

**COMPARATIVE STUDY OF GABAPENTIN AND
CHLORPHENIRAMINE IN THE MANAGEMENT OF
POST-BURN PRURITUS AT KENYATTA NATIONAL
HOSPITAL**

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DECLARATION

I hereby declare that this dissertation is my original work and has not been presented for a degree award at any other university.

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ABBREVIATIONS/ACRONYMS

CGRP: Calcitonin Gene Related Peptide

GABA: Gamma Amino Butyric Acid

H1: Histamine 1

H2: Histamine 2

IL 2: Interleukin 2

KNH/UON ERC: Kenyatta National Hospital/University of Nairobi Ethics and Research Committee

PGE2: Prostaglandin E2

QoL: Quality of Life

TBSA: Total Burn Surface Area

VAS: Visual Analogue Scale

ABSTRACT

COMPARATIVE STUDY OF GABAPENTIN AND CHLORPHENIRAMINE IN THE MANAGEMENT OF POST-BURN PRURITUS AT KENYATTA NATIONAL HOSPITAL

Background: Pruritus is a common complication of burns and it affects the healing of burn wounds due to tissue damage caused by the scratching. It also affects the patient's sleep and daily activities hence interfering with their quality of life.

There is paucity of data regarding the aetiopathogenesis of post burn pruritus and its management. Several treatment options have been used including oral antihistamines, emollient creams, pressure garments and topical antihistamine gels. However, these have had unsatisfactory results and more recently gabapentin has also been found to be effective in the management of pruritus of several aetiologies including burns.

This study therefore sought to compare the efficacy of gabapentin with chlorpheniramine in burns patients suffering from pruritus.

Main objective: To compare the efficacy of gabapentin to that of chlorpheniramine in the management of postburn pruritus.

Study design: A randomized controlled trial.

Materials and methods: Data from 50 patients was collected by use of a data collection sheet .The patients were divided into two arms , one receiving chlorpheniramine and the other gabapentin. Visual Analogue Scale was utilized to grade the severity of pruritus as well as subsequent response to treatment and the data was analysed using SPSS version 22 . Data was presented in form of tables, bar graphs and pie charts. Mann-Whitney U and Kruskal Wallis tests were used to compare the two populations.

1.0 BACKGROUND

Pruritus is defined as a poorly localized, unpleasant sensation that elicits a desire to scratch and is also described as being non-adapting^[1].

Post-burn 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]. It can impact negatively on the quality of life (QoL) of patients recovering from burns by affecting their sleep patterns whereby the patients spend a significant amount of time at night scratching the affected areas instead of sleeping and therefore leading to few hours of sleep with subsequent fatigue the next day.

The pruritus also interferes with the daily activities of the patients when they spend a lot of time scratching their wounds thus distracting them from concentrating on day-to-day activities^[4].

Healing of the burn wound is affected as well by the resultant tissue damage caused by the patient scratching the wounds^[4]. This leads to a delay in healing of the burn wound and especially so if the wounds are extensive.

Pruritus as a complication of burns is therefore an important factor that warrants the clinician's attention during the care of a patient recovering from burns^[4]. It is therefore crucial to not only understand the aetiopathogenesis of this condition but also to find an effective remedy.

There is paucity of data on the aetiopathogenesis of post-burn pruritus and the available treatment options for this condition^[4, 5]. Also lacking is a globally accepted systemic approach in the assessment and management of this distressing symptom^[4-7].

Post-burn pruritus is a widely prevalent complication of burn wounds with statistics reporting a complication rate as high as 73%-93%^[8]. Symptoms are reported to be especially troublesome at night^[4, 9].

Locally, there are no studies which have been carried out on the management of post-burn pruritus.

1.1 LITERATURE REVIEW

Pathophysiology of post-burn pruritus

Pruritic stimuli are transmitted by C fibres extending from the skin to the dorsal root ganglion of the spinal cord where the impulses are conveyed to the higher central nervous system areas such as the somatosensory cortex ^[10] thus involving both the peripheral and central nervous systems.

