Case Presentation of 71 Year Old Man with Hypoglycemia due to Drug-Drug Interactions

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ABSTRACT

Hypoglycemia induced due to drug-drug interaction is an important to consider for differential diagnosis especially in the geriatric patients. The symptoms of hypoglycemia includes: physical symptoms such as anxiety, hunger, palpitations, sweating and hunger. Neurologic impairment include changes in behaviour, decline in cognitive functions. In addition to the well-known hypoglycemic effects associated with treatment of diabetes mellitus, several commonly prescribed medications, such as thiazides, sulfonylureas, metformin, aspirin and some antibiotics can cause hypoglycaemia. We describe a case of hypoglycaemia in a geriatric patient taking anti diabetic drugs metformin, glipizide and anti-platelet drug aspirin together for a period of one week.

Key Words: Hypoglycemia, Geriatric population, Poly-Pharmacy

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INTRODUCTION

Diabetes mellitus is a chronic disease. The United Nation World Health Organization estimates that 220 million people have been affected with diabetes mellitus and may rise to 366 million populations by 2030.[1] In India it is estimated that the populations that may be affected with type 2 diabetes mellitus is 79,441,000 by 2030.[2] People with diabetes mellitus have the risk of hypoglycemia especially in elderly due of presence of co morbidities and poly pharmacy which leads to drug-drug interactions through pharmacokinetic mechanisms, such as inhibition of drug metabolism or through pharmacodynamics

mechanisms, such as increase β-cell function; the impact of these drug-drug interactions. Drug-drug interactions cause a serious adverse drug reaction and one of the way to identify is through literature and reports.[3] Hypoglycemia in patients with diabetes mellitus is a usual health related concern that have an influence on quality of life. We report a case of patient with type 2 diabetes mellitus who experienced hypoglycemia due to co-administration of tablet metformin, tablet glipizide with tablet aspirin.

CASE REPORT

A 71 year old male patient with known case Type 2 diabetes mellitus was presented to emergency department at Government Head Quarters Hospital, Udhagamandalam on 1 July 2014 with complaints of dizziness, fatigue, pale skin, headache, sweating, unconsciousness and rapid heartbeat on consumption of tablet aspirin 150mg once daily from past one week as he is recently diagnosed with Ischemic heart disease. He is also on medication of tablet Isosorbide dinitrate 5mg four times a day. He had never before experienced symptoms of hypoglycemia while taking his anti-diabetic medications of tablet metformin 500 mg twice daily, tablet glipizide 5mg twice daily for past 15 years. The patient is also known case of chronic obstructive pulmonary disease for past two years and on medication of tablet salbutamol 4mg twice daily. On the day of admission the patient blood pressure was 110/70mmHg, pulse rate 72 beats/min, heart rate 110 beats/minute and electrocardiograph finding showed sinus tachycardia, respiratory rate 22 beats/min, and afebrile. The random blood sugar was 49 mg/dl. The laboratory findings included following: haemoglobin 14.7 g/dl, blood urea 62 mg/dl, serum creatinine 1mg/dl, aspartate aminotransferase 41U/L, alanine aminotransferase 22U/L, alkaline phosphates 69U/L, bilirubin total 1.3mg/dl, bilirubin direct 0.6 mg/dl, bilirubin indirect 0.7mg/dl and found to be with in the normal limits. The patient is an abstainer from habits of smoking and consumption of alcohol. The patient was following his diabetic diet appropriately.

On admission the patient was administered via peripheral cannula with of one doses 100 ml/hour of 25% dextrose, he required a continuous infusion of hypertonic 50 ml/hour 5% dextrose over a 24 hour period to maintain normoglycemia and administration of the oral anti-diabetic medications was temporarily interrupted to restore and maintain normoglycemia. The tablet aspirin, isosorbide dinitrate, salbutamol and ranitidine were continued.

