ORIGINAL ARTICLE

Comparison of Efficacy and Safety of Montelukast Versus Gabapentin in the Treatment of Pruritus, in Patients on Hemodialysis

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ABSTRACT

Introduction: Patients with end stage renal disease (ESRD), frequently present with intractable pruritus. In the recent past, many newer therapies have emerged for its treatment with variable results. We studied the antipruritic efficacy and safety of Montelukast sodium, (a leukotriene receptor antagonist), and compared it with Gabapentin in patients on hemodialysis.

Materials and Methods: The study was conducted in the Department of Dermatology, Sharif Medical and Dental College Lahore. It was a Quasi experimental study, 60 patients on hemodialysis, with refractory pruritus were enrolled in each group .Patients were given 10mg of tab Montelukast sodium daily and 300mg of Gabapentin thrice a week for four weeks. Severity of pruritus was assessed using pruritus scoring by Duo.

Results: Pruritus severity score reduced with both the treatments ,but Montelukast showed comparatively higher relief in pruritus score as compared to Gabapentin ($p<0.05$). Patients on Gabapentin complained of increased sedation.

Conclusions: Montelukast is more effective and safe treatment option for the refractory pruritus in patients with hemodialysis as compared to Gabapentin in our population.

Keywords: Hemodialysis, Pruritus, Montelukast.

INTRODUCTION

Patients with end stage renal disease undergoing hemodialysis frequently complain of pruritus. Around 50-90% patients have severe pruritus, which does not improve with dialysis and is not associated with the number of dialysis sessions. [1]The patho physiology of uremic pruritus is not completely understood but it has got a prognostic value and is associated with poor survival. [2, 3]In 25% of patients, it occurs not only during the dialysis sessions but also in between them and in significant patient population it begins with the dialysis. [4]

Treatment modalities include topical emollients along with systemic therapies. Among the commonly used therapies are the oral antihistamines, gabapentin, ondansetron, thalidomide, naltrexone, ultra violet light and topical tacrolimus. [5, 6] Efficacy of various agents has been experienced in a variety of researches with variable results, so the best treatment options are still undecided.

Prevalence of this distressing symptom still remains to be 20-30% despite of continuous improvements and innovations in dialysis technique. [7, 8] This symptom may be related to the release of histamine from mast cells along with various other etiologies. [9] Multiple studies have been conducted so far, comparing the safety and efficacy of various treatment options in such patients. [10] We decided to compare Gabapentin with Montelukast sodium in our study. Montelukast sodium is a leukotriene receptor antagonist with proven efficacy in the treatment of asthma, atopic eczema, allergic rhinitis and chronic idiopathic urticaria. [11] We compared the antipruritic effect of this drug with one of the already established treatment modality, i.e. gabapentin.

Gabapentin is a distinctive antiepileptic drug which modifies various receptor sites involved in dopamine, serotonin, and nor epinephrine release. Its efficacy has already been established in chronic pain related/neuropathic syndromes e.g. HIV-associated neuropathy, post herpetic neuralgia, and pain in diabetic neuropathy [12]. Usefulness of gabapentin in the treatment of uremic pruritus has been proposed in clinical trials and is also mentioned in literature. [13]

We conducted this study to evaluate and compare the efficacy and safety of gabapentin,

given in a dose of 300 thrice weekly, with montelukast given 10 mg daily for four weeks in patients on hemodialysis with pruritus.

The studies that were conducted earlier have compared either Gabapentin with antihistamines [14], or have shown the efficacy of single agent. To the best of our knowledge, this the first study in our country which compares the anti pruritic effects of Gabapentin with Montelukast in uremic pruritus.

METHODS

The study was conducted in the Department of Dermatology, Sharif Medical and Dental College, from October 2010 till May 2011. It was a quasi experimental study. Study was approved from hospital ethical committee. The sample size was calculated using WHO calculator for two groups for a difference in proportion of 20% between the groups giving significance of 0.05 and power of 80%. 60 patients were included in each group and were randomized according to computer generated software.

We included those patients in our study who were on regular thrice weekly hemodialysis and had persistent pruritus for more than three months. They had at least failed to respond to one of the other treatment modalities. We ensured that adequate dialysis is being done by maintaining Kt/V of >1.2, so that unbalanced renal functions itself could not be the cause of pruritus. We excluded all those patients who had Kt/V <1.2, pruritus of less than 3months duration and other pruritic dermatoses and /or systemic diseases leading to generalized itching, e.g. chronic active hepatitis, underlying malignancies, hemoglobin of less than 10gm/dl. Other exclusion criterions were serum parathormone of > 300pg/dl normal is 9-55pg/dl and serum phosphorus of > 7mg/dl.

Patients were informed about the study protocol and an informed consent was taken. Both the groups received treatment for a period of four weeks. The dose of Gabapentin was on alternate days as per recommendation of most of international studies [15]. Montelukast was given daily since <0.2% is excreted in urine.

Investigations prior to start of treatment included a complete blood count, serum levels of calcium, phosphorus, liver function tests, urea, creatinine and parathyroid hormone levels. All the other treatments including emollients were stopped one week prior to the enrollment in study. Severity of pruritus was assessed using pruritus assessment tool at the beginning and after four weeks. (Table –I). A decrease in Pruritus severity score (PSS) by 50% or more was taken as effective response to treatment.

Pruritus severity score by Duo [16]

No	Pruritus Parameters
1	**Severity of pruritus** a) Mild need for scratching (1). b) Need for scratching without excoriation (2). c) Need for scratching with excoriation (4). d) Frustrating pruritus (5).
2	**Distribution of Pruritus** a) Less than two sites (1). b) More than two sites (2). c) Generalized (3).
3	**Sleep disturbance as a result of pruritus** a)waking up of pruritus (1 score for each time per night, up to 10) b) Scratching during night with excoriation (1 score for each time per night, up to5)
Cumulative score= (Severity + Sleep disturbance) x distribution.	