These two pathways (the peripheral and central nervous pathways) therefore provide areas for pharmacological intervention in the management of pruritus. Use of peripherally acting agents such as topical antihistamines and other topical agents has been employed to exploit this pathway. ^[10]

The central nervous system component of conveyance of pruritus stimuli has also been the focus of several studies more recently especially with use of gabapentin. ^[11,12]

The anatomic regions which are most commonly affected by post-burn pruritus are the legs, arms and face. Post-burn pruritus usually occurs in patients with more than 40% TBSA and in patients whose burn wounds take more than three weeks to heal ^[3].

Several mediators of pruritus have been proposed including histamine, prostaglandin E1 (PGE1), serotonin, opioids, CGRP (Calcitonin Gene Related Peptide) and Interleukin 2 (IL-2) as described by Greaves M W and colleagues in 1996 where they concluded that these mediators were potential areas of pharmacotherapy for pruritus ^[10]. Inhibitors of these mediators have been shown to alleviate itch with varying degrees of success.

Antihistamines either H1(histamine 1) or H2 (histamine 2) receptor antagonists in oral form or as topical creams such as doxepin and emollients have been utilized as treatment options and have been found not to be very effective ^[12]

Other topical agents that have been studied include colloidal oatmeal and oils containing liquid paraffin all with varying degrees of success ^[13] as was demonstrated by Matheson JD and his colleagues in a study they conducted in 2001. Their conclusion was that the use of these agents reduced the need for use of oral antihistamines though did not alleviate the itch completely.

Goutos et al carried out a study in the United Kingdom and found that most clinicians favoured the use of antihistamines as opposed to agents working on the central nervous system for treatment of post-burn pruritus ^[14].

Studies conducted by Zachariah JR and colleagues as well as by Carrouger GJ and his colleagues both concluded that there is lack of a clear consensus on the care of patients who do not respond to antihistamines ^[7, 8].

Chlorpheniramine

Chlorpheniramine is a H1 receptor antagonist which exerts its anti-pruritic action by its sedative effect and hence is more useful for nocturnal pruritus as well as blocking histamine receptors which is one of the mediators of the itch pathway. Its main side effect is sedation. It is normally administered at a dose of 4mg every 6 to 8 hours.

Gabapentin

Gabapentin is an antiepileptic drug that has also shown efficacy in conditions associated with chronic pain ^[11] and also in pruritic disorders ^[15, 16]. 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.

It does not directly act on Gamma Amino Butyric Acid (GABA) receptors nor does it affect the reuptake of GABA. It however increases the synthesis of GABA from glutamate by altering the activity of glutamic acid decarboxylase in neurological tissue ^[11, 15].

Its effect on pruritus may be both central and peripheral. It secondarily inhibits CGRP release from primary afferent neurons through a primary increase of GABA in the spinal cord ^[12, 15, 17].

Gabapentin is well absorbed after oral intake and does not induce nor inhibit hepatic enzyme function. It has minimal drug interactions ^[11]. Dosing is initiated for adults at 300mg/day and can be increased up to 1200 mg thrice a day with a high toxicity ratio thus minimizing adverse effects even with high doses.

The most common adverse effect is sedation. Rare adverse effects include pancytopenia, cholestasis, hypersensitivity syndrome and dyskinesia ^[18]. Patients should not be withdrawn abruptly but rather tapered gradually to prevent withdrawal like symptoms ^[19].

Gabapentin is safe for use in paediatric patients, being used for epilepsy at a dose of 20-30mg/kg/day and up to a maximum of 40mg/kg/day in refractory epilepsy. For post-burn pruritus, gabapentin has been used at a dose of 5-10mg/kg/dose up to thrice a day in paediatric patients and 300-900mg/day for adults ^[9].

Chlorpheniramine and Gabapentin in clinical practice.

Chlorpheniramine has been used to treat post-burn pruritus but studies have shown limited efficacy with only 20% of patients getting significant relief when used as sole therapy as evidenced by a study done by Zachariah JR in 2012 ^[7].

