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Norfloxacin-induced hypoglycemia and urticaria

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Abstract

Fluoroquinolone-induced hypoglycemia is not a common adverse drug reaction. However, it has been reported with most of the available agents and appears to be more common in elderly patients with a history of type 2 diabetes who are receiving oral sulfonylureas. The exact mechanism of this effect is unknown but is postulated to be a result of blockage of Adenosine 5'-Triphosphate (ATP)-sensitive potassium channels in pancreatic β -cell membranes. This report highlights hypoglycemia with urticaria as an adverse drug reaction of norfloxacin in a middle aged non-diabetic patient. Clinicians should be alert about the possibility of its potential adverse effect in patients who are receiving norfloxacin therapy.

KEY WORDS: Hypoglycemia, norfloxacin, urticaria

Introduction

Norfloxacin is a fluoroquinolone antimicrobial. It inhibits bacterial DNA synthesis and is used to treat a number of bacterial infections. Fluoroquinolones are generally regarded as safe antimicrobial agents with relatively fewer adverse effects. Norfloxacin is registered for therapeutic use in acute recurrent urinary tract infections, prostatitis, bacterial gastroenteritis, gonorrheal urethritis, proctitis, and cervicitis as well as for prophylactic use in neutropenic patients. Although uncommon, hypoglycemia has been reported with most of the fluoroquinolones.^[1–7]

Case Report

A 48-year-old woman presented in the emergency department with giddiness, restlessness, and rash over thigh and abdomen. The patient reported these symptoms after taking two doses of oral norfloxacin for suspected urinary tract infection from a practitioner. Her medical history suggested one episode of urinary tract infection. There was no history of allergy, diabetes mellitus, hypertension, and ischemic heart disease. On physical examination, she was afebrile with pulse rate of 84/min, blood pressure 124/80 mm Hg, and respiratory rate 20/min. Urticarial rashes were noted on the thigh and abdomen. Other physical findings were unremarkable. The patient's initial laboratory evaluation showed random blood sugar 46 mg/dl and simultaneous serum insulin level was 37.8 μ U/ml (normal range: 6.0–27.0 μ U/ml). Other hematological and biochemical blood tests were within the normal range. Electrocardiogram (ECG), chest X-ray, and abdominal ultrasonography did not reveal any abnormality. She had symptomatic relief after administration of 50 ml of intravenous 50% dextrose; hence, subsequent treatment with intravenous dextrose was not required. Concurrent therapy at the time of the patient's hypoglycemic event consisted of oral paracetamol 500 mg. The patient had received paracetamol for fever. However, no fever was recorded during the hospital stay. From hospital admission until the day of discharge, there was no further episode of hypoglycemia and

her blood glucose level was in the range of 71-140 mg/dl.

Discussion

Hypoglycemia caused by some fluoroquinolones is well established in literature. Published reports are available for ciprofloxacin, gatifloxacin, and clinafloxacin,[1–7] but, to our knowledge, there are no published reports of hypoglycemia with norfloxacin. The proposed mechanism by which the fluoroquinolones induce glycemic abnormalities is not clearly understood. The primary theory of fluoroquinolone-associated hypoglycemia is twofold, consisting of both pharmacokinetic and pharmacodynamic effects. The pharmacokinetic mechanism involves drug–drug interactions, while the pharmacodynamic mechanism comprises the possibility of enhanced pancreatic β -cell stimulation and subsequent increased insulin release.[8] Other investigators have also demonstrated the effect of lomefloxacin and norfloxacin on Adenosine 5'-Triphosphate (ATP)-sensitive potassium channels in pancreatic β -cells.[9] In our patient, laboratory evaluation showed relatively inappropriate insulin elevation at the time of hypoglycemic episodes, consistent with pancreatic β -cell stimulation. Causality analysis by using Naranjo ADR Probability Scale indicated a probable relationship between the adverse effect of hypoglycemia and norfloxacin therapy in this patient.[10] The urticarial rash also strongly supports a probable relationship between the adverse reaction of hypoglycemia and norfloxacin therapy. Hypoglycemic stress can activate the release of Corticotrophin-Releasing Hormone (CRH) by postganglionic sympathetic neurons as well as the hypothalamus. CRH-stimulated mast cell degranulation could lead to urticaria.[11] Concurrently administered drugs should be considered for their potential to cause hypoglycemia alone or as a result of a drug–drug interaction. However, in our case, oral paracetamol is less likely to cause hypoglycemia either alone or as a result of a drug–drug interaction.

Footnotes

Source of Support: Nil,

Conflict of Interest: None declared.

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