secretion of several hormones, including insulin, can be an antidote for sulfonylurea overdose but is not widely used. We present a case of recurrent hypoglycemia induced by sulfonylurea that was successfully managed with the synthetic somatostatin analog, octreotide.[5]

## CASE REPORT

A 62-year-old male was brought to our emergency department with loss of consciousness; he was found in the bathroom by his family. Previously, he complained of headache and fever with watery diarrhea 3-7 times per day for about three days. For this complaint, this patient sought treatment from the midwife and consumed six tablets of sulfonylurea (Glibenclamide®) because a midwife had mistaken it with loperamide for diarrhea. He then developed dizziness, diaphoresis, and vomiting and was unconscious. Physical examination shows Glasgow Coma Scale (GCS) 225, blood pressure 188/79 mmHg, heart rate 85 bpm, respiratory rate 24x/min, and oxygen saturation 99%. His blood result showed Random Blood Sugar (RBS) of 13 mg/dl, normal CBC, unremarkable blood gas analysis, hypokalemia 2.87 mmol/l, normal renal function test, and liver function test (Table 1).

We treated patients with bolus Dextrose 40% 50 cc every low blood sugar measurement, maintenance dextrose 10% infusion. RBS dropped every 1 hour despite increasing glucose infusion. After 5 hours of repeating the results, we administered the first dose of octreotide 50mcg IV, the the hypoglycemic interval lasted 2.5 hours. 7 hours later, the RBS value tended to reduce again when we gave a second dose of 50mcg IV octreotide. The RBS value tended to increase (Figure 1). Therefore, hypoglycemia was resolved, and the patient was moved to a general ward and survived.

**Table 1. Laboratory study of patient**

| Examination | Result | Unit |
|---|---|---|
| Hemoglobin | 12.10 | g/dl |
| Hematocrit | 36.20 | % |
| Leucocyte | 10.99 | $10^3/\mu L$ |
| Thrombocyte | 163 | $10^3/\mu L$ |
| Erythrocyte | 4.46 | $10^6/\mu L$ |
| Neutrophil% | 88.2* | % |
| Basophil% | 0.1 | % |
| Eosinophil% | 0.0 | % |
| Lymphocyte% | 6.7* | % |
| Monocyte% | 5.0 | % |
| Sodium | 136 | mmol/L |
| Potassium | 2.87* | mmol/L |
| Chloride | 103 | mmol/L |
| Ureum | 37.3 | mg/dl |
| Creatinine | 0.4 | mg/dl |
| SGOT | 34 | U/L |
| SGPT | 40 | U/L |
| Albumin | 3.22 | g/dl |
| Bilirubin | 1.15 | mg/dl |