Gabapentin has previously been used for the management of neuropathic pain ^[11, 12]. It has also been found to be effective in burn wound hyperalgesia and allodynia as reported in a study by Gray et al comprising 6 case series ^[20].

It has been shown to be more effective than chlorpheniramine or cetirizine as monotherapy with greater reduction in the intensity of pruritus as well as having a faster onset of action ^[21].

A study by Zachariah and colleagues to evaluate the effect of gabapentin in post-burn pruritus found a reduction in the itch severity score in 87% of the participants, with a significant effect noted in the first month of treatment as evidenced by a mean reduction of 4.99 in itch severity scores which was statistically significant. The overall quality of life of the patients was found to improve significantly with the use of gabapentin ^[9].

Gabapentin is therefore suggested as a second line option in post-burn pruritus in patients who do not respond to antihistamines ^[9].

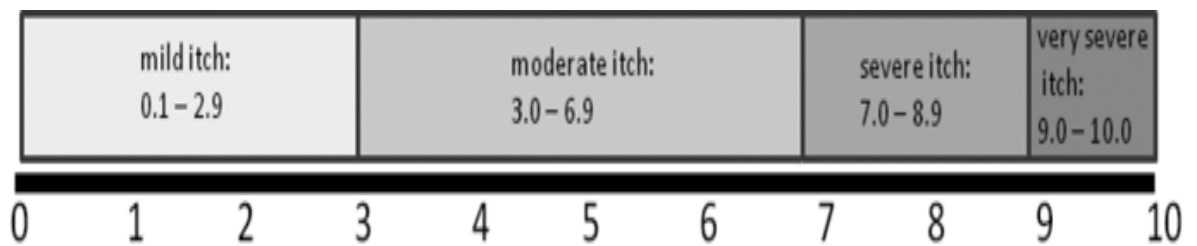
Response to gabapentin alone and in combination with two antihistamines has been found to be higher than chlorpheniramine alone as well as in combination with 2 antihistamines ^[9].

Visual Analogue Scale

Several tools have been developed to try and measure pruritus objectively and in a way that can be reproduced. One such tool is a self report questionnaire developed by C. Majeski and colleagues ^[22] in which seven items were identified to assess itch including the quality, time of day, part of the body affected among others. While being useful in assessing effectiveness of treatment for pruritus ^[22] however, it is quite lengthy and translation to other languages for patients not fluent in English might dilute or distort the intended meaning.

Other tools which employ similar methods include questionnaires such as the 5-D itch scale ^[23] developed by Elman and colleagues which is also lengthy and requires fluency in English. A study by Phan et al comparing the efficacy of the visual analogue scale, the numerical rating scale and the verbal rating scale found the sensitivity of discrimination of pruritus intensity to be higher with the visual analogue scale ^[24].

The Visual Analogue Scale has been proven to be easy to use and reliable for the objective assessment of pruritus. It comprises a 10 cm line that has 1 cm graduations with numbering from 1 to 10. Zero (0) is the score given to no itch while 10 is the most severe form of itch as scored by the patient. The grading is given as 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 ^[25-26].



2.0 STUDY JUSTIFICATION

There is no study which has been carried out in Kenya with regard to the management of pruritus as a complication of burns.

Globally, there is paucity of data regarding the effective management of post-burn pruritus despite the availability of several treatment modalities ^[4, 5]. Most of the studies have been carried out in Caucasian and Asian populations with none having been done in African populations.

This study will possibly lead to the development of treatment protocols which will facilitate the effective management of patients with post-burns pruritus resulting in a positive impact on their quality of life.

2.1 RESEARCH QUESTION

Is gabapentin more effective than chlorpheniramine in the management of post-burn pruritus in a population of burns patients at Kenyatta National Hospital?

2.2 HYPOTHESIS AND OBJECTIVES

2.2.1 Null hypothesis:

Gabapentin has the same efficacy as chlorpheniramine in the treatment of post-burn pruritus.

