Turkish Journal of Geriatrics
2014; 17 (4) 426-430

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Case Report

HYPOGLYCEMIA CAUSED BY CIPROFLOXACIN IN A NON-DIABETIC ELDERLY PATIENT: A CASE REPORT

Abstract

Fluoroquinolones, a commonly used class of antibiotics, can impair glucose homeostasis. Hypoglycemia may be life-threatening in non-diabetic elderly patients with renal impairment. An 80-year-old female patient was admitted to the emergency department with hypoglycemia. The patient was not a diabetic and did not use antidiabetic drugs. Three days prior, she had received ciprofloxacin for a urinary tract infection. During hypoglycemic process, her insulin level was not suppressed. At follow-up in inpatient service, her insulin level had returned to the normal range. Her serum cortisol level was normal, and pancreatic imaging was normal. After ciprofloxacin was discontinued, no further hypoglycemic episodes occurred. Physicians should be careful in prescribing fluoroquinolones in older patients who are prone to hypoglycemia. Moreover, drug-related causes should be considered in cases of unexplained hypoglycemia.

Key Words: Aged; Hypogylcemia; Ciprofloxacin.

Olgu Sunumu

DİYABETİK OLMAYAN YAŞLI BİR HASTADA SİPROFLOKSASİNİN NEDEN OLDUĞU HİPOGLİSEMİ: BİR VAKA SUNUMU

Öz

Antibiyotiklerin yaygın olarak kullanılan bir sınıfı olan florokinolonlar, glukoz dengesini bozabilir. Böbrek yetersizliği olan non-diyabetik yaşlılarda florokinolon kullanımında (özellikle siprofloksasin)hipoglisemi hayatı tehdit edici olabilir. Seksen yaşında kadın hasta acil birimine hipoglisemi ile başvurdu. Hasta diyabetik değildi ve antidiyabetik ilaç kullanmıyordu. Üç gün önce idrar yolu enfeksiyonu için siprofloksasin almıştı. Hipoglisemik süreç boyunca hastanın insülin düzeyi baskılanmadı. Hastanın yatan hasta servisinde yapılan takiplerinde insülin düzeyi normal aralığa döndü. Serum kortizol düzeyi normaldi, ve pankreas görüntülemesi normaldi. Siprofloksasin kesildikten sonra başka hipoglisemi atakları olmadı. Doktorlar hipoglisemiye meyilli olan yaşlı hastalara florokinolon reçete ederken dikkatli olmaları gerekir. Ayrıca, açıklanamayan hipoglisemi durumlarında ilaç-ilişkili nedenler akla gelmelidir.

Anahtar Sözcükler: Yaşlı; Hipoglisemi; Siprofloksasin.

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Geliş Tarihi: 02/09/2014
(Received)

Kabul Tarihi: 16/10/2014
(Accepted)

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Introduction

Fluoroquinolones are among the most commonly used antimicrobial drugs for the treatment of community- and hospital-acquired infections because of their broad spectrum of activity, oral application, good tolerance and safety, and few adverse effects (1). However, some fluoroquinolones have been withdrawn from the market because of adverse effects. For example, temafloxacin causes hemolysis and hypoglycemia (2), and trovafloxacin causes hepatotoxicity (3,4).

Disturbances in glucose homeostasis are one of the drug's most relevant side effects. Both hypoglycemic and hyperglycemic episodes may be observed during fluoroquinolone treatment. Hypoglycemia is rare but life-threatening and can be fatal (5,6). Quinolone-induced hypoglycemia has been reported for all fluoroquinolones (7). Cases of hypoglycemia are particularly common in gatifloxacin treatment of older and diabetic patients (8). Aspinall et al. reported that hypoglycemia is more frequent during gatifloxacin treatment than with other fluoroquinolones. Levofloxacin also poses an increased risk of hypoglycemia (8). The study authors expressed concerns about the significant risk associated with the use of levofloxacin.

