

SHORT REPORT

Comparison of Pregabalin and Ketotifen in treatment of uremic pruritus in hemodialysis patients

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Abstract

This study aims to compare the efficiency of Pregabalin and Ketotifen in treatment of uremic pruritus in hemodialysis (HD) patients. Thirty HD patients were randomly divided into two groups: A (Pregabalin 50 mg three times a day) and B (Ketotifen 1 mg twice a day). Efficacy of treatment and quality of life were weekly evaluated by visual analogue scale (VAS) and Itchy Quality of life, respectively. There was no significant difference between the two groups regarding demographic features, laboratory data, quality of life, and VAS before treatment. In the second week of treatment, the pruritus intensity was significantly lower in the Pregabalin group than the Ketotifen group ($p = 0.026$). The mean of life quality was significantly lower in Ketotifen than Pregabalin group in weeks 1, 2, and 4 ($p = 0.001$, $p = 0.001$, and $p = 0.036$, respectively). There was no significant difference between the two groups regarding the side effects of drugs. This study showed that a higher dose of Pregabalin could be a more effective treatment than Ketotifen without additive side effects in improving the quality of life in dialysis patients.

KEYWORDS

Ketotifen, Pregabalin, uremic pruritus

1 | INTRODUCTION

Uremic pruritus (UP) is an important cause of reduced quality of life in hemodialysis (HD) patients despite the relative knowledge of the reasons and the development of various treatments.^{1,2} Ketotifen is one of the first lines of treatment with low side effects.² Recently, its identified that Pregabalin can effectively treat UP due to binding to $\alpha 2\delta$ subunit of the voltage-gated calcium channels in the dorsal root ganglion of the spinal cord.³ However, fear of the side effects of Pregabalin is the main challenge for its application in UP treatment.⁴

2 | METHODS

This pilot study was approved by the local Ethics Committee (IR.KMU.AH.REC.1396.1771). HD Patients with complaints of pruritus and

non-response to dermal emulsion treatment for at least 3 months were entered to study. Patients over 70 years with a history of opium use, drug allergy to Pregabalin and Ketotifen, epilepsy, irreversible heart failure, ischemia, hypotension (systolic blood pressure below 90 mm Hg), patients with abnormal blood levels of hemoglobin (≤ 10 g/dl), calcium (≤ 8 mg/dl, ≥ 10.5 mg/dl), phosphorus (≥ 5.5 mg/dl) and parathyroid hormone (≥ 300 pg/ml), and non-uremic pruritus such as primary skin diseases (eczema and psoriasis, etc.) were excluded from the study. Thirty HD patients were randomly divided into two groups: A (Pregabalin 50 mg three times a day for 4 weeks) and B (Ketotifen 1 mg twice a day for 4 weeks). The patients were not allowed to use other antipruritic medications. The efficacy and safety of drugs were assessed by a dermatologist after the second and fourth weeks using the visual analogue scale (VAS) and Itchy Quality of life (QoL) and a checklist of drugs' side effects. The data were analyzed by SPSS version 22. p -Values less than 0.05 were considered significant.

3 | RESULTS

Results showed that patients in the Ketotifen group had a higher mean pruritus score than Pregabalin group in the second week (p value = 0.026). The mean QoL score was significantly lower in Ketotifen than Pregabalin group in weeks 1, 2, and 4 (p value = 0.001, p value = 0.001, and p value = 0.036; Table 1). Side effects such as drowsiness, anxiety, headache, dry mouth, constipation, and diarrhea were more common in the Ketotifen group, but no significant difference was seen between the two groups. Complications such as dizziness were more common in the Pregabalin group but were not statistically significant (p value = 0.139; Table 2). One person in the Pregabalin group did not complete the study due to dizziness and one person in the Ketotifen group canceled the course due to personal problem.

