Moxifloxacin-induced Hypoglycemia in a Non-diabetic Patient

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Abstract: Hypoglycemia is a rare life threatening adverse drug reaction associated with various fluoroquinolones like ciprofloxacin, gatifloxacin and levofloxacin. Moxifloxacin was considered safe in this regard. Only one case has been reported for moxifloxacin-induced hypoglycemia in a renal failure patient. Here, we are reporting the second case of hypoglycemia due to moxifloxacin without any major co-morbid condition.

Keywords: Adverse drug reaction, fluoroquinolones, hypoglycemia, moxifloxacin, pharmacovigilance.

INTRODUCTION

Hypoglycemia is a potentially life threatening adverse reaction associated with various drugs like sulfonamides, quinine, and fluoroquinolones. Various fluoroquinolones have different propensities to cause hypoglycemia [1]. Recently, gatifloxacin was given a black box warning and label change by US - FDA due to its dysglycemic action [2]. Levofloxacin is also associated with hypoglycemic reactions [1, 3] but there is scarcity of evidence on linkage between moxifloaxacin and hypoglycemia [1, 4]. We are reporting a case of hypoglycemia due to moxifloxacin.

CASE REPORT

A forty seven years old female patient, weighing 54 kg was admitted to medicine ward of Sir Takhtsinhji General Hospital, a tertiary care hospital, Bhavnagar, Gujarat, India with altered sensorium for one day. Patient was unconscious at the time of admission with normal pulse and elevated blood pressure of 150/100 mm Hg. Relatives gave a history of similar episode on the same day morning. On detailed history, it was known that the patient had high grade fever and dry cough since 3 days for which she had been prescribed tablet moxifloxacin 200 mg orally, 12 hourly and tablet paracetamol 500 mg as and when required. The patient took routine Indian diet (Chapati, sabji, milk) in the dinner. The patient became unconscious on second day morning. Patient was taken to the hospital and her random blood sugar (RBS) was 33 mg/dL (Reference value: 60 - 140 mg/dL) by testing with a glucometer. Patient was given 100 ml of dextrose (25 % w/v) intravenously over 30 minutes and she regained consciousness. After that, she was discharged and advised to continue the same medications for cough and fever (moxifloxacin and paracetamol). On taking the evening dose of moxifloxacin, she again lost consciousness after 3-4 hours and was brought to the Sir Takhtsinhji General Hospital, Bhavnagar, Gujarat on the same day. At that time, her blood sugar was 25 mg/dL by glucose oxidase - peroxidase (GOD/POD) method (normal 70 - 140 mg/dL). All other investigations were normal except complete blood count that showed leukocytosis (total leukocyte count 14,200/cu.mm) with neutrophilia (81% of total leukocyte count). ECG and X-ray chest (postero-anterior view) showed left ventricular hypertrophy and cardiomegaly respectively, suggestive of chronic hypertension. There was no history suggestive of seizure, trauma, diabetes mellitus, signs of meningeal irritation, endocrine abnormality and acute abdomen. There was no history of similar episodes in the past or any significant drug history. There was no history of similar episode in her family. Patient was given 200 ml of dextrose (25 % w/v) intravenously over 30 minutes and followed by 500 ml of dextrose (10 % w/v) intravenously slowly overnight. Moxifloxacin was stopped and the patient was given tablet enalapril 2.5 mg/day for hypertension, tablet paracetamol 500 mg as and when required and tablet famotidine 20 mg orally twice a day from next day onwards of hospitalization. Her random blood sugar was 124 mg/dL in the morning after dextrose drip. Patient was given two tablets of paracetamol in the next three days for fever. The patient recovered quickly and did not get any episode of hypoglycemia thereafter. This adverse drug reaction was reported to the Pharmacovigilance unit, Government Medical College, Bhavnagar, Gujarat, India. Her blood pressure came down to 130/80 mm Hg and her random blood sugar was 134 mg/dL on the third day of hospitalization. On the fourth day, the patient was discharged from the hospital (Table **1**).

An association of hypoglycemia and moxifloxacin was definite according to Naranjo's algorithm with a score of 9 [5]. It was severe according to Modified Hartwig and Siegel's scale (Level 5) [6] and definitely preventable as per Modified Schumock and Thornton scale [7].

DISCUSSION

Fluoroquinolones are one of the most commonly used antimicrobials for community acquired and hospital acquired

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Table 1. Sequence of Events of Moxifloxacin-Induced Hypoglycemia

Day	Random Blood Sugar	Remarks
Day - 1	----	Moxifloxacin (200 mg) and paracetamol (500 mg) was prescribed for cough and fever.
Day - 2 morning	33 mg/dL	Patient became unconscious within a few hours of ingestion of moxifloxacin. Episode of hypoglycemia was treated. The patient was advised to continue medicines.
Day - 2 evening	25 mg/dL	Patient became unconscious after re-challenge with moxifloxacin. Episode of hypoglycemia was treated and moxifloxacin was stopped.
Day - 3 morning	124 mg/dL	Patient was kept under observation.
Day - 4 morning	134 mg/dL	Patient was discharged on next day morning.

resistant infection. Among the fluoroquinolones, ciprofloxacin, gatifloxacin and levofloxacin are found to be associated with severe disturbances with glucose metabolism [1]. Till now, adverse events of dysglycemia were associated with moxifloxacin but causal relationship had not been established in most of these events [1, 8]. Up to the best of our knowledge, this is just the second case that shows a causal relationship between moxifloxacin and hypoglycemia [4]. Contrary to the previous case report, there are no significant co-morbid conditions like renal dysfunction, anorexia and other risk factors like diabetes mellitus that can affect glucose metabolism and can induce or aggravate this disease.

Animal studies and *in vitro* studies have shown that fluoroquinolones increase insulin release by blocking adenosine triphosphate (ATP) sensitive potassium channels and cause depolarization of pancreatic β - cells. It leads to the opening of the voltage gated calcium channels and causes calcium movement through β cells and release of insulin [9, 10]. In our case, moxifloxacin may act through this mechanism to cause hypoglycemia because hypoglycemia was developed within 24 hours of drug consumption which is consistent with hyper insulinemic hypoglycemia in previous studies [11]. Temporal association, the reappearance of event on subsequent administration and no other confounding factor that can contribute to cause hypoglycemia make this reaction more likely due to moxifloxacin. However, no measurements of blood insulin or C peptide were done.

A pooled analysis of evidences based on phase II/III clinical trials and post-marketing surveillance comprising of 14,371 patients (8474 moxifloxacin and 6257 comparator antimicrobials) show that moxifloxacin does not affect glucose metabolism significantly even in diabetic patients. Though, not even a single definite case of hypoglycemia was reported due to moxifloxacin in this analysis [8], this type of rare adverse drug reaction can be seen with the widespread and off label use of moxifloxacin. It may cause hypoglycemia in the non-diabetic patients like in our case. In our study it was empirically prescribed for cough and fever by the private practitioner. It was stopped at our hospital and no further antibiotics were prescribed. The patient was managed symptomatically. Elevated blood pressure reported on admission could be the consequences of hypoglycemia through increased catecholamine levels [12]. Elevated blood pressure is more likely to be the consequences of hypoglycemia rather than a risk factor.

In conclusion, moxifloxacin should be considered as a one of the culprits while dealing with drug-induced hypoglycemia. Clinicians should remain alert to diagnose this type of rare adverse drug reaction as it can lead to serious consequences.

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CONFLICT OF INTEREST

Declared none.

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