Araştırma Yazısı

AĞRILI HEMODİYALİZ HASTALARINDA GABAPENTİN TEDAVİSİ

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Amaç: Üremik nöropatiye bağlı ağrı yüksek yaygınlığına rağmen, teşhis ve tedavi yönünden göz ardı edilmektedir. Bu hastalarda genellikle kullanılan ilaç tedavileri etkin değildir. Biz bu çalışmamızda, hemodiyaliz hastalarında gabapentinin nöropatik ağrıyla birlikte yaşam kalitesi ve depresyona etkisini araştırmayı amaçladık. **Yöntem:** Çalışmaya son dönem böbrek yetmezlikli 22 hemodiyaliz hastası dahil edildi (10 erkek ve 12 kadın, yaş ortalaması 62±3.53). Nöropatik ağrı tespit edilen hastalara 8 hafta süre ile günde 300 mg gabapentin tedavisi verildi. Tedaviden önce ve sonra yaşam kalitesi için SF-36 değerlendirme testi (fiziksel ve mental komponent skoru), depresyon için Beck depresyon envanteri (BDI) ve ağrı içinde Mc Gill ağrı anketi kısa formu (SF-MPQ: VAS; Visual Analogue Score, PPI; Present Pain Intensity, total SF-MPQ) uygulandı. **Bulgular**: Gabapentin tedavisi ile birlikte ağrı skorlarında önemli derecede azalma tespit ettik. Total SF-MPQ skoru 21.32±8.74 den 7.5±5.72, VAS 6.4±2.15 den 2.45±1.81, PPI 3.18±1.1 den 1.3±0.88 düştü. Ayrıca SF-36 ve BDI skorlarında da anlamlı iyileşmeler tespit ettik ($p<0.001$). Hemodiyaliz hastalarında sık karşılaşılan bir sorun olan ağrıya gabapentin tedavisinin etkili olduğunu, bununla birlikte yaşam kalitesi ve depresyonda iyileşme sağladığını tespit ettik.
Anahtar kelimeler: Depresyon, gabapentin, hemodiyaliz, ağrı, yaşam kalitesi**.**

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GABAPENTIN IN THE TREATMENT OF PAIN IN HEMODIALYSIS PATIENTS

Aim: Despite its high prevalence, pain induced by uremic neuropathy is usually underrecognized during diagnostic process and undertreated. In most of the patients, traditional drugs are ineffective. In this study, we investigated the effect of gabapentin on neuropathic pain along with quality of life (QOL) and depression in hemodialysis (HD) patients. **Methods:** Twenty two patients with chronic renal failure who were on HD were included in our study (10 males and 12 females, mean age 62±3.53). We administered 300 mg/day gabapentin for 8 weeks to patients in whom neuropathic pain was detected. We administered SF-36 Evaluation Test (Physical Component Score and Mental Component Score) for QOL, Beck's Depression Inventory (BDI) for depression and Short Form of McGill's Pain Questionnaire (SF-MPQ: VAS; Visual Analogue Score, PPI; Present Pain Intensity, total SF-MPQ) before and after the treatment. **Results:** With gabapentin treatment, we found a statistically significant decrease in pain scale scores. Total SF-MPQ decreased from 21.32±8.74 to 7.5±5.72, VAS scale decreased from 6.4±2.15 to 2.45±1.81, PPI decreased from 3.18±1.1 to 1.3±0.88. We also determined significant improvements in SF-36 and BDI scales ($p<0.001$). **Conclusion:** Gabapentin treatment improved pain which is a frequently encountered problem in HD patients and also made significant improvements in depression and quality of life.
Keywords: Depression, gabapentine, hemodialysis, pain, quality of life**.**

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INTRODUCTION

Neuropathic pain is a chronic debilitating condition that is typically refractory to treatment with most currently available pharmacotherapeutic agents, such as opioids and non-steroid anti inflammatory drugs (NSAIDs). Neuropathic pain has diverse etiologies, including diabetes, HIV infection, herpes zoster infection, spinal cord injury, and postamputation syndrome (1-5).

