

Cilnidipine-Induced Spontaneous Hypoglycemia in a Young Female: A Case Report

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Abstract

Cilnidipine is a calcium channel blocker and used as a latest antihypertensive agent. Incidences of adverse drug event with the molecules of this class of antihypertensive agents among the hospitalized patients are common but such an event with cilnidipine is rare. Here, we present a case on a 27-year old non-diabetic female patient who developed spontaneous hypoglycemia after administering cilnidipine orally to manage her high blood pressure. When the adverse drug event was identified, the cilnidipine therapy was stopped and patient recovered from hypoglycemia. No further incidence of hypoglycemia happened during her hospitalization time.

Keywords: Cilnidipine; Antihypertensive agent; Adverse drug event; Hypoglycemia

Introduction

Cilnidipine is a fourth generation calcium channel blocker. Globally, as an antihypertensive agent, cilnidipine has been demonstrated as an effective compound in various studies in patients even with severe hypertension [1].

Drug-induced hypoglycemia is an adverse drug event (ADE) found among hospitalized patients of all ages ranging from mild to moderate to severe symptoms. Quinolone antibiotics, some beta-blockers, MAO-inhibitors and some other classes of drugs are frequently found with hypoglycemic events [2].

In this study, a spontaneous hypoglycemic event was found with cilnidipine in a non-diabetic young patient. After discontinuation of cilnidipine, the adverse event was resolved.

Case Report

A 27-year old female patient was admitted at ICU department in a tertiary level private hospital with the history of hypertension, postpartum preeclampsia and acute kidney injury. The patient did not have a history of smoking, alcohol, allergy or contact with other unwell persons. After 35th week of gestation, the patient gave birth of a baby through lower uterine caesarean section (LUCS) procedure at the same hospital. She had a family history of hypertension and diabetes. On physical examination, she was found with acute distress and shortness of breath. Her pulse rate was 115 beats/minute, respiratory rate was 26 breaths/minute, blood pressure was 178/95

mm Hg, body temperature was 101°F, Glasgow Coma Scale (GCS) was E2V3M4, SpO₂ was 88% (on room air), random blood sugar was 7.4 mmol/L, serum albumin was 2.4 g/dl, lactate dehydrogenase (LDH) was 911 U/L, bilirubin (total) was 0.6 mg/dl and C-reactive protein (CRP) was 277.3 mg/L. Her electrolytes reports showed that sodium 144 mmol/L, potassium 4.5 mmol/L, chloride 105 mmol/L and magnesium 2.9 mg/dl. Her serum creatinine was 2.1 mg/dl. She was prescribed with injection Paracetamol (1 g, IV, SOS) for hyperthermia management. As prophylactic antibiotic, she was prescribed with injection Ceftriaxone (1 g, IV, 12-hourly). The patient was on normal hospital diet containing 1800 Kcal/day and did not get any energy or nutritional supplements through oral or intravenous route. To manage her raised blood pressure, initially, she was treated with tablet Metoprolol (50 mg, twice daily, orally), tablet Prazosin (1 mg, three times daily, orally). Patient's blood pressure was monitoring in every 2 hours interval and recorded as uncontrolled in most of times. 206/101 mm Hg was recorded as her highest blood pressure and this life-threatening too much high blood pressure was recorded in several checking-times. To manage those incidences of excessive high blood pressure, cilnidipine (10 mg, twice daily, orally) was added to the prescription as add on therapy. After about 8 hours of taking first dose of cilnidipine, she developed hypoglycemia (2.2 mmol/L) as the first episode and spontaneous hypoglycemic events were repeatedly observed with the same medication. To manage her hypoglycemia, 25% dextrose solution was given accordingly. After completing the fourth dose of cilnidipine, the medication was suspected for that

adverse event and stopped. After discontinuation of cilnidipine, the spontaneous hypoglycemic event did not appear anymore and no dextrose supplement required. The patient was treated conservatively at ICU and discharged to the cabin two days later. She had been well until our last contact with her.

Discussion

Drug-induced hypoglycemia is an adverse drug event and among all hospital admissions, 23% ADEs are drug-induced hypoglycemia. Most of the reports on drug-induced hypoglycemia found in patients with glucose-lowering medications like, sulfonylureas and insulins [2]. However, the patient of this case report is non-diabetic.

Hypertension is one of the reflexes of aberrant sympathetic nerve stimulation which is highly regulated by N-type Ca^{2+} channels [3]. Cilnidipine is a long acting Ca^{2+} channel antagonist that uniquely blocks both the sympathetic N-type and L-type Ca^{2+} channels and it shows its direct inhibitory activity on the release of sympathetic neurotransmitters [1]. Studies found that once daily dosing of cilnidipine is a satisfactorily effective antihypertensive agent that can affect the heart rate also [3]. Insulin resistance is a metabolic abnormality that can cause hyperglycemia [4]. In a study on diet-induced obese (DIO) mice, researchers found that cilnidipine restricts the progression of insulin resistance and improves glucose tolerance without affecting body's adiposity. In association with obesity-related metabolic disorders, excessive fat accumulation in the body enhances the risk of insulin resistance and fat reducing approaches may improve the condition. Avoiding the involvement of body's weight or adiposity, cilnidipine modifies glucose metabolism and/or insulin sensitivity [5].

A number of study showed that L-type and/or N-type calcium channel drugs like, cilnidipine, generally affect insulin resistance and their inhibitory role on sympathetic nerves affects the insulin signaling pathways, which in turn, affects the intracellular signaling molecular activities, including adipocytes. In adipocytes, adipocytokines such as, adiponectin and TNF-alpha, are influenced by a number of cellular factors that regulate insulin resistance [6,7]. In addition, adiponectin regulates glucose metabolism by improving insulin signaling and glucose uptake by the liver and skeletal muscles. Insulin sensitivity is positively affected by the inflammatory markers which are regulated by adiponectin [8]. Researchers found that cilnidipine regulates the level of adiponectin in white adipose tissue and serum which is an insulin-sensitizer [9]. Another study demonstrated that in patients with essential hypertension, 21% insulin sensitivity is attained by using cilnidipine [5]. The aforementioned findings suggested that cilnidipine therapy improves insulin resistance and/or glucose metabolism and spontaneous hypoglycemia may be developed. In this case report,

a non diabetic-patient developed spontaneous hypoglycemia with cilnidipine therapy and the event resolved just after discontinuing the medication.

Conclusion

Cilnidipine-induced spontaneous hypoglycemia is a significant adverse drug reaction and without a prompt corrective management of this hypoglycemic event, serious life-threatening complications may be developed in patient.

Conflict of Interest

There is no conflict of interest.

Acknowledgement

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