Most hypoglycemic episodes are related to interactions with oral antidiabetic drugs and depend on the potentiation of oral antidiabetic drugs, such as sulfonylureas or insulin, in older diabetic patients (9-14). However, fluoroquinolones may induce hypoglycemia in some non-diabetic patients (15). Hypoglycemia typically occurs within the first 3 days of fluoroquinolone therapy.

Some of the factors that affect the development of hypoglycemia include age, renal dysfunction, inadequate nutrition, hepatic failure, malignancy and corticosteroid use (8). In the literature, ciprofloxacin is associated with the lowest risk of hypoglycemia. However, rare cases of hypoglycemia have been described in elderly diabetic patients (9). In this case report, we present a patient without diabetes who experienced hypoglycemia associated with ciprofloxacin use.

Case Report

An eighty-year-old female patient without any history of diabetes admitted to infectious disease policlinics with the complaint of pain during urination. She was diagnosed to have urinary tract infection and was prescribed ciprofloxacin (500 mg orally twice per day).On the third day of antibiotic treatment, she was brought to emergency room by her husband because of confusion, diaphoresis and slurred speech. In the emergency room her blood pressure was 100/70 mmHg, body temperature was 36.5 °C and pulse was 98 beats/min. Her respirations were deep and were 22/minute. Capillary blood glucose level measured by finger-stick was 47 mg/dl. After rapid administration of 20% glucose solution, blood samples were taken for further measurement of hormonal parameters (cortisol, thyroid function tests, insulin and c peptide). Dextrose infusion was continued until the blood glucose returned to normal and confusion dissolved. Cranial CT was ordered after neurology consultation and we didn't detect any pathological finding.

The laboratory findings were as follows: urea:79 mg/dl, creatinine: 2.4 mg/dl, serum sodium: 140 mEq/L, potassium: 5.8 mEq/L, insulin 42.4 µU/ml (3-17 µU/ml) and c-peptide 16.41 ng/ml (normal range 0.78-5.9 ng/ml), aspartate aminotransferase/alanine aminotransferase level 34/44 IU/L.

In the past medical history, she had hypertension for ten years and has been treated with valsartan plus hydrochlorothiazide combination. Three days prior to presentation, a quinolone was added to her medications. In the differential diagnosis of hypoglycemia, we questioned the patient and she declared that she didn't use any oral anti-diabetic agent accidently or consciously. Since she had hypoglycemia, low blood pressures and hyperpotassemia at the time of admission, we searched for a possible adrenal insufficiency and it was excluded since serum cortisol level was measured as 34 µg/dl (normal range 3.7-19 µ). Because of the elevated insulin and c-peptide levels, we performed pancreatic imaging, and it was normal.

After 4 hours of dextrose infusion, her consciousness returned to normal. There was no hypoglycemic attack over the following five days. We sent blood samples to measure insulin levels during the normoglycemic period; her insulin level was 13.3 µU/ml (normal range 3-17 µU/ml). For her urinary tract infection, we obtained a urine culture and prescribed second-generation cephalosporin adjusted to creatinine clearance. Treatment for UTI was continued for one week and stopped. Urine culture was negative after the treatment. During the follow up, her glomerular filtration rate was low as 49 ml/h and her serum potassium level was 5.8-5.4 mg/dl. Given the low creatinine clearance and elevated potassium level, we changed her antihypertensive drug to a calcium channel blocker. In routine laboratory evaluation, we observed subclinical hyperthyroidism and performed thyroid ultrasonography revealing multinodular goiter. After thyroid scintigraphy, thyroid fine needle aspiration was performed. Since the pati-

ent did not exhibit any hyperthyroid symptoms; we advised her to reduce the iodine in her diet. After discontinuing ciprofloxacin, we did not observe any hypoglycemic episodes.

