Hyponatremia and Hyperkalemia Caused by Moxifloxacin Use: A Case Report

Moksifloksasin Kullanımının Neden Olduğu Hiponatremi ve Hiperkalemi: Olgu Sunumu

Kubilay İşsever[1], Erkut Etçioğlu[2], Emel Gönüllü[3]

[1] *Sakarya University Medical Faculty Department of Internal Medicine,Turkey*

[2] *Sakarya University Medical Faculty Department of Family Medicine,Turkey*

[3] *Sakarya University Medical Faculty Department of Internal Medicine,Division of Rheumatology, Turkey*

Yazışma Adresi / *Correspondence:*
Erkut Etçioğlu

Sakarya Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, Korucuk Mahallesi Konuralp Bulvarı No:81/1 Korucuk Kampüsü, Adapazarı/Sakarya
T: **+ 90 553 574 78 37** E-mail: **erkutetcioglu@gmail.com**

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Orcid:
Kubilay İşsever https://orcid.org/000-0002-1376-1488
Erkut Etçioğlu https://orcid.org/0000-0002-8117-7929
Emel Gönüllü https://orcid.org/0000-0002-6990-4206

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Abstract

Moxifloxacin is an antibiotic of quinolone group and its usage frequency for inpatients increases day by day. Reported side effects for this antibiotic include nausea, vomiting, stomachache, headache, hypoglycemia or hyperglycemia, anemia, arthralgia, myalgia and tendon rupture. Solely, side effects regarding electrolyte imbalance are rarely reported. Since an infiltration in the right basal region of the lung was found on chest X-ray, prophylactic moxifloxacin was started. The plasma sodium (Na) level of the patient decreased to 129 (135-145) mEq/L on the fifth day of the treatment while the potassium (K) level increased to 5,8 (3.5-5.5) mmol/L on the fifth day of the treatment. When blood and urine culture test results came out as negative, moxifloxacin treatment was discontinued on its 5th day. Three days after the discontinuation, Na and K levels reached to normal levels. This situation made us think that hyperkalemia and hyponatremia occurred as a side effect of moxifloxacin treatment. If hyponatremia and/or hyperkalemia occur during treatment of moxifloxacin, adverse effects must be thought and the treatment must be discontinued immediately.

Keywords Moxifloxacin; Adult Still's Disease; Hyperkalemia; Hyponatremia

Öz

Moksifloksasin, kinolon grubu bir antibiyotiktir ve yatan hastalarda kullanım sıklığı her geçen gün artmaktadır. Bu antibiyotik için bildirilen yan etkiler arasında mide bulantısı, kusma, karın ağrısı, baş ağrısı, hipoglisemi veya hiperglisemi, anemi, artralji, kas ağrısı ve tendon rüptürü vardır. Elektrolit dengesizliği ile ilgili yan etkiler literatürde nadiren bildirilmiştir. Akciğer grafisinde akciğer sağ bazal bölgede görülen infiltrasyon alanına yönelik profilaktik moksifloksasin tedavisi başlandı. Hastanın plazma sodyum (Na) seviyesi tedavinin beşinci gününde 129 (135-145) mEq / L'ye düşmüş, potasyum (K) seviyesi tedavinin beşinci gününde 5,8 (3.5-5.5) mmol / L'ye yükselmiştir. Kan ve idrar kültürü test sonuçları negatif olarak sonuçlanmasıyla moksifloksasin tedavisi 5. gününde kesildi. Tedavinin kesilmesinden üç gün sonra Na ve K seviyeleri normal seviyelere ulaştı. Bu durum, hiperkalemi ve hiponatreminin moksifloksasin tedavisinin bir yan etkisi olabileceğini düşündürdü. Moksifloksasin tedavisi sırasında hiponatremi ve / veya hiperkalemi ortaya çıkarsa, yan etkiler düşünülmeli ve tedavi derhal kesilmelidir.

