ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 05 | May - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ROLE OF OCTREOTIDE IN MANAGEMENT OF SULPHONYLUREA - INDUCED REFRACTORY HYPOGLYCEMIA : A CASE REPORT

Diabetology

Dr Akshay Kothari * Visiting Diabetologist , Grant Govt Medical College And Sir J.J Group Of Hospitals, Mumbai. *Corresponding Author

Dr Kiran Shah Visiting Diabetologist , Grant Govt Medical College and Sir J.J Group of Hospitals, Mumbai.

ABSTRACT

Hypoglycemia in diabetes is generally the result of interplay of relative or absolute therapeutic exogenous or endogenous insulin excess and compromised physiological and behavioral defenses against falling blood glucose concentrations. Thus, it is fundamentally iatrogenic, the result of treatments that include insulin or an insulin secretagogue such as glimepiride. The long-acting, synthetic somatostatin analog, octreotide, can be used to correct refractory hypoglycemia caused by sulfonylurea. There have been few records of it being used in a clinical environment. We present a case in which a subcutaneous injection of octreotide was successful in treating sulfonylurea-induced refractory hypoglycemia. The patient was referred to our hospital for recurrent hypoglycemia caused by sulfonylurea. His medications included tablet glimepiride 4 mg once daily along with tablet metformin 1000mg once daily. His plasma glucose level on arrival was 45 mg/dl. He was treated with 50 ml of 25% glucose solution and administered continuous drip of 5% glucose solution through a peripheral vein, but his hypoglycemia recurred several times. Finally, 100 mcg of octreotide was subcutaneously injected. Thereafter, hypoglycemia did not recur, and additional injections of glucose were not required. The subcutaneous injection of octreotide can be an effective and safe method of treating prolonged, and refractory hypoglycemia caused by sulfonylureas and alleviate impending complications, morbidity, and/ or mortality. The octreotide subcutaneous injection can be used as outpatient department treatment and can greatly reduce the cost of hospitalization.

KEYWORDS

Sulfonylurea, Hypoglycemia , Somatostatin analog octreotide

INTRODUCTION

The most often prescribed drug class for the management of patients with type 2 diabetes (T2D) is sulfonylureas[1]. These drugs are generally prescribed, owing to their low cost and tolerability[2]. The most well-known is glimepiride, third-generation sulfonylureas. When first-line agents fail to meet target glycated hemoglobin, the American Diabetes Association (ADA) recommends adding a sulphonylurea considering cost as an important factor[3]. These agents cause hypoglycemia by inducing the pancreas to secrete insulin; hence, hypoglycemia is a significant side effect[4]. When compared to other oral antidiabetic agents, glimepiride is more likely to cause hypoglycemia[5-6]. A potential complication of treatment of hypoglycemia with intravenous dextrose is recurrent hypoglycemia. Dextrose administration leads to hyperglycemia which successively potentiates insulin release from the pancreas resulting in recurrent hypoglycemia. Re-administration of dextrose perpetuates this cycle, leading to high dextrose requirements and therefore the need for frequent monitoring of blood sugar levels[7-8]. So we need a medication that effectively treats sulfonylurea-induced chronic and persistent hypoglycemia without causing side effects and is simple to use. We report a case of sulphonylurea-induced refractory hypoglycemia managed with a synthetic somatostatin analog, octreotide[8].

Case

A fifty-eight years old male, non-addict, was brought to our emergency department with gradually increasing giddiness, sweating, weakness, dyspnea on exertion, and unsteadiness for the last 15 minutes. His medical history included long-standing T2D without any associated macrovascular and microvascular complications. He reported good adherence with his medications which included glimepiride four mg and metformin one gram was taken once daily. The patient was tachycardic, tachypneic, diaphoretic, and disoriented when he arrived. The initial glucose meter reading was 36 mg/dL, measured using Accu-check Performa(Roche), and the metabolic panel blood glucose level was 45 mg/dL. The patient's serum creatinine level was 0.9 mg/dL. There was no obvious reason found for hypoglycemia on history as the patient had been following the same routine of diet exercise and medications. His laboratory parameters were within normal limits and are mentioned in the following table.

Table: Laboratory Parameters

Parameter	Observed value	Normal range
Hemoglobin	11.9	12.5-18cgms%
WBC	8000	4000-11000
HbA1c	6.8	<5.5%
SGOT	23	5-40 U/L
SGPT	15	5-40 U/L
S. Creatinine	0.9	0.4-1.4 mg/dl
eGFR CKD-EPI Creatinine 2009 Equation	87	90mL/min/1.73m^2
TSH	1.19	0.25-5.5 uIU/ml
S.Cortisol level	11.9	3-21 microgram/dl

WBC: White blood cell count, HbA1c: Glycated hemoglobin, SGOT: serum glutamic-oxaloacetic transaminase, SGPT: serum glutamic-pyruvic transaminase, TSH: Thyroid stimulating hormone.