2.2.2 Main objective:

To compare the effectiveness of gabapentin to that of chlorpheniramine in the treatment of patients with postburn pruritus.

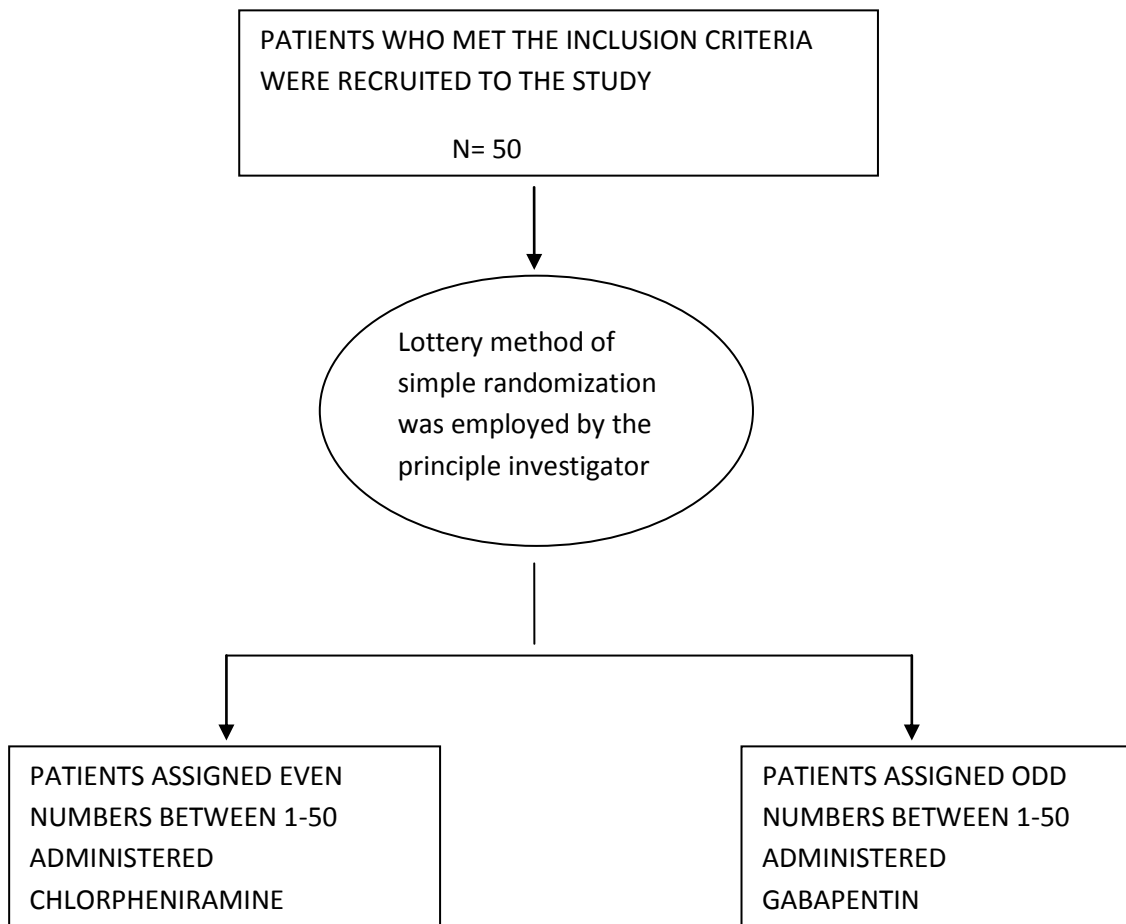
2.2.3 Specific objectives

1. To determine the effectiveness of gabapentin in the management of post-burn pruritus.
2. To determine the effectiveness of chlorpheniramine in the management of post-burn pruritus.
3. To compare the severity of sedation in patients on treatment with chlorpheniramine and gabapentin for postburn pruritus.

3.0 MATERIALS AND METHODS

3.1 Study design

Diagram 1: Randomized controlled trial



The patients were blinded to the drug that they received but the principle researcher and the caregivers were not blinded.