Mean decrease in PSS between the two groups was compared using two sample independent t-tests. A P-value of <0.05 was considered significant.

Patients were also inquired about any side effects on follow up. Investigations including complete blood count, liver and renal function tests were repeated after four weeks as well.

RESULTS

60 patients were enrolled in each group. Before the start of therapy average PSS (Pruritus severity score) was 34 (range of 29-45). Most of the patients had severe generalized pruritus. Pre and post treatment PSS scores were compared for the individual drug. Gender distribution of patients is shown in Table-II

Table II:

Group	Group A (Montelukast)	Group B (Gabapentin)	Total
Males	29	34	63
Females	31	26	57
Total	60	60	120

When compared to pre-treatment PSS, both these drugs were successful in achieving a reduction in this score, but the reduction by Montelukast was statistically significant. ($p<0.05$) 43% patients on Montelukast achieved reduction in PSS by > 50%, while 23% patients on gabapentin had similar reduction. Response with both drugs was not significantly different among males and female patients.

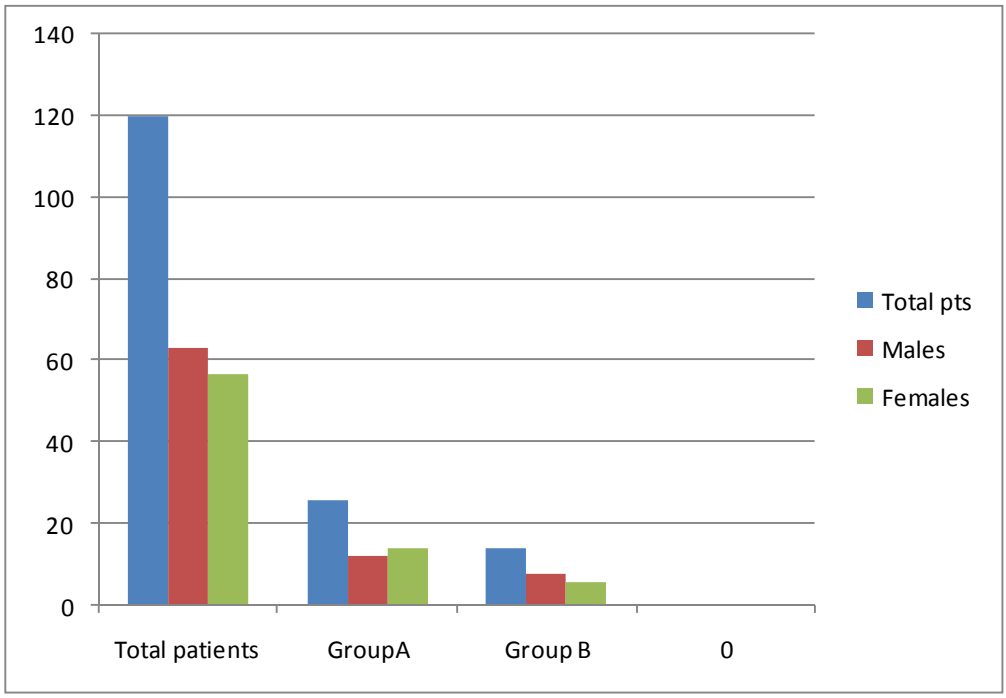

Figure I: Treatment Response among Male and Female Patients.

45% of the patient on gabapentin reported dizziness and sedation, while those on Montelukast did not complain of any major side effect. Only 1% had complaints of mild abdominal pain and dyspepsia.

DISCUSSION

Pruritus in patients with end stage renal disease and on hemodialysis can cause considerable morbidity. [2] Our study revealed that anti pruritic effect and safety profile of Montelukast is significantly better than that of Gabapentin. It can be a preferable agent for dialysis related pruritus that does not respond to other options.

Certain differences were observed on comparison with various international studies. Gabapentin has been shown to be effective in 80% of patients with uremic pruritus [17] Razeghi et al also observed that gabapentin showed a major reduction (73%) as compared to placebo. [18]Some of these researchers used gabapentin four times per week [13, 17] but we don't think that this minor dosage difference could have altered the results significantly.

Diego et al [9] also compared gabapentin with desloratidine and found this drug to be less effective as compared to antihistamine. He too reported that excessive sedation, somnolence and fatigue were frequently reported (47%) by the patients and some of the patients in his study even discontinued the therapy due to sedation.

Alireza et al [19] proved safety and efficacy of montelukast in dialysis patients in 2007 as compared to placebo. He reported a reduction in symptoms of 35% of patients.

We did not observe any significant side effect from montelukast in our study but Alireza et al had some major side effects with the above mentioned drug although in minor proportion. One of his patients died of myocardial infarction and one developed anemia. Both these side effects were reported to be "suspected unexpected serious adverse reaction". [20] Fortunately, we did not observe any serious adverse effect with either agent.

The difference in response rates may be due to some racial, genetic or environmental factors. It may also be due to difference in duration of therapy.

CONCLUSION

To the best of our knowledge, this is the first study of its kind which compared the therapeutic effect and safety of two treatment modalities. Based upon our results we recommend the use of montelukast as one of the treatment options in patients having intractable pruritus with hemodialysis, who do not respond to conventional therapies. We also suggest future studies to compare the efficacy of montelukast with other treatment modalities like H1receptor antagonist etc. Results can also be validated by a conducting large scale, double- blind, cross-over placebo controlled trials.

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