4 | DISCUSSION

Our study showed that high dose of Pregabalin is a more effective than Ketotifen in improvement of pruritus. Recently, it has been suggested that nervous system activity may play an important role in the mechanism of UP. Lee et al showed that Pregabalin (75 mg twice daily) reduced chronic pruritus.⁵ Despite the evidence of efficacy Pregabalin in UP,⁶⁻⁸ it was found that only 4% UP patients have been used Pregabalin.⁴ This low statistic can be due to the fear of drugs side effects and uncertainty of the effective dose with minimal side effects in previous studies. Otsuka et al indicated that a maximum dose of 150 mg of Pregabalin in dialysis patients has no serious side

effects.⁹ Different studies showed that Pregabalin has more complications in elderly patients, opium users, dialysis patients with underlying disease.^{10,11} So, to use high doses of Pregabalin, we used stricter restrictions on patient selection. In most studies, such as ours, dizziness has been the most common complication.^{4,8-11} In our study, there is no considerable side effects in both groups. The Limitations of this study were the sample size and short duration of Follow up (30 days). First, start the dose of Pregabalin 50 mg three times a day, while studies have shown that gradually increasing the dose of Pregabalin can improve the results and reduce the side effects.⁹ We suggested study design with higher sample sizes and comparison of different doses of this drug.

AUTHOR CONTRIBUTIONS

Najmeh Shamspour and Azadeh Mohebbi were involved in the study design. Azadeh Mohebbi, Mahin Aflatoonian, Maryam Khalili, Maryam Mousavi evaluate patients in inclusion and exclusion criteria. Najmeh Shamspour, Elahenaz Parsimood, Mohsen Seifi, and Jalal Azmandian collected lab tests data. Najmeh Shamspour, Maryam Mousavi, Jalal Azmandian and Mohsen Seifi gave coded drugs to patients. Azadeh Mohebbi, Mahin Aflatoonian, Saman Mohammadi, Elahenaz Parsimood evaluated the patient with questionnaires Azadeh Mohebbi and Najmeh Shamspour wrote the initial draft of the article. Batoul Khoundabi performed statistical analyzes. All authors were involved in editing and finalizing the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

TABLE 1 Comparison of uremic pruritus and life quality between Pregabalin and Ketotifen groups

Items	Groups	Baseline	After 1 week	After 2 weeks	After 4 weeks	p -Value group ^c	p -Value time ^c
VAS	Pregabalin	2.5 ± 0.52	1.42 ± 0.51	1.29 ± 0.47	1.29 ± 0.47	0.223	0.021 ^a
	Ketotifen	2.0 ± 0.67	1.64 ± 0.49	1.71 ± 0.46	1.57 ± 0.51		
p -Value ^b		0.152	0.223	0.026 ^a	0.234		
Life quality	Pregabalin	3.00 ± 1.19	7.28 ± 1.19	8.14 ± 1.19	7.42 ± 1.21	0.048 ^a	0.026 ^a
	Ketotifen	3.71 ± 1.19	4.92 ± 1.19	4.57 ± 1.19	5.85 ± 1.20		
p -Value ^b		0.637	0.001 ^a	0.001 ^a	0.036 ^a		

^aSignificant in 0.05 levels.

^bPaired comparisons by groups.

^cTotal effects for group and time by GEE models.

TABLE 2 Comparison of complications between Pregabalin and Ketotifen groups

Items	Time	Drowsiness	Anxiety	Headache	Dry mouth	Constipation	dizziness
Ketotifen	After 1 week	N = 2 (14.28)	N = 2 (14.28)	N = 2 (14.28)	N = 4 (28.57)	N = 4 (28.57)	N = 1 (7.14)
	After 4 weeks	N = 2 (14.28)	N = 2 (14.28)	N = 2 (14.28)	N = 4 (28.57)	N = 4 (28.57)	N = 1 (7.14)
Pregabalin	After 1 week	N = 2 (14.28)	N = 0 (0)	N = 1 (7.14)	N = 1 (7.14)	N = 2 (14.28)	N = 4 (28.57)
	After 4 weeks	N = 2 (14.28)	N = 0 (0)	N = 1 (7.14)	N = 1 (7.14)	N = 2 (14.28)	N = 4 (28.57)
p -Value		1	0.142	0.541	0.139	0.357	0.139

Note: Data presented as number and percentage.

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