Discussion

Fluoroquinolone-induced hypoglycemia has been described infrequently, especially in older diabetic patients with renal failure who use sulfonylurea; fluoroquinolones are known to potentiate oral antidiabetic drugs (12,13). Renal failure predisposes patients with or without diabetes to hypoglycemia. This results from numerous factors, including chronic malnutrition, anorexia, decreased renal clearance, decreased drug clearance, decreased clearance of endogenous insulin and decreased renal gluconeogenesis. Aspinall et al. (8) studied whether drug class affected the glucose disturbances associated with fluoroquinolones; in their study, only 25.1% of patients exhibited diabetes. They reported that the odds ratio for severe hypoglycemia with gatifloxacin was 4.3, while with levofloxacin and ciprofloxacin the ratios were 2.1 and 1.1, respectively, in diabetic patients. In patients without diabetes, the odds ratio was 1.9 for gatifloxacin, 1.6 for levofloxacin, and 0.7 for ciprofloxacin. In addition, hypoglycemia requiring hospitalization was more common with gatifloxacin and levofloxacin than with ciprofloxacin (8). According to this study, ciprofloxacin was safer than the other drugs. However, our patient used ciprofloxacin and was neither a diabetic nor did she use oral antidiabetic drugs.

Mohr et al. (15) found that there were no significant differences in the risk of dysglycemia between gatifloxacin and levofloxacin. In contrast to our patient, the authors did not observe any hypoglycemic events with ciprofloxacin use. In another study, published by Park-Whylli et al., the odds ratio for hypoglycemia was 4.3 in gatifloxacin-treated patients and 2.9 in levofloxacin-treated patients; however, there was no risk associated with moxifloxacin, ciprofloxacin or cephalosporins (6). In a further study, there was no risk of dysglycemia with ciprofloxacin. This study included 17,108 patients receiving a fluoroquinolone, and the dysglycemia rates were as follows: gatifloxacin 1.01%, levofloxacin 0.93%, ceftriaxone 0.18%, and ciprofloxacin 0% (15).

The mechanism of fluoroquinolone-induced hypoglycemia is similar to that of sulfonylureas, which stimulate insulin secretion by inhibiting K-ATP channels in the islets of Langerhans. This inhibition leads to the depolarization of the beta cell membrane and the opening of voltage-dependent calcium channels, allowing calcium movement into the cells with subsequent insulin release. Hany et al. reported that the enhancement of insulin secretion is a group effect of fluoroquinolones and depends on their ability to block K-ATP channels in pancreatic beta cells. As we mentioned above, chronic renal failure itself may predispose patients to hypoglycemia whether or not they are diabetic. The conditions underlying this relationship include chronic malnutrition, anorexia, vomiting, decreased renal clearance, decreased drug clearance, insulin clearance and diminished renal gluconeogenesis. Several authors have reported levofloxacin-induced hypoglycemia in chronic renal failure patients (13, 14).

Ciprofloxacin, like the other fluoroquinolones, is primarily eliminated through the kidneys. Hypoglycemia-induced ciprofloxacin has been reported in diabetic patients using oral hypoglycemic drugs. There may be an interaction between ciprofloxacin and antidiabetic drugs.

We believe that the cause of hypoglycemia in our patient was her moderate renal dysfunction and the use of ciprofloxacin. We used the Naranjo adverse drug reactions (ADR) scale to document the possibility of a relationship between ciprofloxacin and hypoglycemia. Our score was four, indicating that ciprofloxacin-related hypoglycemia is a possibility. We did not assess the following parameters in our patient: response to placebo, rechallenges with ciprofloxacin, and the blood level of ciprofloxacin. Our patient was older and exhibited renal impairment, but she exhibited no history of diabetes or any use of oral antidiabetic drugs.

Although fluoroquinolones are frequently used, 80.4% of physicians are unaware of hypoglycemia induced by fluoroquinolone. Hypoglycemia in elderly patients is a life-threatening problem, especially in the case of the administration of oral antidiabetic drugs in the presence of chronic renal failure and inadequate nutrition. Hypoglycemia can cause irreversible brain injury or dementia. Although hypoglycemic episodes may resolve, patients can suffer serious health problems. Therefore, the condition requires hospitalization.

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