Although its high prevalence, pain induced by uremic neuropathy is usually underrecognized during diagnostic process and undertreated. In most of the patients, traditional drugs are ineffective.

Gabapentin, a potent anticonvulsant drug, has an unknown mechanism of action. Initially approved only for use in controlling seizures, it showed promise in the treatment of chronic pain syndromes; especially neuropathic pain (6), Gabapentin is eliminated primarily through the kidney and removed by hemodialysis (HD). It has a significantly longer half-life in HD patients than in those with normal renal function and HD patients need lower doses at less frequent intervals than the patients with normal renal function do. The recommended dose for HD patients is 200–300 mg after each HD session (6).

In this study we investigated the effect of gabapentin on neuropathic pain along with quality of life, anxiety and depression in HD patients.

MATERIAL AND METHODS

Twenty two patients with chronic renal failure who were on HD were included in our study (10 males and 12 females, mean age 62±3.53). There was a 1-week washout period between the sequential treatment phases. All patients had histories of neuropathic pain of more than 8 weeks. We administered 300 mg/day gabapentin for 8 weeks to patients in whom neuropathic pain was detected.

SF-MPQ comprises 15 adjectives that describe the sensory and affective dimensions of pain as well as a visual analogue scale (VAS) and present pain index (PPI). The SF-MPQ comprises a 15-item adjective checklist that is rated on a 4-point intensity scale (0.none, 1.mild, 2.moderate, 3.severe) as well as two single-item measures of present pain (7).

In order to evaluate QOL of the patients, a short form of Medical Outcomes Study (SF-36) (8) was used, which has been adapted to the Turkish population. The test consisted of 36 items, which were assigned to 8 dimensions, namely functional capacity (10 items), physical aspect (4 items), body pain (2 items), general health status (5 items), vitality (4 items), social aspect (2 items), emotional aspect (3 items) and mental health (5 items). Each scale was scored with a range from 0 to 100. The first 5 items were physical component scale (PCS) and the last 5 items were mental component scale (MCS) (9). It has been shown that these 2 summary scales adequately represent values of their individual scale components with 80 and 85% variability (10). The higher the scale the better the QOL. This scale has been commonly used and validated in patients with ESRD (11).

Depression was assessed by using the BDI, which was validated and commonly used in patients with ESRD (12-14). Patients were grouped as normal (BDI, 0-9), mild (BDI, 10-18), moderate (BDI, 19-29) and severe depression (BDI, 30-63). It is reported that 85% of western dialysis patients with BDI scores of 11 or higher met DSM-IV criteria for diagnosis of major depression (13). A BDI score of 21 has been suggested as a cut-off value for the diagnosis of depression in a Korean population (15). The validation and reliability study in a Turkish population was made by Hisli (16) and a BDI score of 17 or greater as a cut-off value for diagnosis of depression.

The Local Ethics Committee approved the study design. Informed consent was obtained from each patient.

RESULTS

Baseline characteristics of the patients are shown in Table 1. With gabapentin treatment, we found a statistically significant decrease in pain scale scores. Total SF-MPQ decreased from 21.32±8.74 to 7.5±5.72, VAS scale decreased from

Table 1. Baseline Characteristics of the Patients

Parameter	Mean ± SD	Minimum	Maximum
Age (years)	62±3.53	41	88
Dialysis duration (months)	49.6 ± 47.8	8.0	168
Hematocrit (%)	33.4 ± 4.0	28.1	44,8
Serum albumin (g/dl)	3.9 ± 0.3	3.5	4.4
Calcium (mg/dl)	8.9 ± 0.7	7.4	10
Phosphate (mg/dl)	5.0 ± 0.9	2.7	6.1
Parathyroid hormone (pg/ml)	288 ± 117	139	497
Kt/V	1.33 ± 0.17	1.2	1.7
CRP	9.7 ± 8.8	1.0	27.9

CRP: C Reactive Protein, Kt/V: Coefficient of efficiency of dialysis

6.4±2.15 to 2.45±1.81, PPI decreased from 3.18±1.1 to 1.3±0.88. We also determined significant improvements in SF-36, BDI scales ($p<0.001$). Their results are shown in Table 2. During the 8-week treatment, no adverse effects requiring drug cessation was seen in the study group.