*Abnormal result

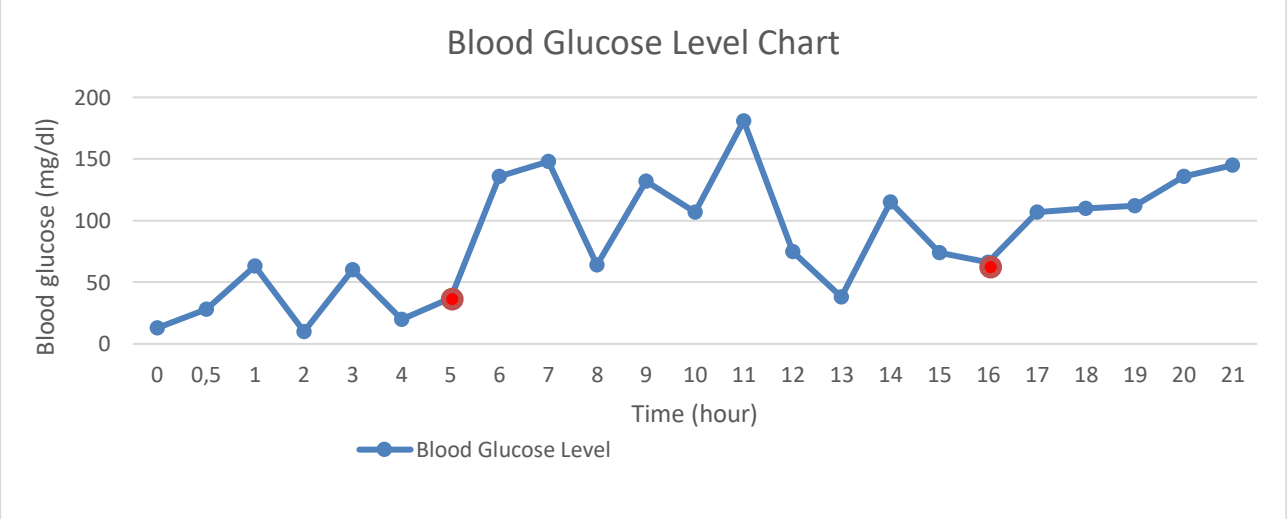


**Figure 1. Blood glucose level chart. Octreotide is administered in the 5th hour and 16th hour.**

## DISCUSSION

In this case, the first dose of octreotide 50 mcg was given intravenously at 5 hours, and the interval with the second dose was 11 hours. RBS value tended to reduce after 7 hours of the initial dose, and there were three episodes of hypoglycemia occurred. After the second dose, the blood sugar level can be maintained with minimal dextrose 10% infusion. If hypoglycemia recurs, the octreotide dose is 50-100 mcg subcutaneously with additional doses at 6–12-hour intervals. Typically, 1-3 doses are sufficient. Both SC and IV administration are acceptable, although the usual

route is SC. Shorter duration of action with IV administration, requiring dosing every 4 hours compared with every 6 hours with the subcutaneous route.[6]

Octreotide is FDA-approved for the treatment of acromegaly, metastatic carcinoid symptoms, and vasoactive intestinal-secreting tumors. It has also been used for the cessation of upper gastrointestinal bleeding and to correct refractory hypoglycemia caused by sulfonylurea overdose.[7] Octreotide is well-tolerated; most likely adverse effects are usually mild GI symptoms. Accidental overdoses of 2,400 to 6,000 µg/day have occurred, causing mild, similar symptoms as described above, indicating that octreotide has a wide therapeutic window.[8] Another agent for inhibiting insulin release is diazoxide; it is less effective than octreotide and has the potential to cause hypotension.[9]

Octreotide prevents rebound hypoglycemia after treatment of sulfonylurea overdose with dextrose. By mimicking somatostatin, octreotide suppresses the secretion of gastrin, cholecystokinin, growth hormone, glucagon, and insulin. G-protein-coupled somatostatin-2 receptors bind voltage-gated calcium channels on pancreatic beta cells.[10-11] When octreotide binds to the somatostatin receptors, the calcium channels close, preventing calcium influx and subsequent secretion of insulin (Figure 2). This mechanism lends to the effectiveness of octreotide for treating sulfonylurea-induced hypoglycemia, as it binds "downstream" from where sulfonylureas exert their effects on the β cells and prevents an event necessary for insulin secretion.[9,12]

This case has a similar result with the ingestion of 500 mg glibenclamide described by Carr and Zed; it described fewer hypoglycemic episodes and lower dextrose requirements with octreotide 50 µg every 8h for three doses.[12] In Another case, ingestion of 15mg Glibenclamide by McLaughlin showed no hypoglycemic episode after octreotide therapy with routine multiple dose octreotide subcutaneous injection.[13]

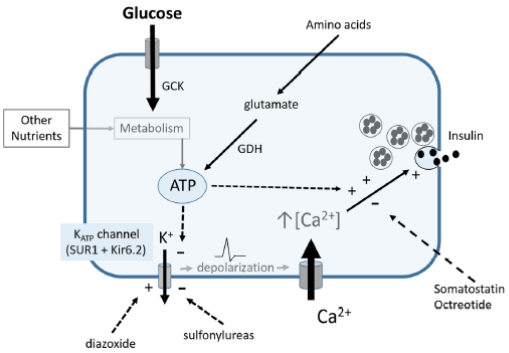


**Figure 2. Mechanism of sulfonylurea antidotes.[5]**

Although octreotide does not have FDA, American Diabetes Association, and Joint British Diabetes Societies approval for hypoglycemia induced by sulfonylurea, currently, octreotide is used in intoxication from insulin secretagogues.[1] Lastly, it should be remembered that octreotide is not a substitute for IV dextrose and does not decrease the need for frequent glucose assessments.

## CONCLUSION

Octreotide is safe and acts as a specific antidote for sulfonylurea toxicity and should be considered as first-line therapy for sulfonylurea-induced hypoglycemia. Using octreotide for hypoglycemia other than sulfonylurea overdose is not recommended.

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