Comparative study of gabapentin and chlorpheniramine in the management of postburn pruritus at Kenyatta National Hospital

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Abstract

Introduction: Postburn pruritus is a common complication that not only affects healing of the burn wounds but also the patient's quality of life. Several treatment options including chlorpheniramine have been used with unsatisfactory results. This study compares the efficacy of gabapentin with chlorpheniramine in burns patients suffering from pruritus in an African population.
Main objective: To compare the efficacy of gabapentin to that of chlorpheniramine in the management of postburn pruritus.
Study design: A randomised controlled trial.
Materials and methods: Patients with postburn pruritus were divided into two arms, one receiving chlorpheniramine and the other gabapentin. Visual Analogue Scale (VAS) was utilised to grade the severity of pruritus as well as subsequent response to treatment. Comparative analysis of the two groups was done using the Mann-Whitney U and Kruskall Wallis tests.
Results: There was a general decrease in the mean VAS score for patients on chlorpheniramine and gabapentin from Day 1 to Day 28: 6.5 to 0.4 for gabapentin and 5.7 to 2.4 for chlorpheniramine respectively. There was an insignificant difference in VAS scores on Day 1 (p-value = .071) and Day 7 (p-value = .905) but thereafter patients administered chlorpheniramine had significantly higher VAS scores as compared to patients administered gabapentin (Day 14 p-value = .002, Day 21 p-value < .001 and Day 28 p-value < .001).
Conclusion: Either chlorpheniramine or gabapentin could be utilised in the management of postburn pruritus. However, patients with high VAS of pruritus respond better when managed with gabapentin.

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Introduction

Pruritus is defined as a poorly localised, unpleasant sensation that elicits a desire to scratch. It is usually non-adapting.[1] Postburn pruritus refers to itchiness involving the skin in and around a burn wound. It is a common and distressing feature of burn wounds[2-4] that interferes with the patient's day-to-day activities. Management of this condition has mainly been by the use of antihistamines such as chlorpheniramine. Chlorpheniramine is an H_1-receptor antagonist which exerts its anti-pruritic action by its sedative effect as well as blocking histamine receptors which are one of the mediators of the itch pathway. Gabapentin is an antiepileptic drug that has also shown efficacy in conditions associated with chronic pain[5,6,7,8] and also in pruritic disorders.[9,10] Its primary effect is in the inhibition of voltage-dependent calcium ion channels located in the spinal cord, especially the superficial laminae of the dorsal horn inhibiting the release of neurotransmitters.

The most common adverse effect of both drugs is sedation. Rare adverse effects include pancytopenia, cholestasis, hypersensitivity syndrome and dyskinesia.[8] The drugs should not be withdrawn abruptly but rather tapered gradually to prevent withdrawal-like symptoms.[9] This study compares the efficacy of these two drugs in the management of pruritus in the African population at Kenyatta National Hospital – a tertiary referral hospital in Kenya.

Materials and method

This study was carried out in the department of plastic surgery, Kenyatta National Hospital, after receiving approval from the ethics and research committee. Patients with postburn pruritus were randomised to two arms of treatment. In one arm, patients were given chlorpheniramine at a dose of 0.2 mg/kg to a maximum recommended dose of 12 mg per day for children and adults to a maximum dose of 24 mg/day. In the other arm of treatment patients were given gabapentin at a dose of 5 mg/kg/dose three times a day (children), while adults were started at a single dose of 300 mg per day with a provision to escalate to 300 mg, three times a day. VAS scores were taken for each patient in both arms of the study before the commencement of the medication. Once the administration of the medication began, VAS scores were subsequently recorded at weekly intervals for a period of four weeks at which point the final score was taken.

Patients were categorised into various groups based on their VAS: 0 = no pruritus; 0.1–2.9 = mild pruritus; 3–6.9 = moderate pruritus; 7–8.9 = severe pruritus and 9–10 = very severe pruritus. During treatment a point was allocated for a patient on therapy who subsequently moved from a group with more pruritus to one with less, two points if two groups were moved and three points if three groups were moved (e.g. patient who moved from severe pruritus to mild pruritus would earn two points for the therapy administered). The total points scored were then compared for the two arms of therapy.

Drug-related side-effects such as sedation were monitored in both groups. The collected data was analysed using the statistical package for social sciences (SPSS) version 22.0. Mann-Whitney U test was used to compare the two populations.