Visual analogue scale 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, visual analogue scale scores were subsequently recorded at weekly intervals for a period of 4 weeks at which point the final score was taken.

The dosage of the medication was as follows:

Chlorpheniramine:

Patients 12-18 yrs: 0.2mg/kg increased to a maximum of 12 mg per day depending on patient response.

Adults: 0.2mg/kg increased to a maximum of 24mg per day depending on patient response.

Gabapentin

Patients 12-18 yrs: 5mg/kg/dose up to thrice a day depending on the patients response.

Adults: 300mg once daily increased to 300mg thrice a day depending on patient response.

3.2 Study setting

The study was carried out in the plastic surgery ward (4D), the burns unit and the plastic surgery outpatient clinic at the Kenyatta National Hospital (KNH).

3.3 Study population

Patients with postburn pruritus and were admitted in ward 4D and burns unit as well as those attending the plastic surgery outpatient clinic.

3.4 Sample size

The study sample size was determined through comparison of proportions between the two groups. The number of participants per group required to detect a difference $p_1 - p_2$ in the proportions with significance level α and power $1 - \beta$ was:

$$n = \frac{p_1(1 - p_1) + p_2(1 - p_2) (Z_{1-\frac{\alpha}{2}} + Z_{(1-\beta)})^2}{(p_1 - p_2)^2} \quad [27]$$

Where

$p_1 = 87\%$ Expected proportion of Group 1

$p_2 = 67\%$ Expected proportion of Group 2 (67%)

$\alpha = 0.05$ Significance level (probability of a type I error)

Power $(1-\beta)= 80\%$ Where β is the probability of a type II error

$$Z_{1-\frac{\alpha}{2}} = 1.96$$

$$Z_{(1-\beta)} = 0.84$$

Substituting the formula and inclusion of 10% attrition the sample size per group is $24.9 \approx 25$ thus **n = 50**

3.5 Study duration

The study was carried out between February 2015 to April 2015.

3.6 Inclusion criteria

1. All burn patients between the age of 12- 80 years admitted in ward 4D or burns unit with a score above zero(0) in the VAS for pruritus
2. All burn patients between the ages of 12-80 years attending the plastic surgery outpatient clinic with a score above zero (0) in the VAS for pruritus
3. Patients who consented to participation in the study

3.7 Exclusion criteria

1. Patients aged below 12 years
2. Patients above 80 years
3. Patients who did not have Pruritus
4. Patients already on gabapentin or chlorpheniramine for other medical conditions.
5. Patients who declined to participate in the study

3.8 Study limitations

1. Patients enrolled in the study were at different stages of healing of their burn wounds.
2. Some of the outpatients might not have been compliant on their medication.

3.9 Study delimitations

1. Post burn pruritus tends to affect burns in the limbs and face; therefore most of the patients with pruritus were likely to have burns in these areas thus providing a form of standardization of the presentation.

3.10 Data collection

Patients who met the inclusion criteria and gave informed consent were consecutively sampled and assigned a random patient number from 1 to 50. This was done using simple random sampling applying the lottery method of assigning numbers. The principle investigator did the randomization.

Their age, extent of burn (depth and burn surface area) and area of most intense pruritus was recorded (see the appendix).

The Visual analogue scale (VAS)(see the appendix) was used to assess and grade the severity of the pruritus in each patient at the beginning of the study and regularly at 7 day intervals during the study period. The follow up period was 4 weeks, during which time the medicine was administered and after which the final score of itch severity was taken.

The study population was divided into two arms; patients with even numbers were assigned to the chlorpheniramine arm and patients with odd numbers were assigned to the gabapentin arm.

Each arm had the following data collected:

1. Biodata comprising age and sex.
2. Site of burn wound, percentage of BSA as well as site of most intense pruritus.
3. Visual analogue scale score of pruritus.
4. Dosage of the drug given.
5. Adverse effects(if any) of the drug given.

