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Case Report

CASE STUDY: ORAL HYPOGLYCEMIC DRUGS OVERDOSE INDUCED GENERALISED TONIC-CLONIC SEIZURES

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ABSTRACT

Metformin is an oral hypoglycemic agent of the biguanide class, and glimepiride is an oral hypoglycemic agent of the sulfonylurea class frequently used to treat Type-II diabetes mellitus. Under certain conditions, overdose or long-term use of metformin and glimepiride can cause lactic acidosis and hypoglycemia. Metformin overdose can cause severe hypoglycemia in the absence of other anti-diabetic drugs. Potential mechanisms of metformin-induced hypoglycemia include decreased hepatic glucose production, decreased glucose absorption, and low oral intake. Hypoglycemia, in turn, leads to loss of consciousness, headache, confusion, and neurological symptoms such as insomnia, delirium, and in rare conditions may lead to coma, seizures, and death. Here, this case study is of 23-years-old female patient and non-diabetic presented with alleged consumption of metformin (8 g), glimepiride (32 mg) with three-episodes of generalized tonic-clonic seizures (GTCS), fever with chills, and loss of consciousness. In general, diabetic patient's hypoglycemia condition can be more often due to drug overdosage or dietary restrictions. However, in non-diabetic patients, hypoglycemia is considered a jeopardy situation because it may lead to several fatal effects.

Keywords: Metformin, Glimepiride, Over-dose, Hypoglycemia, Seizures.

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INTRODUCTION

Metformin is the most frequently prescribed oral hypoglycemic drug of the biguanide family [1]. Metformin inhibits hepatic gluconeogenesis (The metabolic process of making glucose from its breakdown products or the breakdown products of lipids or proteins), glycogenolysis (the metabolic process of conversion or breakdown of glycogen into glucose molecule) enhances peripheral glucose utilization in patients with non-insulin-dependent diabetes [2,3]. Metformin also reduces hyperglycemia by gastrointestinal tract absorption of glucose and increases insulin signaling and utilization of glucose [4]. Accidental and intentional metformin overdoses are reported commonly in India. Metformin acts by increasing cellular insulin sensitivity. Their action is anti-hyperglycemic rather than hypoglycemic and does not cause severe hypoglycemia even in overdose [5]. In general, metformin can be prescribed as dual therapy with sulfonylureas (glimepiride, gliclazide). The excess consumption or overdosage of sulfonylureas primarily leads to hypoglycemia. Anti-hyperglycemic agents exert their effect by stimulating insulin release from the beta cells of the pancreas. In overdose, particularly in non-diabetic patients, cause prolonged and profound hypoglycemia. The onset of hypoglycemia occurs within a few hours of ingestion and, without treatment, may progress in severity. The severity includes cerebral hypoglycemia that may cause permanent neurological injury or death [5]. Hypoglycemia leads to loss of consciousness, headache, confusion, and reeling sensation. Neurological symptoms such as hypothermia, insomnia, delirium, and rare conditions may lead to coma, seizures, and death. In a hypoglycemia condition, a low blood sugar level can lead to hypoxia condition that may cause neurological damage. A study in rats proves that hypoxia and hypoglycemia condition leads to a reduction in cerebral oxygenation and might disrupt the cell membrane-bound.

Na+ - K+ activated ATPase with an increased net influx of sodium (Na+) ions into cells and raise the difference in electrolyte imbalance and increases the osmolality of the brain leads to the accumulation of fluid causes cerebral edema [6]. The neurological injury occurs either by cerebral edema or by other conditions that may lead to seizures.