Results

A total of 50 patients were recruited into the study with 25 patients in each group: chlorpheniramine (Group A) or gabapentin (Group B).

The median age of patients was 28 years with an interquartile range of nine years. The age range for patients was nine to 65 years, with a mean age of 33 years (34.5 years Group A; 31.6 years Group B). Thirty-one patients (62%) were male (15 Group A; 16 Group B) while 19 (38%) were female (10 Group A; 9 Group B). Thirty-two patients had second-degree superficial burn wounds (14 Group A; 18 Group B). Eleven patients had mixed second-degree burn wounds (6 Group A; 5 Group B). Seven patients had both second-degree and third-degree burns (4 Group A; 3 Group B). Most of the patients (33; 66% – 16 Group A; 17 Group B) had intense pruritus localised on the trunk (66%) and the lower limbs (31; 62% – 17 Group A;14 Group B).

The mean VAS score for patients on chlorpheniramine reduced from 5.7 to 2.4 from Day 1 to Day 28 (Figure 1), while for gabapentin from 6.5 to 0.4 (Figure 1). (The difference was of statistical significance as from Day 14 to Day 28.) Patients in the chlorpheniramine arm were all started at a dose of 4 mg twice a day but due to poor response their frequency of administration was increased to 4 mg three times a day for eight of the 25 (32%) patients in that arm.

Patients in the gabapentin arm were all started off at a dosage of 300 mg once daily and none of them required adjustment of dosage or frequency of administration.

Figure 2 demonstrates the pruritis scoring during the treatment in the two arms of patients.

The majority (21; 84%) of patients who were administered chlorpheniramine moved only one level of pruritus, while for gabapentin 12 (48%) patients moved two levels of pruritus and 28% moved three levels (Figure 3). This was of statistical significance (p-value < .001).

All patients administered chlorpheniramine had a mild degree of sedation on Day 7 and Day 14 while 64% of patients administered gabapentin had at least a moderate degree of sedation on Day 21 and Day 28.

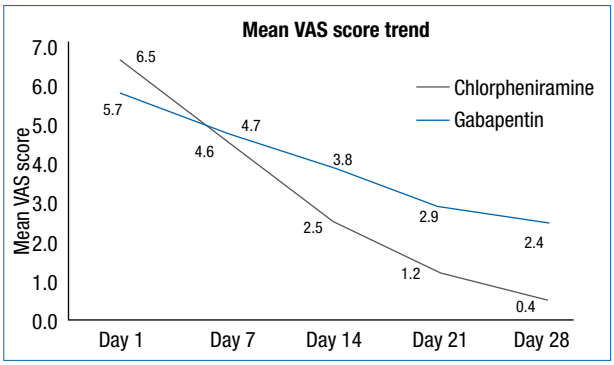

Figure 1. Mean VAS score for chlorpheniramine and gabapentin from Day 1 to Day 28

