

Hypoglycemia Following Celecoxib Use in a Non-Diabetic Patient: A Case Report

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Abstract

Background: Hypoglycemia typically arises due to insulin or insulin-producing drugs used to treat diabetes. It can also occur from exposure to other medications like alcohol. To diagnose hypoglycemia, the first step is to determine whether it is hyperinsulinemia or non-hyperinsulinemia. To differentiate between the two, the drug history of the patient should be examined.

Case presentation: A 23-year-old male was diagnosed with hypoglycemia and hypoglycemia due to Celecoxib consumption. After ruling out potential causes, drug complication was concluded as the most probable cause. The patient was advised to discontinue Celecoxib and follow-ups at 3, 6 and 12 months showed normal blood glucose levels and no hypoglycemic symptoms.

Conclusion: Research results suggest that celecoxib and valdecoxib may be used as glucokinase-activating compounds and lead to hypoglycemia. These drugs reduce blood glucose levels by exerting their effects not only on the liver, but also in the pancreas.

Keywords: Hypoglycemia, Diabetes, NSAIDs

1. Introduction

Hypoglycemia is often caused by insulin or insulin-producing drugs used for diabetes treatment, or by exposure to other medications, including alcohol. However, several other disorders such as vital organ failure, sepsis, non-cellular tumors, insulinoma, and gastric surgeries and medications can also lead to hypoglycemia. The Whipple Triad can be used to diagnose hypoglycemia, which includes: 1) symptoms of hypoglycemia, 2) low plasma glucose concentration (less than 70 mg/dl), and 3) improvement of symptoms after an increase in plasma glucose levels. Lower levels of venous glucose can typically occur during pregnancy and prolonged fasting [1].

Severe hypoglycemia can lead to serious complications, increase the risk of cardiovascular events, and even mortality during and after the initial episode. Therefore, it should be managed as a

medical emergency. The factors that contribute to this condition are well understood [2].

The initial step in the differential diagnosis of hypoglycemia is to establish whether it is attributed to hyperinsulinemia or non-hyperinsulinemia. This determination requires a comprehensive evaluation of the patient's medical history [3]. In this review study, an examination was conducted on a patient who exhibited symptoms of hypoglycemia caused by the consumption of celecoxib.

2. Case Presentation

A 23-year-old male patient with a history of discopathy a year prior to the current referral occasionally used painkillers to alleviate his pain. His back pain worsened in the week leading up to the referral, prompting him to take two doses of methylprednisolone,

three doses of ketorolac, and diclofenac 100 mg orally. He discontinued diclofenac due to digestive issues and started taking celecoxib 100 mg along with gabapentin 300 capsules and vitamin B1. After taking celecoxib for four days, the patient experienced heaviness, apprehension, palpitations, sweating, tremors, and severe weakness. These symptoms improved when the patient consumed sweet food. The patient did not visit a doctor during this time. On the sixth day of using celecoxib, the symptoms recurred, and a self-administered glucometer test revealed low blood sugar (58 mg/dl), causing the patient to seek medical attention due to anxiety.

During the initial examination, the patient's blood pressure was measured several times and was found to be 160/90 mmHg. The patient expressed dissatisfaction with hospitalization and was subsequently examined as an outpatient.

The following tests were requested and found to be normal except for FBS, which was in the hypoglycemic range: CBC, LFT, Na, K, TFT, RFT, Ca, 2hpp, HbA1C, lipid profile, CPeptide, ESR, urinary and morning free cortisol, urinary VMA, metanephrine, and urinary normetanephrine.

60mg/dL	FBS
88mg/dL	BS(2hpp)
5.8	HbA1C
13 mg/dL	BUN
0.9 mg/dL	Cr
102 mg/dL	Triglycerides
194 mg/dL	Cholesterol
53 mg/dL	HDL
112 mg/dL	LDL
22U/L	AST
37U/L	ALT
140mmol/L	Na
3.9mmol/L	K
9.1mg/dL	Ca
3mm/hrs	ESR
9.7µIU/mL	Insulin
16.8µg/dL	Cortisol 8 am
62micg/24H	Urine free cortisole
149micg/day	Urinary Metanephrine 24hrs
395micg/day	Urinary Normetanephrine 24hrs
2.60ng/mg	C-Peptide
2.76micIU/mL	TSH
7.2µg/dL	T4
61pg/mL	Aldosterone
22.80micIU/ml CLIA	Renin
9.3mg/24hrs	Urinary VMA 24hrs

Table 1: Laboratory Tests Requested For the Patient Mentioned in the Study

In the investigation of other causes of secondary hypertension, renal parenchymal ultrasound, renal artery Doppler ultrasound, and abdominal contrast CT scan were performed, all of which showed no pathological findings.

The patient's symptoms, including apprehension, heart palpitations, tremors, and severe weakness, improved after discontinuing celecoxib and starting amlodipine 5mg tablets to control blood pressure. The patient's blood pressure returned to normal, so the amlodipine tablets were stopped. Additionally, the patient's fasting

and postprandial glucose tests came back within the normal range.

At the 3, 6, and 12-month follow-up, the patient had no hypoglycemic symptoms, normal blood pressure, and normal blood glucose tests.

3. Discussion

COX-1 and COX-2 are the two primary isoforms found in the enzyme cyclooxygenase (COX). The term "non-steroidal anti-inflammatory drugs" (NSAIDs) refers to a class of diverse

substances recommended for their anti-inflammatory, antipyretic, and pain-relieving effects. These effects are achieved by inhibiting COX [4].

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is widespread among patients with musculoskeletal conditions. Several studies have linked NSAIDs with serious gastrointestinal issues like ulcers, bleeding, and perforation of the digestive tract. Moreover, using these drugs in combination with risk factors such as advanced age, a history of stomach ulcers, or other medications can further elevate the chances of experiencing these side effects. The fewer NSAID-related side effects studied suggest the possibility of severe NSAID-induced hypoglycemia in hospitalized patients treated with hypoglycemic drugs [5].

Several cases of hypoglycemia have been reported following the use of aspirin and indomethacin but have rarely been reported following the use of other nonsteroidal anti-inflammatory drugs [6]. Research results suggest that celecoxib and valdecoxib may be capable of being used as glucokinase-activating compounds, potentially leading to hypoglycemia [7]. The findings gathered from preclinical studies confirm the hypothesis that these drugs lower blood glucose levels by exerting their effects not only in the liver but also in the pancreas. Diabetics are expected to see significant improvements in their glucose control, leading to the function of GKAs [8].

Hypoglycemia is rare in untreated diabetic individuals. When present, it can be mistaken for other conditions. This case study shows the significance of gathering a thorough medical history and recognizing the various medications that can lead to hypoglycemia.

4. Acknowledgment

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5. Conflict of interest

There is no conflict of interests.

6. Ethical Approval

The present study has the approval of the ethics committee of Hamadan University of Medical Sciences with the number IR.

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7. Authors' contribution

First author: Designing the study and interpreting the results and scientific editing of the article (50%), second author: participation in the writing of the article (20%), third author: data collection (20%), fourth author: data collection (10%).

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