# Comparison of the Efficacy of Gabapentin with Loratadine in Patients of Chronic Kidney Disease with Uremic Pruritus

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## Abstract

**Objective:** To evaluate the efficacy of gabapentin versus loratadine in reducing the severity of uremic pruritus in patients of chronic kidney disease and to compare the side effects of both drugs.

**Material and Methods:** This comparative study was carried out in the Department of General Medicine and Nephrology, Mayo Hospital, Lahore. 256 patients of uremic pruritus, fulfilling the inclusion criteria, were enrolled in the study and divided randomly into two groups. Group A received loratadine 10mg daily and group B received gabapentin 100mg daily, for four weeks. Patients were asked to grade the severity of pruritus on a Numerical Rating Scale (NRS) and also answer the Dermatology Life Quality Index Questionnaire (DLQI). These proformas were filled once at the start of the study, and then at two and four weeks. Data was analyzed using version 25.0 of SPSS.

**Results:** Results showed a notable reduction in severity of pruritus with gabapentin as compared to loratadine (Group-A: 3.28 vs. Group-B: 4.03, p-value=0.004). Improvement in DLQI score was significantly higher for patients in gabapentin group (Group-A: 3.44 vs Group-B: 4.25, p-value=0.003). No significant difference was observed regarding safety profile of both drugs.

**Conclusion:** Results of this study demonstrate that gabapentin is more effective in reducing severity of pruritus and improving DLQI score when compared with loratadine. Both drugs are equally safe as no significant difference was seen in side effects.


**Keywords:** Chronic kidney disease, Uremic pruritus, Gabapentin, Loratadine

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## Introduction

Chronic kidney disease (CKD) is a condition defined as abnormality in kidney structure or function for more than three months. Uremic pruritus remains a frequent symptom of chronic kidney disease. The etiology of uremic pruritus is proposed to be multifactorial, involving both central and peripheral factors.[1] It is a distressing dermal condition which can lead to disrupted sleep, depression and reduced quality of life. Furthermore, severe uremic pruritus is linked to a higher mortality risk.[2]

The prevalence of uremic pruritus varies between 30% and 64% in the literature[3] Increased frequency and severity has been linked to longer dialysis duration.[4] Interestingly, the incidence of uremic pruritus is highest in Asia, including China, Japan and Pakistan.[5] Among studies conducted in Pakistan, the frequency of uremic pruritus was shown to range from 49%- 74 %.[6-8]

Despite medical advancements, there is presently no permanent cure for pruritus caused by chronic kidney disease. Due to its obscure pathophysiology, treatment options are limited and inadequate.[9] Drugs including

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gabapentin, opioid receptor modulators, antihistamines, topical capsaicin and emollients, and ultraviolet B (UVB) light are only some of the treatments available today.[10,11] In many cases, especially in developing nations like Pakistan, uremic pruritus goes undertreated and patients are just offered routine antihistamines.[6] The basis of using antihistamines in uremic pruritus emerged from elevated plasma levels of histamine in these patients. However, antihistamines have been ineffective in successfully treating this condition, indicating that histamine is not the only culprit involved in its pathogenesis.[12] Since there are likely several molecular routes contributing to its etiology, the relative effectiveness of any one therapeutic strategy is low. A combination of therapies is typically used to treat CKD associated pruritus. There are, however, no recommendations on how the various therapeutic modalities should be implemented.[10] Gabapentin is a potent antiepileptic agent, clearly demonstrated in the treatment of convulsions and neuropathic pain. Given that neuropathic pain and pruritus have similar pathophysiological pathways, gabapentin may be considered as another therapeutic option for uremic pruritus. Its specific pharmacological action is not fully understood but it may be involved in preventing neuropathic processes that lead to a pruritic sensation in uremia by limiting neuronal calcium influx.[13] Gabapentin is excreted mainly through the kidneys, and is removed by hemodialysis. The recommended dose in chronic renal failure with creatinine clearance (CrCl) <15ml/min is 100-300 mg/day. Lower limit of this dosage range is recommended for CrCl <7.5 ml/min. Supplemental doses in hemodialysis are 100-300 mg, post dialysis.[14] Recent data has shown gabapentin to be a promising drug for uremic pruritus, with favorable efficacy and safety profile. A limited number of studies have been conducted comparing gabapentin with oral antihistamines in uremic pruritus, with inconsistent results.[15-17] Therapeutic decision making is still controversial because findings from many reports have been refuted by additional studies, so the optimal treatment modality is still disputed.