CASE REPORT

A female patient of age 23 years old weighted 50 kg was brought to the hospital due to alleged consumption of a combination of drugs metformin (8 g) and glimepiride (35 mg). The patient has shown complaints of seizure phenomenon and fever with generalized tonic-clonic seizures for about three episodes with loss of consciousness. Patient conditions were drowsy, not following commands, irritable, low General Random Blood Sugar (51 mg/dL), GTCS (three episodes), and O_2 Saturation – 84% mild hypoxia condition. The patient immediately shifted to ER, the patient was intubated with endotracheal tube done and mechanical ventilation provided for 2 days. arterial blood gases (ABG) analysis when the patient was in the ER showed pH – 7.36, $PaCO_2$ – 32.5 mmHg, PaO_2 – 51 mmHg, SpO_2 – 84%, bicarbonate 22.4 mmol/L, lactate 1.1 mmol/L, and blood glucose 3.4 mmol/L, these were abnormal values based on the patient condition. The immediate threat to life is hypoglycemia and mild hypoxemia, the potential for progression to coma, and further episodes of seizures. This patient already exhibited clinical features of moderate hypoglycemia confirmed by blood analysis and complaint of two episodes of seizures. Patient hypoglycemia requires immediate correction with the establishment of intravenous administration of a bolus dose of 50 ml of 50% dextrose solution. The investigations were MRI-brain epilepsy protocol showed no abnormality, CT-scan of the brain showed no abnormalities. Lumbar puncture was performed to obtain cerebro-spinal fluid, the analysis showed: Fluid appearance – clear, cell count – 01 cells/cubic mm, type of cells – 100% lymphocytes, lymphoglobulins – negative, T-protein – 35 mg/dL, and glucose – 98 mg/dL. A complete blood picture analysis showed the elevated erythrocyte sedimentation rate – 40 mm/h, total white blood cell count – 17800 cells/cubic mm, neutrophils – 88%, and other parameters were within normal range. Renal function test showed elevated serum creatinine – 1.7 mg/dl and blood urea – 63 mg/dL, serum electrolytes were within normal range. After reaching a sufficient oxygen saturation, the ABG analysis showed pH – 7.41, $PaCO_2$ – 40 mmHg, PaO_2 – 89 mmHg, SaO_2 – 95 mmHg, bicarbonate 24.2 mmol/L, lactate 0.9 mmol/L, and blood glucose 4.9 mmol/L. The patient does not know to have any history of psychiatric illness or suicidal ideation or attempt. She does have a

Table 1: Improved Blood glucose levels (mg/dL) of patient

Day-1	Day-2	Day-3	Day-4	Day-5	Day-6
51 mg/dL	86 mg/dL	94 mg/dL	101 mg/dL	98 mg/dl	111 mg/dL

Table 2: The treatment regimen of the patient

Name of the drug	Route of administration	Dose	Frequency
Inj. Phenytoin	Intravenous (IV)	1 g	Thrice a day
Inj. Ceftriaxone	Intravenous (IV)	1 g	Twice a day
Inj. Pantoprazole	Intravenous (IV)	40 mg	Once a day
Inj. Mecobalamin	Intravenous (IV)	1 amp	Once a day
Inj. Dextrose-NS	Intravenous (IV)	50 ml Bolus dose	On day-1 and later stopped

g: Gram, mg: Microgram, Amp: Ampule, ml: Milliliter

family history of diabetes mellitus. Based on her psychological status of being reluctant to get counseling, her representatives were counseled by the neuropsychiatric regarding taking care of the patient. The patient got prescribed antiepileptic drugs, antibiotics, and neuroprotectives. On day 6, the patient shifted to the general ward with normal mental status and vital signs. The patient was tolerating the oral intake and did not develop any more hypoglycemic attacks. Table 1 shows the blood glucose levels of the patient and continuously monitored according to the range.

The patient got treated according to the symptomatic approach as the maintenance of blood glucose level is the primary criteria for the treatment, the treatment based on the patient's condition as the occurrence of seizure is due to hypoglycemia after correction of hypoglycemia patient has been treated with drug regimens as shown in Table 2.

DISCUSSION

In this case report, we report a young female patient who developed significant hypoglycemia due to alleged consumption of oral hypoglycemic agent combination of two drugs Metformin, and glimepiride. Metformin overdose usually results in life-threatening lactic acidosis. This complication can be in any patient who appears unwell. Severe or worsening lactic acidosis mandates immediate hemodialysis. Sulphonylurea overdose invariably results in profound and prolonged hypoglycemia [7,8]. Dextrose is a specific antidote for sulphonylurea poisoning. However, attempts to maintain euglycemia by continuous infusion of concentrated dextrose are problematic, as it stimulates further insulin release and rebounds hypoglycemia, and may require administration of excessive volume and osmolar loads [7]. Octreotide, a synthetic octapeptide analog of somatostatin, effectively suppresses insulin secretion. It is the antidote for sulphonylurea poisoning and has a very benign adverse effect profile [9]. Hypoglycemia, if untreated, may lead to a severe imbalance between the patient's symptoms. Preventing the reoccurrence of hypoglycemia is the criterion of providing good care to the patient.

CONCLUSION

This case study concludes that during treatment of hypoglycemic seizures due to overdose of oral hypoglycemic drugs, it is important to understand the drugs activity and its overdose effects, to provide effective treatment. If different activity and poisoning effects of drug overdose are not known may cause a severe deficit in enabling proper therapy. This case study acts as an add-on to the existing data in overdose of anti-diabetic drug-induced hypoglycemic seizures.

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AUTHOR'S CONTRIBUTION

Mr. Anvesh Kumar Kuchipudi was involved in the collecting, organizing of the data, case study analysis, reviewing, and editing of the manuscript. Ms. Vathsalya Poranki was involved in the case study analysis, drafting, reviewing the case study, and editing the manuscript.

ETHICAL COMMITTEE

Ethical approval is not applicable for this case report in our Institutional Ethical Committee.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

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