On conclusion of the study, the raw data was filed in form of both hard and soft copies and stored for future reference. This was necessary in view of future publication of this study.

3.11 Quality control

The principal investigator recruited the patients, obtained informed consent and collected the data in order to ensure quality control.

3.12 Data analysis and presentation

Data was entered into a password protected database, which was correlated with hard copies of the same to ensure accuracy.

Data was analyzed by use of the Statistical Package for Social Sciences (SPSS) version 22.0 Descriptive univariate analysis of socio-demographic characteristics (such as age and gender) was analyzed and presented using percentages, pie charts, frequency tables and graphs.

Mann-Whitney U test(see the appendix) was used to compare the two populations.

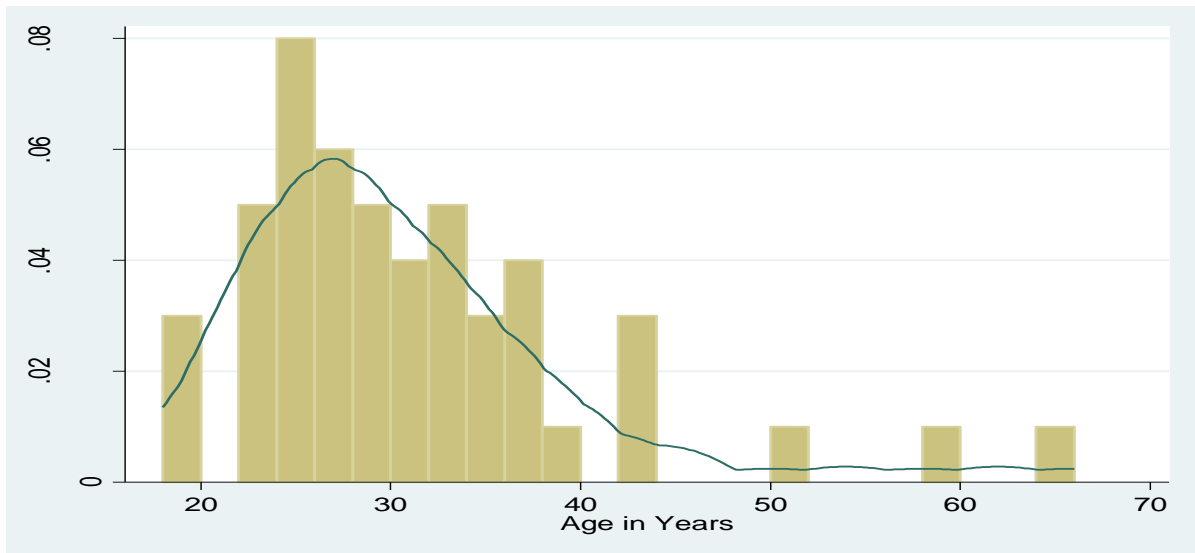
3.13 ETHICAL CONSIDERATIONS

1. Ethical approval was sought from the KNH/UON Ethics and Research Committee
2. Patients who consented to inclusion into the study were guaranteed the utmost observance of confidentiality and were allowed to drop out at any time during the study period.
3. The study was to be stopped in those patients who acquired undue or life threatening adverse effects and appropriate treatment of their adverse effects instituted.
4. The study participants were not to incur any extra financial costs.
5. The principal investigator would not benefit in monetary terms from this study and neither did he have any conflicting interests in the manufacturing companies or marketing any of the two drugs.
6. The results were to be published to allow other medical practitioners to benefit from the study.