## Material and Methods

This randomized controlled trial was carried out in the department of General Medicine and Nephrology, Mayo Hospital, Lahore from May 2022 to October 2022. Approval was taking from internal review board No. 9669/REG/KEMU/2021 dated 01/06/2021), and also it was registered with Clinical Trials with ID NCT05750875. A sample size of 256 patients (128 in each group) was calculated Using a 5% level of significance, 95% power of test, and an expected percentage of loratadine as 58% and gabapentin as 16%.[17] Non-probability convenience sampling was used for patient enrollment. Consenting adults of either gender greater than 18 years of age having stage 3 or above CKD, regardless of dialysis status with persistent pruritus ≥ 4 points, occurring at least 3 times a week, for 2 weeks, in a 1-month period, were recruited for the study. Chronic skin conditions, pruritus due to any other cause, history of drugs causing pruritus or prior allergic reaction to either gabapentin or loratadine resulted in exclusion from the study. Approval was taken from the Institutional Review Board (IRB) and Advanced Studies and Research board (ASRB) of King Edward Medical University/ Mayo Hospital, Lahore (Reference number 9669/REG/KEMU/2021). All consenting patients, fulfilling the inclusion criteria, presenting to the Medical and Nephrology Departments of Mayo Hospital, were enrolled in the study. Any topical or systemic antipruritic drugs were discontinued at least one week prior to the study. A baseline evaluation was conducted on demographic, clinical and laboratory data. Calculations were made for glomerular filtration rate (GFR) and CKD was staged accordingly. Patients were assigned at random to two groups, A and B. Group A received loratadine 10mg and group B received gabapentin 100mg, daily for four weeks. The hemodialysis patients received their dose after the dialysis session. The severity of pruritus was graded on a numerical rating scale (NRS, numbered 0-10). Minimal clinically important difference in chronic pruritus was considered a 2-3 point decrease in NRS.[18] Participants were also asked to answer the Dermatology Life Quality Index Questionnaire at 0 and 4 weeks, to measure impact of the condition on their life. It was deemed clinically significant when the DLQI score changed by at least four points.[19] Subjects were also asked to report any side effects, namely drowsiness, dizziness, fatigue, blurred/double vision, gastrointestinal symptoms, headache, dry mouth, palpitations or any allergic reaction. The data was analyzed using SPSS 25.0. The reduction in NRS and DLQI scores was calculated and mean reduction was compared between the two groups. Independent sample t-test was then applied and p-value <0.05 was accepted as significant.

## Results

Out of 256 patients with 128 participants in each group, 60.9% were male and 39.1% were female. Majority

of the participants (57.4%) belonged to CKD stage V and 46.5% were undergoing dialysis at the time of our study. Mean age of patients in group A was 47.8±13.17 and the mean age of patients in group B was 53.8 ± 13.48. Table 2 and 3 show minimum, maximum and mean reduction in severity of pruritus and DLQI score

**Table 1:** *Patient demographics at baseline*

| | Mean duration of pruritus (months) | Mean frequency of pruritus (per week) | Mean severity of pruritus at baseline (NRS) | Mean DLQI score at baseline |
|---|---|---|---|---|
| **Group A** | 2.69 ± 0.64 | 4.47 ± 1.07 | 6.38 ± 1.24 | 11.31 ± 2.08 |
| **Group B** | 2.81 ± 0.73 | 4.74 ± 1.35 | 6.53 ± 1.16 | 11.53 ± 1.83 |

A: Loratadine , B: Gabapentin

**Table 2:** *Reduction in Severity of Pruritus from baseline till 2nd and 4th week in Study Groups*

| | Reduction in Severity of Pruritus | | | |
|---|---|---|---|---|
| | Baseline-2nd Week | | Baseline-4th Week | |
| | Group-A | Group-B | Group-A | Group-B |
| **n** | **128** | **128** | **128** | **128** |
| **Mean±SD** | 2.09± 0.73 | 2.56± 0.80 | 3.28± 1.02 | 4.03± 0.96 |
| **Minimum** | 1 | 1 | 1 | 2 |
| **Maximum** | 4 | 4 | 6 | 6 |
| **p-value *** | **0.018** | | **0.004** | |

** Comparison between Groups (Independent sample t-test)*
*A: Loratadine B: Gabapentin*

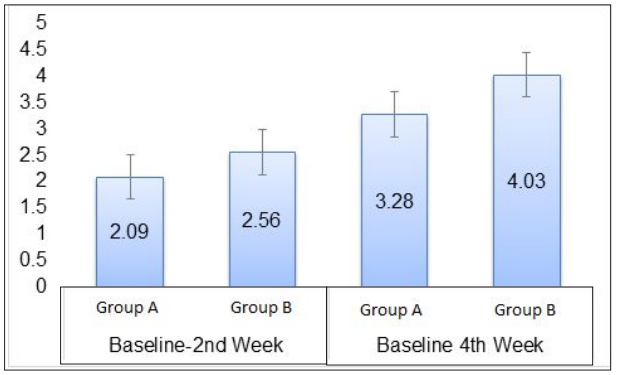


**Figure-1:** *Reduction in Severity of Pruritus from baseline till 2nd and 4th week in Study Groups*

**Table 3:** *Reduction in DLQI from baseline till 4th week in Study Groups*

| | Reduction (Baseline-4th Week) | |
|---|---|---|
| | Group-A | Group-B |
| **n** | **128** | **128** |
| Mean ±SD | 3.44±0.91 | 4.25±1.19 |
| Minimum | 2 | 2 |
| Maximum | 5 | 6 |
| **p-value*** | **0.003** | |

** Comparison between Groups (Independent sample t-test)*
*A: Loratadine B: Gabapentin*

respectively in both groups. It can be seen that Group B had a statistically significant greater reduction in both pruritus severity and DLQI score.