DISCUSSION

The chronic pain of neuropathy has multiple etiologies and pathophysiologic manifestations (eg, ongoing pain described as shock like or burning, hypersensitivity such as allodynia). By definition, neuropathic pain results from a primary lesion in or dysfunction of the nervous system. It serves no physiologic purpose, causes physical as well as social and psychological impairment, and merits specific intervention for the alleviation of symptoms (1,3).

The antiepileptic agent gabapentin has been the subject of numerous case reports and case series in the literature and has been specifically studied as an initial or add-on treatment for neuropathic pain. Pain and peripheral neuropathy are frequent complications of ESRD.

There is no study up to now evaluating gabapentin efficacy on neuropathic pain in HD patients. Our study is the first study to evaluate gabapentin efficacy on neuropathic pain in HD patients. We found clear improvement in pain scores of the patients with gabapentine treatment; total SF-MPQ, VAS scale, PPI decreased from with gabapentin in the present study.

Depression is the most common psychological disorder among dialysis patients and the prevalence of depression, ranging 13-30%, has been reported in dialysis patients (17-20). As renal insufficiency progresses, patients may experience symptoms that may affect their daily lives. Several reasons

Table 2. Parameters before and after gabapentin therapy

Effect of Gabapentin on Scales			
Parameters	**Pre-treatment (n:22)**	**Post-treatment (n:22)**	**p**
Total SF-MPQ	21.32±8.74	7.5±5.72	p<0.001
VAS	6.4±2.15	2.45±1.81	p<0.001
PPI	3.18±1.1	1.3±0.88	p<0.001
PCS	41.31±21.8	70.21±14.2	p<0.001
MCS	55.26±19.78	80.20±9.51	p<0.001
BDI	13.82±4.44	7.05±3.26	p<0.001

Total SF-MPQ; Total Short Form of McGill's Pain Questionnaire, VAS; Visual Analogue Score, PPI; Present Pain Intensity, PCS; Physical Component Score, MCS; Mental Component Score, BDI; Beck's Depression Inventory.

such as loss of renal function, loss of role at work and in family, loss of sexual function account for the high prevalence of depression in HD patients. It was demonstrated that serial measurement of depression is one of the predictors of mortality in HD patients (10). For that reason, diagnosis and treatment of this common problem may be very important for improvement of high risk of death rate in this group of patients.

There is no study up to now evaluating gabapentin efficacy on depression in HD patients. There are only studies on depressive patients having bipolar disorder with normal renal function. Young et al (21) determined that depression was relieved with gabapentin therapy in 15 bipolar depressive patients also in Wang et al's study (22) gabapentin was helpful in bipolar depression and Hamilton Depression Rating Scale was improved from 32.5±7.7 to 16.5±12.8. Value of BDI decreased from with gabapentin in the present study.

Rodrigues et al (23) showed that QOL improved with gabapentin therapy in the patients with primary orthostatic tremor. There is no study investigating the effect of gabapentin on QOL in HD patients. Our study is the first study to evaluate gabapentin efficacy on QOL in HD patients. We found clear improvement in QOL scores of the patients with gabapentine treatment. From two components of QOL; PCS and MCS increased from with gabapentin in the present study.

In conclusions, Gabapentin treatment improved pain which is a frequently encountered problem in HD patients and also made significant improvements in depression and QOL.

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