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Hypotension, the Influence of Mirtazapine in a Patient with Chronic Renal Failure

Hipotansiyon, Kronik Böbrek Yetmezlikli Hastada Mirtazapinin Etkisi

ABSTRACT

In patients with end-stage renal disease (ESRD), depression is the most commonly identified psychiatric illness; however, its prevalence varies since it is assessed by using different methods in different studies and in different populations. The commonly accepted view in the treatment of depression is a combination of psychotherapy and pharmacologic treatment. Mirtazapine is an antidepressant used in the treatment of major depressive illness which affects both noradrenergic and serotonergic activity. This paper is a case report of a 40 year old man with a history of renal failure who developed hypotension while receiving mirtazapine therapy. We believe that hypotension was a conclusion of the mirtazapine in our patient and hemodialysis had no influence on hypotension. Hypotension improved after the metabolization of mirtazapine (approximately thirty-six hours).

KEY WORDS: Hypotension, Chronic renal failure, Mirtazapine, Hemodialysis

ÖZ

Son dönem böbrek yetmezliği olan hastalarda depresyon en sık tanımlanan psikiyatrik hastalıktır, fakat depresyon prevalansı farklı çalışmalarda, farklı popülasyonlarda, farklı yöntemlerle değerlendirildiğinden değişiklikler göstermektedir. Depresyon tedavisinde kabul gören genel görüş tedavide psikoterapi ve ilaç tedavisinin kombinasyonu şeklindedir. Mirtazapin hem noradrenerjik hem de serotonerjik aktiviteyi etkileyen ve majör depresyon ile duygu durum hastalıklarında kullanılan anti depresan ilaçtır. Bu makalede, 40 yaşında böbrek yetmezliği öyküsü olan erkek hastada mirtazapin tedavisi sırasında gelişen hipotansiyon sunulmuştur. Düşüncemize göre, hipotansiyon mirtazapin kullanımın bir sonucu oluşmuştur ve hipotansiyon üzerine diyalizin bir etkisi yoktur. İlaç metabolize edildikten sonra hipotansiyon düzelmiştir (Yaklaşık 36. saat).

ANAHTAR SÖZCÜKLER: Hipotansiyon, Kronik böbrek yetmezliği, Mirtazapin, Hemodiyaliz

Demet YAVUZ[1]
Rahman YAVUZ[2]

1 Samsun Training and Research Hospital, Clinic of Nephrology, Samsun, Turkey
2 Ondokuz Mayıs University, School of Medicine, Department of Medical Education, Samsun, Turkey

INTRODUCTION

In patients with ESRD, depression is the most common psychological disorder with a prevalence proportion as 20% to 25% as per last forecasts. Several studies have linked depression with mortality in ESRD, which is a sign that makes early diagnosis and treatment essential (1). Major depressive disorder is a clinical syndrome that lasts for 2 weeks and during these two weeks, the patient experience s either depressed mood or anhedonia along with at least 5 of the 9 'Diagnostic and Statistical Manual of Mental Disorders IV' criterion symptom domains and it is associated with adverse outcomes (2). For the treatment of psychiatric disorders in patients with renal failure, drugs are commonly used. While choosing the drug and adjusting the dosage in ESRD patients, some factors are taken into consideration. The drug metabolizes through the renal or the hepatic pathway, and it might be eliminated through hemodialysis (3).

A limited number of studies on the treatment of depression are found for patients with ESRD. There are a number of treatment alternatives such as psychotherapy, electroconvulsive therapy, pharmacologic

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Correspondence Address:
Rahman YAVUZ
Ondokuz Mayıs University
School of Medicine, Department of Medical Education, Atakum, 55139
Samsun, Turkey
Phone : +90 362 312 19 19
E-mail : rahmanyavuz55@hotmail.com

therapy(4). Mirtazapine is a tetracyclic piperazinoazepine, which enhances central noradrenergic and serotonergic (5). After single and multiple oral administration, Mirtazapine is rapidly and well absorbed from the gastrointestinal tract and peak plasma concentrations are reached within 2 hours. Mirtazapine binds to plasma proteins in proportion as % 85. It indicates pharmacokinetics whereon a dosage range of 15 to 80 mg. An approximately 30% decrease in oral mirtazapine clearance is caused by liver and moderate renal impairment while a % decrease is caused by a severe renal impairment (6). Mirtazapine may have a few cardiac effects which causes very orthostatic hypotension (7). Regardless of the severity degree, patients with renal failure well tolerated the 15 mg/day dosage of drug. Further research is needed to evaluate repeated dose pharmacokinetics and tolerability of mirtazapine in patients with renal failure (8).

