ORIGINAL ARTICLE

COMPARING THE EFFICACY AND SAFETY OF PREGABALIN VS GABAPENTIN IN UREMIC PRURITUS IN PATIENTS OF CHRONIC KIDNEY INJURY UNDERGOING HAEMODIALYSIS

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Background: World has been facing an epidemic of non-communicable diseases including heart, metabolic and renal diseases. Renal diseases have been commonly diagnosed and managed in low- and middle-income countries. Objective was to compare efficacy and safety of Pregabalin and Gabapentin in uremic pruritus among patients of chronic kidney injury undergoing haemodialysis. It was a comparative cross-sectional study, conducted at the Department of nephrology Abbottabad International Medical Institute. February 2021 to January 2022**. Methods:** Total of 90 cases were included in the study, which were diagnosed as chronic kidney disease stage 5 undergoing haemodialysis and presented with pruritus. Pruritus was gauged on numeric rating scale and patients score of more than 6 were included. Patients were randomly divided into two groups via lottery method. Group A received Pregabalin while group B received Gabapentin. Efficacy and safety were assessed in both groups at the end of six months. **Results:** Out of 90 dialysis dependent chronic kidney disease patients with significant pruritus included in the study, 61 (52.7%) patients were males and 29 (46.3%) were females. At the end of 6 weeks, we found out that 35 (38.9%) had no pruritus, 25 (27.8%) had mild, 19 (21.1%) had moderate while 11 (12.2%) had severe pruritus. After applying the chi-square test we found that Pregablin was statistically significantly more efficacious then Gabapentin (*p*-value-0.026). Sedation, nausea and blurred vision were found more in patients who took Pregabalin (*p*-value<0.001). **Conclusion:** Pregablin emerged out to be more efficacious with regards to reducing pruritus of the two medications compared in our study population while patients who took Gabapentin experience significantly a smaller number of side effects as compared to patients who were given Pregabalin.

Keywords: Chronic kidney disease; Gabapenton; Pregabalin; Pruritus

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INTRODUCTION

World has been facing an epidemic of non-communicable diseases including heart, metabolic and renal diseases.[1] Renal diseases have been commonly diagnosed and managed in low- and middle-income countries.[2,3] Multiple options have been used to manage these patients depending upon type and extent of disease and expertise avaibale.[4]Extra-renal conditions arise commonly in these patients due to prolong metabolic changes related to renal damage or treatment used.

Hemodynamic changes occur in almost all patients suffering from acute or chronic renal conditons.[5]Patients with chronic renal disease may have complex pathophysiology of various systems leading to multiple health related problems. These problems may become too cumbersome in some patients leading to poor health related quality of life.[6] Uremic pruritus by now has been an established entity with CKD may it be dialysis dependent or non-dependent.[6]

Various studies have been done to look for best management option for pruritus in patients suffering from chronic kidney disease. Swama *et al*.[7] in 2019 published a comprehensive review regarding various treatment options for uremic pruritus. They chalked out various topical and systemic therapies which may be effective for management of pruritus. Haber et al. in 2020 conducted a randomized controlled trial regarding gabapentin and doxepin in the management of uremic pruritus. They came up with the conclusion that statistically significant difference in all parameters existed in both the groups.[8]Ravindran *et al.* in 2020 compared safety and efficacy of Pregabalin versus Gabapentin for the treatment of uremic pruritus in patients with chronic kidney disease on maintenance haemodialysis.[9] They found that both medications were equally effective

in treatment of uremic pruritus but Pregablin was safer. They encouraged use of 25mg Pregablin for this purpose. Burden of chronic kidney disease is increasing with each passing day in Pakistan. More emphasis is laid on managing renal issues or haematological problems and clinicians pay less attentions to definitive treatment of associated symptoms believing that renal replacement may be cure of problems. A recent local study highlighted huge burden of uremic pruritis in our part of the world.[10]Limited local data has been generated regarding efficacy and safety of various management options to treat this common problem in patients suffering from CRF undergoing haemodialysis. We therefore planned and conducted this study with the rationale to compare efficacy and safety of Pregabalin and Gabapentin in uremic pruritus among patients of chronic kidney injury undergoing haemodialysis.

MATERIAL AND METHODS

After getting approval from the Ethical Committee, a comparative cross-sectional study was carried out in Dialysis Unit, Medicine Department, Abbottabad International Medical Institute, Abbottabad from February 2021 to January 2022. Sample size was calculated by WHO Sample Size Calculator with population prevalence proportion of pruritis in CKD patients as 55%[11] and margin of error as 10%. Non probability Consecutive sampling technique was used to gather the sample.

Inclusion criteria: Known patients of CKI, who were on regular haemodialysis, aged between 25–80 years and having persistent pruritus were included in the study.

Those already on antihistamines or those with dermatoses of skin were excluded. Patients with liver involvement or any other local or systemic cause of pruritus were not included as well. Patients with CKD related anaemia or those taking any medications with pruritus as known adverse effect were excluded as well.

Chronic kidney disease was diagnosed by consultant nephrologist/medical specialist on the basis of set criteria.[12] Patients meeting the inclusion criteria were selected and randomly placed into two groups via lottery method. Group A received oral Pregabalin 25mg OD at night while group B received oral Gabapentin 100mg OD at night.[9]Numerical rating scale was designed and recorded at start of the study and after 6 weeks, to assess the baseline itch severity score and improvement at the end of the study respectively. In NRS 0 = no pruritus, <3 = mild pruritus, 3 to <7 = moderate pruritus, 7–10= severe pruritus.[13,14]

Patients were asked a simple question about the intensity of their itch in last 24 hours and following NRS score was noted:

0	1	2	3	4	5	6	7	8	9	10

Both efficacy and adverse effects were recorded during six weeks of treatment at time of routine follow up.