Assessing the reaction for causality using the Naranjo probability scale for adverse drug reactions, it is categorized the reaction as possibly caused by tablet aspirin along with his anti-diabetic medications. On Day 2 and 3 the blood sugar readings were obtained and found to be within the range and all his vital parameter was found to be normal. The patient was continued with the same treatment up to day 3 as prescribed previously. On day 4 the post prandial blood sugar was 174 mg/dl, fasting blood sugar was 115 mg/dl and random blood sugar was 220 mg/dl and was prescribed with tablet metformin 500 mg twice daily with his previous medications until the day 11. On day 12, the patient was discharged and had no complaints of hypoglycemia and the same medications were prescribed on discharge.

DISCUSSION

In this patient the occurrence of hypoglycemia was due to drug-drug interaction between tablet glipizide a sulfonylurea, metformin a biguanide and tablet antiplatelet drug aspirin.

As per the guidelines of type 2 diabetes mellitus treatment, the combination of sulfonylurea and metformin is the next step to manage hyperglycaemia when cannot be controlled with lone oral anti-diabetic drug. When these drugs are given in combination there is a decline in hepatic glucose production which may impair the regaining of the patient from hypoglycemia and medications must be stopped immediately.[4] In this patient these drugs were stopped until the patient attainted normoglycemia.

The episode of hypoglycemia in this patient has no association with factors of alcohol intake, stress, organ illness, infection and neither imbalance of food intake and oral anti-diabetic usage.

Hypoglycemia in elderly diabetic patient is a concern due changes in blood brain circulation, comorbid conditions and aging.[5] The diabetic patients are at greater predominance of developing cerebrovascular and cardiovascular condition requiring to be on antiplatelet drug aspirin.[6] In the present report the patient was on anti- platelet drug aspirin for his management of ischemic heart disease. Literatures have reported that the common reasons of hypoglycemia in diabetic patient when sulfonylurea drug given is caused via several mechanisms. The pancreatic mechanisms involve inhibition of the efflux of K+ from pancreatic ß-cells via a sulfonylurea receptor which may be closely linked to an ATP-sensitive K+-channel which leads to

depolarization of the ß cell membrane, as a consequence, voltage-dependent Ca++-channels on the ß-cell membrane then open to permit entry of Ca++. The resultant increased binding of Ca++ to calmodulin results in activation of kinases associated with endocrine secretory granules promoting the exocytosis of insulin-containing secretory granules. The sulfonylureas also reduce serum glucagon levels contributing to its hypoglycaemic effects. The precise mechanism by which this occurs remains unclear but may result from indirect inhibition due to enhanced release of both somatostatin and insulin.[7] But with concomitant use of aspirin along with oral anti-diabetic drugs even at the therapeutic dose there is a greater chance to cause hypoglycemic episodes.[8,9] The mechanism of aspirin causing hypoglycemia when given along with glipizide and metformin is unknown but the probable mechanism includes reduction of hepatic gluconeogenesis and increase of insulin secretion, increases glucose utilization in peripheral tissues due to disconnection of oxidative phosphorylation or reduction of the concentration of circulating non esterified fatty acid by suppression of lipolysis. In the study reported by the M Gossell-Williams *et al* the risk of hypoglycaemia was found in 37 patients out of 104 sets (35.5%) with the aspirin along with oral anti-diabetic drug of sulfonylureas and metformin presenting one of the most offending drugs presenting 13 of 37.[10] Consistent with few published reports, the hypoglycemia in our patient was documented within one week of aspirin administration along with oral hypoglycemic agents glipizide and metformin thus an intravenous dextrose was required for the management of hypoglycemia. The sequential course of hypoglycemic event coincided with oral aspirin administration with glipizide and metformin. The condition of hypoglycemia resolved within a few days of stopping the medication.

CONCLUSIONS

It is challenging to conclude the most likely mechanism for the hypoglycemia seen in this patient; however, his hypoglycemia was mostly due to the concurrent use of antiplatelet drug aspirin, glipizide and metformin. It is tough to remember all potential interactions that may affect drug therapy in diabetic patients nevertheless an effort must be done by the prescriber and the pharmacist to give a special attention when the drugs

like aspirin, glipizide and metformin are given together in diabetic patients.

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