While in the emergency room, he was given 50 ml of 25% of dextrose, and his capillary blood glucose level rechecked after 15 minutes was 190 mg/dl. The patient was conscious, oriented, and responding to oral commands was asked to eat and transferred to the ward. His diabetes medications were withheld. Two hours later the patient again complained of giddiness. His capillary blood glucose level was rechecked and found to be 50 mg/dl. Another 50 ml of 25% dextrose was repeated along with a continuous drip of 5 % dextrose at the rate of 40 ml/hour and capillary blood glucose levels were checked every two hourly Figure 1.

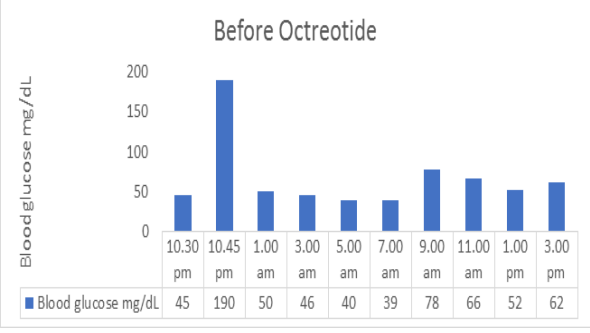

Figure 1

Intravenous bolus doses of 25% dextrose were given intermittently. A decision was made to administer 100 micrograms of octreotide subcutaneously. After receiving octreotide his capillary blood glucose levels showed a steady increase and there were no further episodes of hypoglycemia. His capillary blood glucose levels remained above 200 mg/ dl Figure2 .

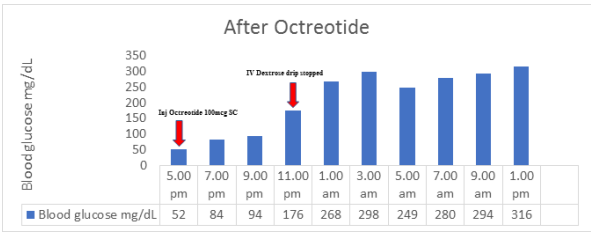

Figure 2

Upon discharge, he was re-started on metformin. His glimepiride was stopped.

DISCUSSION:

Hypoglycemia complicating sulfonylureas use is well documented in the literature, is of varying magnitude and duration[9]. The goal of sulfonylurea-induced hypoglycemia treatment is to restore euglycemia. To avoid chronic hypoglycemia, sulfonylurea-induced hypoglycemia is treated with quickly metabolized carbohydrates such as intravenous dextrose or oral glucose tablets and gels, accompanied by a continuous intravenous infusion. For sulfonylurea-induced refractory hypoglycemia, repeated boluses and titration of the continuous intravenous dextrose infusion may be needed[10]. If this first treatment fails, other options should be considered.

Glucagon or diazoxide therapy has been used in the past. Glucagon stimulates glycogenolysis and gluconeogenesis by binding to hepatic glucagon receptors. Glucagon, on the other hand, induces pancreatic insulin secretion, which can intensify the hyper-insulinemic state induced by sulfonylureas by increasing blood glucose levels and binding to pancreatic receptors[11]. The increased use of octreotide, glucagon, and diazoxide therapy has fallen out of favor.

The FDA has approved octreotide, a long-acting synthetic somatostatin analogue, for the treatment of acromegaly, metastatic carcinoid symptoms, and vasoactive intestinal secreting tumors. It's also been used to treat refractory hypoglycemia caused by sulfonylurea overdoses and to avoid upper gastrointestinal bleeding[12-15] Octreotide can be given intravenously or subcutaneously, and both methods have the same bioavailability [16-17]. Octreotide binds to somatostatin-2 receptors on pancreatic beta cells, stopping calcium from entering the cells and inhibiting insulin secretion. Since it binds ' downstream' from where sulfonylureas exert their effects on beta cells and prevents an event needed for insulin secretion, octreotide is successful in the treatment of sulfonylurea-induced hypoglycemia. Since supplemental dextrose alone was inadequate to treat sulfonylurea-induced hypoglycemia in our patient, octreotide was used. Many patients can benefit from subcutaneous doses of 50-100mcg per 8 hours. Since the dosage and length of octreotide administration are smaller than those prescribed for other indications, adverse effects should be less common when octreotide is used for sulfonylurea-induced refractory hypoglycemia for a short period time.

CONCLUSION

In diabetics, extreme refractory hypoglycemia is a significant side effect of sulfonylurea treatment. The use of octreotide as soon as hypoglycemia is detected is successful in restoring hypoglycemia quickly and safely. Octreotide is an appealing agent for reversing extreme hypoglycemia caused by glimepiride use because of its ease of administration, quick onset, and favorable side effect profile.