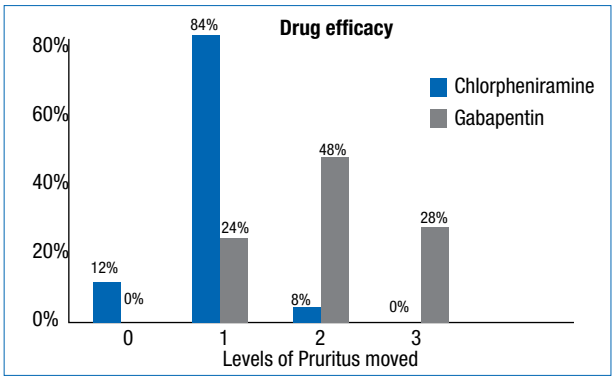

Figure 3. Levels of pruritis moved

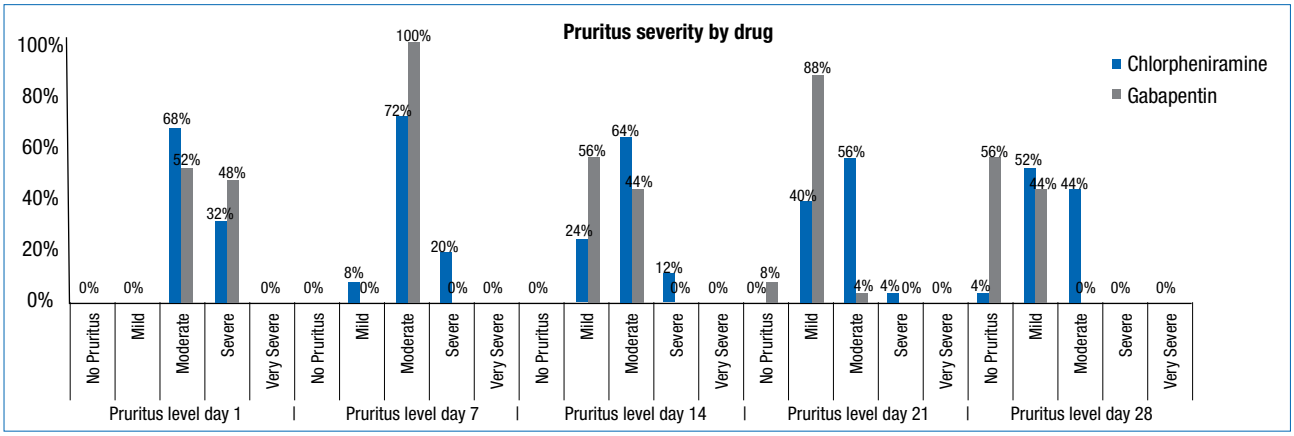

Figure 2. Pruritus severity from Day 1 to Day 28

Discussion

Most of the participants in this study had second-degree deep burns (64%), while 22% of the participants had mixed second-degree burns. The area most affected by pruritus was the trunk followed by the lower limbs. The severity of pruritus at recruitment of the study varied with the highest score being eight on the VAS and the lowest three. The highest scores were seen in patients with postburn pruritus involving the lower limbs. On the other hand, burns involving the upper limbs were associated with a lower score of pruritus. Ioannis Goutos and Peter Dziewulski[2] demonstrated similar findings by noting that postburn pruritus affects lower limbs most.

Gabapentin was found to be more effective in the treatment of postburn pruritus as evidenced by a higher mean reduction of VAS scores for patients administered gabapentin (6.36) as compared to chlorpheniramine (3.32). This reduction was higher in patients with severe pruritus. Although this study had intended to escalate the dose of gabapentin to the maximum recommended dose of 900 mg, the majority of the patients responded well on a lower dose of 300 mg per day. None of the patients thus had a dose adjustment upwards. This finding was also noted with Ana Alice in the management of pruritus using a single dose of 300 mg for management of notalgia pruritus.[11] She reported reduction of pruritus by up to 50% with a single dose of gabapentine. Patients with mild pruritus responded almost similarly on either chlorpheniramine or gabapentin.

It is therefore evident that while the two drugs are able to treat postburn pruritus, gabapentin is more effective as seen in this study.

The superior efficacy of gabapentin as evidenced in this study over antihistamines (chlorpheniramine), mirrors similar findings from several studies such as one conducted in 2011 by Ahuja RB.[12] He compared gabapentin with cetirizine (also an antihistamine) for the treatment of postburn pruritus and found gabapentin to be more effective by reducing VAS scores to a greater magnitude than cetirizine. In the same study,[12] several patients were able to reach itch-free status i.e. VAS scores of 0–1. In his study, however, he escalated the dosage from 300 mg upwards. This has also been the finding in this study with 14 (56%) of the patients in the gabapentin arm achieving scores of 0–1 by the end of the study.

The only side-effect experienced in this study was sedation. Both gabapentin and chlorpheniramine caused sedation in the majority of the patients. Gabapentin however caused sedation of more magnitude than chlorpheniramine. The sedation caused, however, did not interfere with the day-to-day activities of the patients and no patient requested for the stoppage of the medications. No other neurological side-effects were experienced.

In conclusion, in our study we found that postburn pruritus could be managed by either chlorpheniramine or gabapentin. Both drugs are safe with relatively mild side-effects and result in improving the quality of the patient's life. Patients with mild pruritus could, however, be managed with chlorpheniramine since it is cheaper and has fewer sedative effects with a similar efficacy compared to gabapentin. Patients with moderate to severe pruritus are, however, best managed with gabapentin as demonstrated in this study. It is more effective in reducing pruritus of the worst severity. There is, however, a need to carry out further studies in patients who may use these medications on a long-term basis since postburn pruritus may persist even up to one year after burns. There is also a need to compare tid dosage as recommended by the manufacturer vis-à-vis od dosage as demontstrated in this study which was effective in our patients.

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