4.0 RESULTS

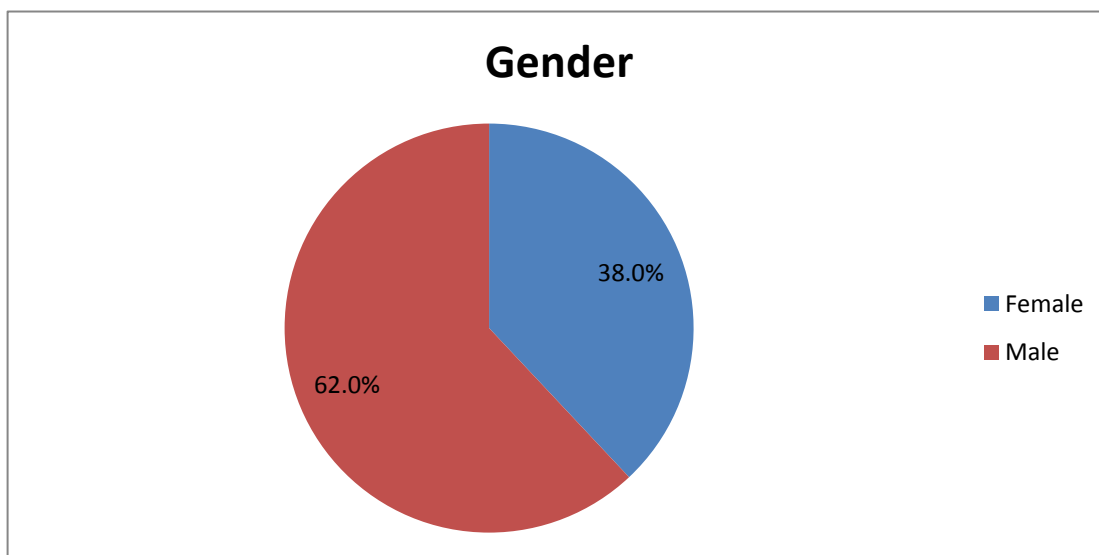
50 patients were recruited into the study

FIGURE 1: age of respondents



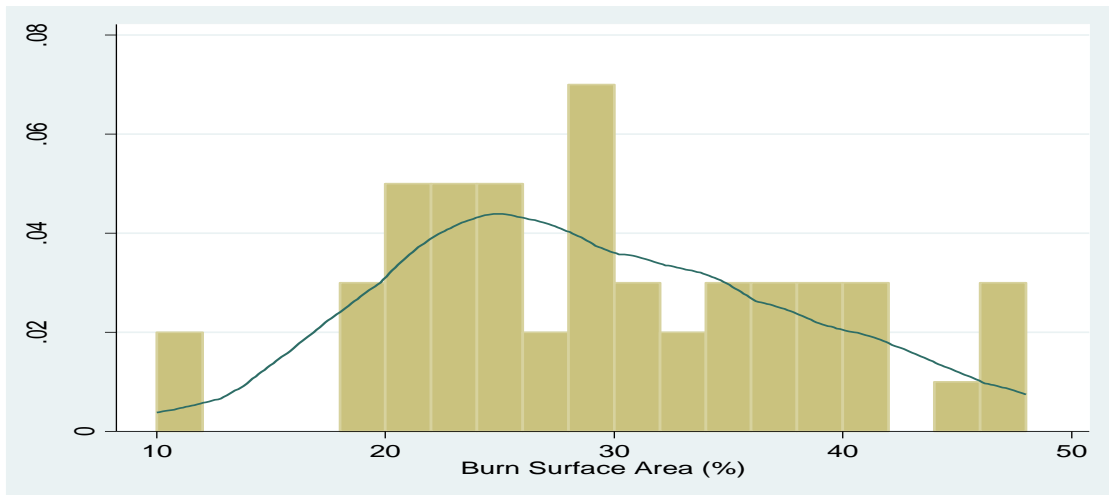
The median age of the respondents was 28 years with an interquartile range of 9 years.