Anahtar kelimeler *Moksifloksasin; Erişkin Still Hastalığı; Hiperkalemi; Hiponatremi*

INTRODUCTION

The quinolone group of antibiotics has become the most popular class of antibiotics in recent years due to its broad spectrum of antibacterial effects. Especially new generation quinolones (moxifloxacin, gemifloxacin, etc.) has started to be preferred frequently in clinical practice due to its efficacy for gram positive, gram negative and anaerobic bacteria, good pharmacokinetics, easy posology as using once or twice daily and safe side effect profile.[1] In spite of the side effects of quinolone antibiotics, which are widely used in many diseases such as sinusitis, urinary tract infections, atypical pneumonia, chronic bronchitis and tuberculosis. Reported side effects for this antibiotic include nausea, vomiting, stomachache, headache, hypoglycemia or hyperglycemia, anemia, arthralgia, myalgia and tendon rupture.[2] There are very few reports about the side effects related to fluid-electrolyte balance. In this case report, we aimed to report the side effects of hyponatremia and hyperkalemia after moxifloxacin use in a patient treated in rheumatology department. The informed consent form was signed by the patient and his consent was obtained.

CASE

A forty-six years old male patient was presented to another clinic with complaints of fever, weakness, and high blood pressure two weeks prior to his admission to our hospital. After intravenous (IV) antihypertensive (unknown name) medication, disseminated erythematous macules and papules presented on his body. The patient admitted to the dermatology outpatient clinic and hospitalized with prediagnosis of drug allergy. He was treated with intravenous prednisolone 40 mg / day, antihistaminic tablets twice daily and topical treatment for 3 days in the dermatology department. The patient complained about fever and fatigue, and a posteroanterior chest X-ray revealed an infiltration siteat the right basal region. As a result, prophylactic moxifloxacin was started as pneumonia treatment after consulting with pulmonary diseases specialist. However, on the sixth day of the treatment the patient was discharged on his will. The patient was admitted to the outpatient clinic and hospitalized again with complaints of high fever and rash three days later. The next day, rheumatology consultation was requested and the patient was taken over by rheumatology department with Adult Still's Disease pre-diagnosis. Redness and rashes which appeared on his back, involved his abdomen and localized on lower extremities were added to his complaints.

He had a history of hypertension. The patient was receiving 16 mg of candesartan cilexetil and 12.5 mg of hydrochlorothiazide combination treatment. However, he had not used these drugs for about 10 days. The patient's family history was unremarkable. Physical examination revealed no pathological findings other than non-eruptive erythematous rashes on the abdominal region and back. Moxifloxacin, which was previously planned by dermatology department, was administered on the day before patient transfer to rheumatology department.

The test results revealed as sodium (Na): 129 (135-145) milliequivalents per liter (mEq / L), potassium (K): 5 (3.5-5.5) millimoles per liter (mmol/L), alanine aminotransferase (ALT) : 73 (0-50) international units per milliliter (IU / ml), aspartate aminotransferase (AST) : 41 (0-50) IU / ml, leuocyte : 10.100 (4600-10200) / mm3, C reactive protein (CRP) : 129 (0-5) milligrams per liter (mg / L), anti-HAV IgM: negative, anti-HBc IgM: negative, anti-CMV Ig M: negative, anti-rubella: negative, Acid Fast Bacilli (AFB) in sputum examination: negative, rheumatoid factor (RF): negative, Erythrocyte Sedimentation Rate (ESR): 37 nanometers per hour (nm/h) (<15), ferritin: 1102 (20-500) nanograms per milliliter (ng/mL), parvovirus B19: negative, Antinuclear Antibody (ANA) : negative, Anti-Extractable Nuclear Antigen (Anti-ENA): negative, C3 and C4 level: normal, Brucella Rose Bengal and Wright: negative, Mono Test: negative, urine sediment: normal. Transthoracic echocardiography examination revealed an ejection fraction (EF) of 60% and no vegetation. Prediagnosis of infective endocarditis was ruled out.