CASE REPORT

This paper presents a predialysis patient who is treated with mirtazapine due to the fact that depressive disorder. It is possible for mirtazapine to have caused hypotension and detrimental influences on renal function. Our case was a 40 year old man with a history of renal failure, depression and stage III chronic kidney disease. The patient had no history of hemodialysis. The patient's depressive disroder had started a year ago. He was diagnosed with moderate depression and we started the antidepressive pharmacotherapy with 15 mg mirtazapine. The physical examination of the man showed him to be afebrile, with a blood pressure of 123/76 mm Hg, and a pulse of 86. On admission, his blood urea nitrogen value was 60 mg/dL and creatinine value was 2.4 mg/dL. Urinalysis was found to be normal before mirtazapine. He had been having treatment with sevelamer, acetylsalicylic acid, and lansaprazole.

Before taking mirtazapine, the patient was haemodynamically stable. However, 2 hours after the administration of mirtazapine he had an arterial pressure of 90/55 mmHg. 8 hours after administration, the arterial pressure value became 85/51 mmHg, 24 hours after administration the pressure became 94/51 with associated symptoms. The pressure became 105/72 mmHg 36 hours after administration and 40 hours after the administration, blood pressure was 121/75 (Figure 1). Haemorrhagic or infectious complications were ruled out while secondary hypotension due to mirtazapine began to be considered. Sinus tachycardia was seen in the electrocardiography. The patient's general condition began to deteriorate 8 hours after the administration of mirtazapine. Metabolic acidosis and increased creatinine level were observed. The first hemodialysis was performed two hours after the administration of mirtazapine while the second one was performed 30 hours after. Blood pressure did not increase after both hemodialysis while hypotension did not improve. The hypotension resolved 36 h after the administration of mirtazapine which may be due to the metabolization of mirtazapine.

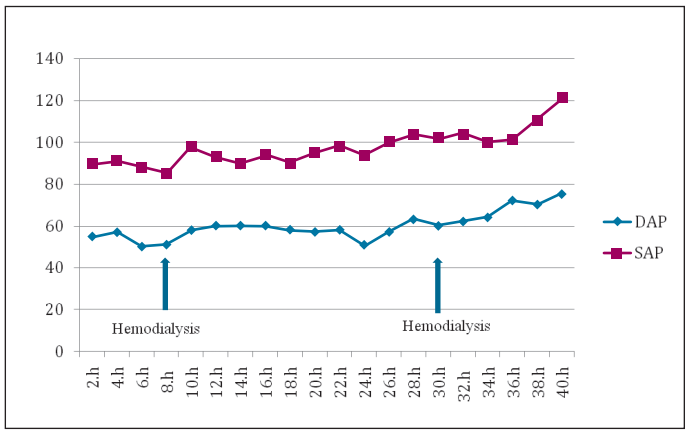

Figure 1: *Systolic and diastolic blood pressure measurements after mirtazapine treatment.*

DISCUSSION

Depression is common in patients with end-stage renal disease and it has been associated with increased mortality (4). While screening for depression in the general medical population remains controversial, a strong case for depression screening in patients with end-stage renal disease can be made when the high prevalence of depression and its significant impact on morbidity and mortality are considered (4). Dissimilar pharmacological medication have been tested in this patient community.

To reduce psychiatric symptoms and increase the patient's quality of life, depression is treated with modern antidepressants such as mirtazapine which is a new antidepressant drug. Mirtazapine antagonizes presynaptic α2-receptors and postsynaptic 5-HT2 receptors. It is also an antagonist of peripheral histamine and alpha-1 adrenergic receptors, which are responsible for sedation (3). Mirtazapine was shown to be superior to placebo while it was at least equally effective but often better tolerated than tricyclic antidepressants and selective serotonin reuptake inhibitors. Effective mirtazapine doses are 15 to 45 mg per day, and its elimination half-life of 20 to 40 h allows a daily single dose (9). Following oral administration, its bioavailability becomes 50%, and peak plasma levels are reached after 2 h, following administration of a single dose. (9).

Our patient had not followed hemodialysis programme before administration of mirtazapine and he had compensated renal failure under medical treatment. The patient had not previously used another antidepressant. The introduction of mirtazapine was associated with hypotension. The patient's general condition deteriorated 8 h after the administration of mirtazapine. Metabolic acidosis developed, and creatinine level increased. We hypothesize that the hypotensive effect of mirtazapine increased renal failure. Hypotension did not improve after hemodialysis, it improved after the metabolization of mirtazapine (approximately thirty-six hours). This is possibly because the drug is not eliminated through the renal pathway or through the hemodialysis membranes (3).

The use of sertraline proved to be promising in the treatment of dialysis-associated hypotension in an end-stage renal disease patient (10). However, mirtazapine was associated with hypotension in this study. There is only one case report of rhabdomyolysis in a patient after an overdose of mirtazapine (3), but our patient used therapeutic doses of mirtazapine.

In conclusion, we would like to state that in patients with a renal failure who are being treated with medical treatment and who do not currently apply hemodialysis treatment, the use of antidepressant drugs, especially mirtazapine, may endanger the residue renal function, due to the haemodynamic effects of the drug. (3)

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