Characteristics of participants and the distribution of the characteristics of both groups were described by using the descriptive statistics. Chi-square was applied to look for the difference in parameters of efficacy and safety in both the groups. Statistical analysis was performed using Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Differences between groups were considered significant if *p*-values were ≤0.05.

RESULTS

Out of 90 dialysis dependent chronic kidney disease patients with significant pruritus included in the study, 61(52.7%) patients were males and 29 (46.3%) were females. Table-1 summarized the general characteristics of study participants. At the end of 6 weeks, we found out that 35 (38.9%) had no pruritus, 25 (27.8%) had mild, 19 (21.1%) had moderate while 11 (12.2%) had severe pruritus.

Table-2 summarized the results of chi-square analysis. It was revealed that Pregablin was statistically significantly more efficacious than Gabapentin (*p*-value-0.026) in relieving the symptoms of pruritus. Sedation, nausea and blurred vision were found more in patients who took Pregabalin (*p*-value<0.001).

Table-1: Characteristics of dialysis dependent chronic kidney disease patients included in the study

Study parameters	n (%)
Age of Patients (years)	
Mean±SD	39.63±8.71 years
Range (min-max)	19-64 years
Gender	
Male	61 (67.7%)
Female	29 (32.3%)
Mean duration of chronic kidney disease	3.47±4.81 years
Medication used	
Pregabalin	41 (45.5%)
Gabapentin	49 (54.5%)
Pruritus after 6 weeks of treatment	
No	35 (38.9%)
Mild	25 (27.8%)
Moderate	19 (21.1%)
Severe	11 (12.2%)
Adverse effects	
Sedation	45 (50%)
Nausea	23 (25.5%)
Blurring of vision	31 (34.4%)
Others	03 (3.3%)

Table-2: difference in efficacy and safety parameters in both groups: Chi-square test

Factors studied	Pregablin	Gabapentin	*p*-value
Pruritus			
No	20 (47.8%)	15 (30.6%)	0.023
Mild	14 (34.1%)	11 (22.4%)	
Moderate	04 (9.8%)	15 (30.6%)	
Severe	03 (7.3%)	08 (16.3%)	
Sedation			
No	11 (26.8%)	34 (69.4%)	<0.001
Yes	30 (73.2%)	15 (30.6%)	
Nausea			
No	23 (56.1%)	44 (89.8%)	<0.001
Yes	18 (43.9%)	05 (10.2%)	
Blurring of vision			
No	16 (39.1%)	43 (87.7%)	<0.001
Yes	25 (60.9%)	06 (12.3%)	

DISCUSSION

Chronic kidney disease has been on a rise in almost all parts of the world including developing country like ours. Renal replacement therapy is usually mode of treatment in patients with advanced CRF till transplant is arranged. Renal failure and haemodialysis may give rise to number of extra-renal manifestations in these patients. Uremic pruritus is one of these extra renal manifestations which sometime become too cumbersome for the patients. Management of these allied symptoms sometimes become very important to improve overall quality of life of patients.

Rayner *et al*. in 2012 compared Pregablin and Gabapentin for treatment of uremic pruritus. They studied 71 patients and revealed that both medications were effective in relieving symptoms of pruritus bur Pregablin was more tolerable to patients as compared to Gabapentin.[15] Our results were slightly different in this regard as Pregablin turned out to be more efficacious medication out of the two for managing pruritus and Gabapentin was more safe and well tolerated by the patients included in the study.

A prospective cross-over study was conducted on Pregabalin versus Gabapentin in the treatment of neuropathic pruritus in maintenance haemodialysis patients by Solak *et al*.[16]They came up with the findings that in both neuropathic pain and pruritus, both drugs were equally effective. In our study, Pregablin emerged out to be more efficacious of the two medications compared while patients Gabapentin showed lesser number of side effects as compared to Pregabalin. We studied sedation, nausea and blurred vision and found out that patients who were in Pregablin group experienced more adverse effects.

Ishida *et al*. in 2018 compared adverse effects in patients of CKD undergoing haemodialysis using Pregablin and Gabapentin.[17]It was concluded that both medications showed significant side effects in CKD patients and authors advised to use these very cautiously. Our study stated same as both groups showed significant number of side effects including sedation, nausea and blurred vision but patients taking Pregablin significantly showed more side effects. Risk vs benefit for use of both medications is needed to be weighed by the treating team before starting the treatment.

Leung *et al*. in 2016 published detailed review regarding use of Gabapentin in patients of CKD having pruritus.[18]They concluded that Gabapentin significantly reduced pruritus in these patients and common side effects reported were somnolence, dizziness, and fatigue. We compared Pregablin with Gabapentin both for efficacy and safety and found out Pregablin superior to Gabapentin in terms of efficacy. Gabapentin however turned out to be safer of two medications.

Limitations of this study include study design. Randomized controlled trial would have been best design to compare efficacy and safety. Long term follow-up of patients may have yielded better results. Pragmatic design and dose variation of both medications as per patients' requirement may also have provided better information.

CONCLUSION

Pregablin emerged out to be more efficacious of the two medications compared in our study population while patients who took Gabapentin experience significantly less number of side effects as compared to patients who were given Pregabalin.

Conflict of interest: None

AUTHORS' CONTRIBUTION

NJK: Data collection, wrote manuscript, did statistical analysis and proof reading. Wahaj: Data collection, wrote manuscript, did statistical analysis and proof reading. SH: Data collection and analysis. AG: Conceived the study, supervised whole study and did proof reading. NI: Data collection and

analysis, did proof reading. AA: Data collection and statistical analysis. MAA: Data collection and proof reading

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