Existence of high fever lasting more than 1 week (≥ 39 degrees celsius (C°)) with typical non-itchy, salmon-pink maculopapular skin rash from major criteria and RF negativity from minor criteria of Yamaguchi criteria confirmed the diagnosis as Adult Still's disease.[3] Paracetamol and moxifloxacin were given on the first day while intravenous immunoglobulin (IVIG), paracetamol, first generation antihistaminic and moxifloxacin were administered on the second day of takeover. On the third day, prednisolone 60 mg/day IV was added to the treatment while IVIG was discontinued. On the third day of prednisolone treatment, fever and rashes regressed. Acute phase reactants regressed as CRP was found as 41 (0-5) mg / L and ferritin was found as 600 (20-500) ng/mL on the 3rd day, and CRP was 7 (0-5) mg / L, ferritin was 120 (20-500) ng on the 5th day of prednisolone treatment.

Na and K levels were 129 mEq / L and 5 mmol / L on the 2nd day of the moxifloxacin treatment while levels were 130 mEq / L and 5.8 mmol / L, respectively,on the 5th day of treatment. Considering that paracetamol and prednisolone cannot cause this condition, as soon as blood and urine culture results were found as negative, moxifloxacin treatment was discontinued. Na and K levels were 134 mEq / L and 4.4 mmol / L on the 1st day; 134 mEq / L and 4.5 mmol / L on the 2nd day and 135 mEq / L and 4.6 mmol / L on the 3rd day of discontinuation, and considered as normal. Thus, our hypothesis about causation of hyponatremia and hyperkalemia by moxifloxacin was supported. (Table-1)

As the clinical symptoms of the patient regressed as a result of the examinations and treatments, prednisolone treatment was continued in tablet form and he was discharged with recommendations and suggestions of rheumatology follow up.

Table-1: Daily changes in electrolyte values after moxifloxacin use and discontinuation

	Mox. 2nd day	Mox. 5th day	Mox. Post-Stop 1st day	Mox. Post-Stop 3rd day
Na (mEq/L)	129	130	134	135
K (mmol/L)	5	5.8	4.4	4.6

Na: Sodium, K: Potassium, Mox.: Moxifloxacin

DISCUSSION

Quinolones are highly tolerated drugs that have been extensively evaluated for their widespread clinical use, particularly ciprofloxacin and ofloxacin, and their efficacy and side-effect profiles are well observed in randomized double-blind trials.

Fluoroquinolones can prolong the QT interval by inhibiting cardiac potassium voltage-gated channels (KCHN2), potentially leading to torsades de pointes.[4]

Among these side effects, those related to electrolyte imbalance are perhaps the least known side effects of fluoroquinolones. In one case report, moxifloxacin-induced syndrome of inappropriate antiduretici hormone secretion (SIADH) was reported.[5] Moxifloxacin as the cause of hyponatremia and again, SIADH as the underlying mechanism have been reported in another case.[5] Stimulation of gamma-aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) receptors is thought to affect changes in antidiuretic hormone (ADH) secretion by affecting neuroendocrine cell physiology in the brain. Thus, mechanism which makes moxifloxacin cause SIADH is thought to be related with this receptor stimulating or function changing affect of the drug.[6]

Although there have been reported cases of SIADH and hyponatremia as side effects, there is no reported case of hyperkalemia as a side effect in the literature. Although it was thought that angiotensin-converting enzyme (ACE) inhibitors and thiazide group antihypertensive drugs used by our patient in daily routine may cause this condition,

the patient discontinued these drugs 10 days before this clinical picture. Therefore, it is not possible to attribute the hyperkalemia which occurred in the patient to these drugs. The coexistence of hyponatremia with hyperkalemia implies the suspicion of hypoaldosteronism. Hyponatremia and hyperkalemia may occur in hypoaldosteronism or type 4 renal tubular acidosis with increased urinary sodium excretion and increased potassium reabsorption from renal tubules.[7,8] Inability to analyse urinary sodium and potassium excretion took place as the limitation of our case report. There is no clear information about whether moxifloxacin caused this clinical picture via hypoaldosteronism.

CONCLISION

Hyperkalemia and hyponatremia due to moxifloxacin use should be kept in mind and treatment must be discontinued immediately if these side effects occur.

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