## Discussion

This study compared the effect of gabapentin and loratadine in alleviating uremic pruritus in patients with chronic kidney disease. At 2 and 4 weeks post-treatment, gabapentin was more effective than loratadine at reducing the severity of pruritus. Mean reduction in severity of pruritus from baseline till 2nd week (Group-A: 2.09± 0.73 vs Group-B: 2.56±0.80, p-value=0.018) showed significantly higher reduction for gabapentin and similar trend was seen for baseline till 4th week (Group-A: 3.28±1.02 vs Group-B: 4.03±0.96, p-value=0.004). Similarly the reduction in DLQI score was greater in gabapentin group (Group-A: 3.44 vs Group-B: 4.25, p-value=0.003). Only 15 (11.7%) and 6(4.7%) patients in loratadine group experienced headache and dry mouth respectively. While in gabapentin group 16(12.5%) patients experienced drowsiness, 11(8.6%) dizziness and 7(5.5%) patients reported fatigue. No statistically significant difference was seen regarding safety profile of both drugs. According to an Iranian Study by Noshad, et al., gabapentin was more effective than antihistamine in treating uremic pruritus and its psychogenic problems with no significant side effects. Improvement in severity of pruritus and quality of life was significantly higher with gabapentin as compared to antihistamine.[15] 2 patients (10%) in gabapentin group and 16 patients (80%) in hydroxizine group continued to have pruritus (P.001). Results of our study are consistent with the findings of Iranian study showing higher efficacy of gabapentin as compared to antihistamine loratadine.

Another Iranian study by Amirkhanlou, compared gabapentin and ketotifen for treating uremic pruritus in hemodialysis patients. As per findings of this study both drugs were equally effective for treating this condition.

Complete response to treatment (Gapapentien:53.8% vs. Ketotifen: 50%) and side effects did not show any significant difference.[16] These results are in contrast to our study as reduction in severity of pruritus as well as improvement in DLQI score was significantly higher with gabapentin. However, results regarding side effects are consistent with this study as both groups did not show any significant difference in adverse events.

In his research, Diego Marquez found that compared to no treatment, desloratadine significantly reduced uremic pruritus while gabapentin was only mildly effective. Both treatments resulted in lower visual analogue scores (5.89 to 3.4 with desloratadine; p = 0.004, 5.95 to 4.6 with gabapentin; p=0.07;), but only desloratadine was statistically important. The final pruritus score with gabapentin and desloratadine did not change (4.6 versus 3.4, p=0.16).When compared to gabapentin, desloratadine was better tolerated.[17] Contrary to this, our study showed both drugs to decrease the severity of pruritus as well as improve DLQI scores but still gabapentin showed higher efficacy in both these domains.

A study carried out by Khan, et al. in Abbottabad, Pakistan, compared pregabalin and gabapentin in the treatment of uremic pruritus. It showed that at the end of 6 weeks treatment period with gabapentin, 30.6% patients had no pruritus and 22.4% reported mild pruritus only.[20]

In order to alleviate pruritus, antihistamines have been widely used. These drugs work by blocking the histamine H1 receptor. According to reports, anti-histamines were commonly administered as first-line treatment for uremic pruritus, with over half of doctors prescribing an oral anti-histamine and one-quarter prescribing a topical anti-histamine.[8] In most cases, antihistamines are the primary medicine of choice for nephrologists worldwide. Antihistamines have been recommended as a first line of treatment since they rarely cause adverse effects. However, there is no evidence that antihistamines are actually effective in the treatment of uremic pruritus, and various reviews have hypothesized that the apparent benefit is due to drowsiness instead of an actual anti-pruritic action in patients taking them. As a result, they have restricted utility in uremic pruritus.

In cases of neuropathic pain, doctors often prescribe gabapentin, an anticonvulsant and calcium channel blocker that works centrally. Gabapentin is reported to be effective in neuropathic pruritus and can be used in chronic itch unresponsive to other agents. A suppression of calcium influx into neurons is hypothesized to be responsible for gabapentin's therapeutic effects. Researchers have shown that some patients experience side events while taking gabapentin for uremic pruritus. The most frequently reported adverse effects were drowsiness, vertigo, and sedation, and they were all noticed after the first dose. Nonetheless, they are frequently modest and typically subside within 5–10 days.[13]

## Conclusion

Results of this study demonstrate that gabapentin is superior in reducing severity of uremic pruritus and improving DLQI score when compared with loratadine. Both drugs are equally safe as no significant difference was seen in side effects. Gabapentin has shown promising results however, further large multi-centered trials are required to validate this effectiveness and to establish routine use of gabapentin in the treatment of uremic pruritus. Moreover, synergistic effect of gabapentin along with other available treatment options needs to be explored further.

**Conflict of Interest** *None*

**Funding Source** *None*

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## Authors Contribution

**NNZ:** Conceptualization of Project
**TN, BA:** Data Collection
**NNZ, NN, HF:** Literature Search
**TN, BA:** Statistical Analysis
**NNZ, MI:** Drafting, Revision
**NNZ, TN:** Writing of Manuscript