Ethics Approval: Not applicable
Consent Publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.
Conflict of interests: The authors declare that they have no competing interests.
Funding: None
Author Contributions: Author and co-authors have equally contributed to the manuscript.
Acknowledgements: None

REFERENCES:

1. American Diabetes Association (2016). 7. Approaches to Glycemic Treatment. *Diabetes care*, *39 Suppl 1*, S52–S59. https://doi.org/10.2337/dc16-S010
2. Rogers M., Sands C., Self T. (2011) Sulfonylurea-induced hypoglycemia: the case against glyburide. *Consultant* 51: 2. [Google Scholar] [Ref list]
3. American Diabetes Association (2021). 9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes-2021*. *Diabetes care*, *44*(Suppl 1), S111–S124. https://doi.org/10.2337/dc21-S009
4. Burge, M. R., Schmitz-Fiorentino, K., Fischette, C., Qualls, C. R., & Schade, D. S. (1998). A prospective trial of risk factors for sulfonylurea-induced hypoglycemia in type 2 diabetes mellitus. *JAMA*, *279*(2), 137–143. https://doi.org/10.1001/jama.279.2.137
5. Ahrén, B., Foley, J. E., Dejager, S., Akacha, M., Shao, Q., Heimann, G., Dworak, M., & Schweizer, A. (2014). Higher Risk of Hypoglycemia with Glimepiride Versus Vildagliptin in Patients with Type 2 Diabetes is not Driven by High Doses of Glimepiride: Divergent Patient Susceptibilities?. *Diabetes therapy : research, treatment and education of diabetes and related disorders*, *5*(2), 459–469. https://doi.org/10.1007/s13300-014-0082-y
6. Riddle M. C. (2019). A Verdict for Glimepiride: Effective and Not Guilty of Cardiovascular Harm. *Diabetes care*, *42*(12), 2161–2163. https://doi.org/ 10.2337/dci19-0034
7. Zammitt, N. N., & Frier, B. M. (2005). Hypoglycemia in type 2 diabetes: pathophysiology, frequency, and effects of different treatment modalities. *Diabetes care*, *28*(12), 2948–2961. https://doi.org/10.2337/diacare.28.12.2948
8. Dougherty, P. P., & Klein-Schwartz, W. (2010). Octreotide's role in the management of sulfonylurea-induced hypoglycemia. *Journal of medical toxicology : official journal of the American College of Medical Toxicology*, *6*(2), 199–206. https:// doi.org/ 10.1007/s13181-010-0064-z
9. Ha, W. C., Oh, S. J., Kim, J. H., Lee, J. M., Chang, S. A., Sohn, T. S., & Son, H. S. (2012). Severe hypoglycemia is a serious complication and becoming an economic burden in diabetes. *Diabetes & metabolism journal*, *36*(4), 280–284. https:// doi.org/ 10.4093/dmj.2012.36.4.280
10. Rowden, A. K., & Fasano, C. J. (2007). Emergency management of oral hypoglycemic drug toxicity. *Emergency medicine clinics of North America*, *25*(2), 347–viii. https://doi.org/10.1016/j.emc.2007.02.010
11. Thoma, M. E., Glauser, J., & Genuth, S. (1996). Persistent hypoglycemia and hyperinsulinemia: caution in using glucagon. *The American journal of emergency medicine*, *14*(1), 99–101. https://doi.org/10.1016/S0735-6757(96)90029-7
12. Braatvedt, G. D. (1997). Octreotide for the treatment of sulphonylurea induced hypoglycemia in type 2 diabetes. *New Zealand Medical Journal*, *110*, 189–190.
13. Green, R. S., & Palatnick, W. (2003). Effectiveness of octreotide in a case of refractory sulfonylurea-induced hypoglycemia. *Journal of Emergency Medicine*, *25*(3), 283–287. doi:10.1016/S0736-4679(03)00204-X
14. Carr, R., & Zed, P. J. (2002). Octreotide for sulfonylurea-induced hypoglycemia following overdose. *Annals of Pharmacotherapy*, *36*(11), 1727–1732. doi:10.1345/aph.1C076
15. McLaughlin, S. A., Crandall, C. S., & McKinney, P. E. (2000). Octreotide: An antidote for sulfonylurea-induced hypoglycemia. *Annals of Emergency Medicine*, *36*(2), 133–138. doi:10.1067/mem.2000.108183
16. Kutz, K., Nüesch, E., & Rosenthaler, J. (1986). Pharmacokinetics of SMS 201–995 in healthy subjects. *Scandinavian Journal of Gastroenterology. Supplement*, *119*, 65–72. doi:10.3109/00365528609087433
17. Chanson, P., Timsit, J., & Harris, A. G. (1993). Clinical pharmacokinetics of octreotide. Therapeutic applications in patients with pituitary tumours. *Clinical Pharmacokinetics*, *25*(5), 375–391. doi:10.2165/00003088-199325050-00004