FIGURE 2: pie chart illustrating gender of respondents



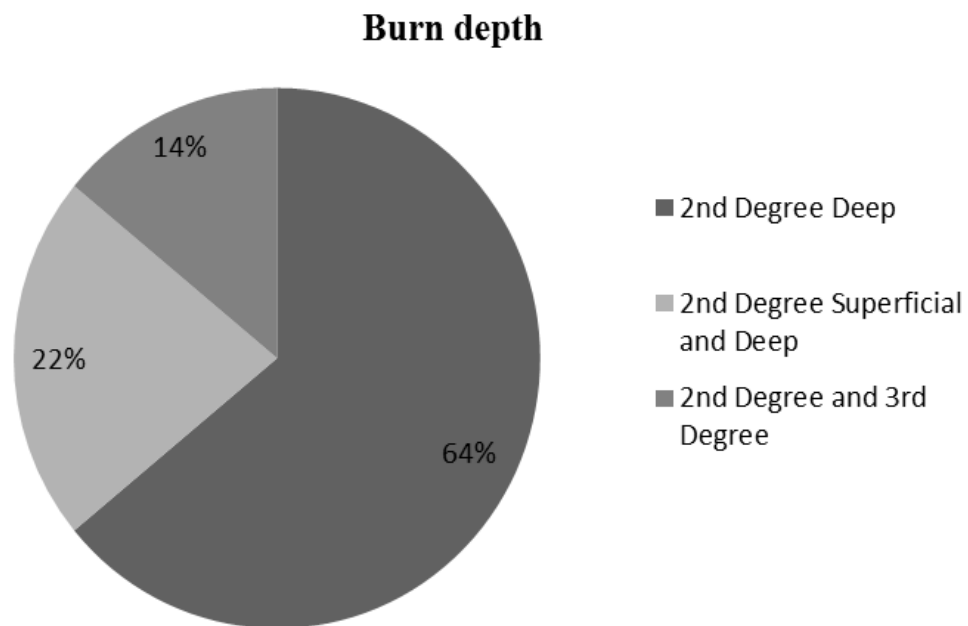
Majority 31(62%) of the respondents were male as compared to 19(38%) female respondents

FIGURE 3: chart illustrating burn surface area (%)



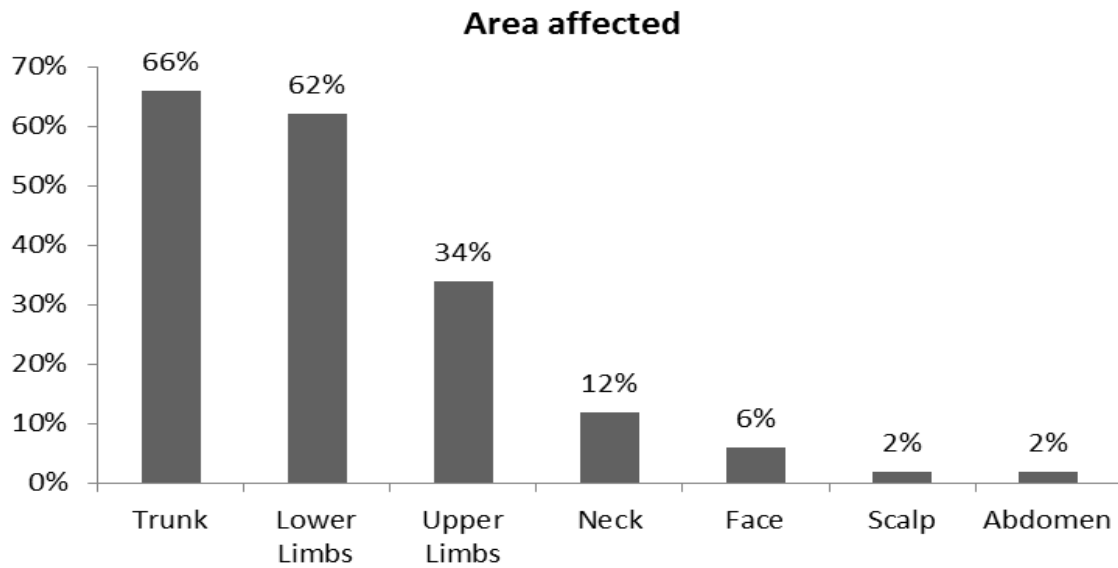
The median burn surface area was 28% with an interquartile range of 14%.

FIGURE 4: pie chart illustrating depth of the burn wound



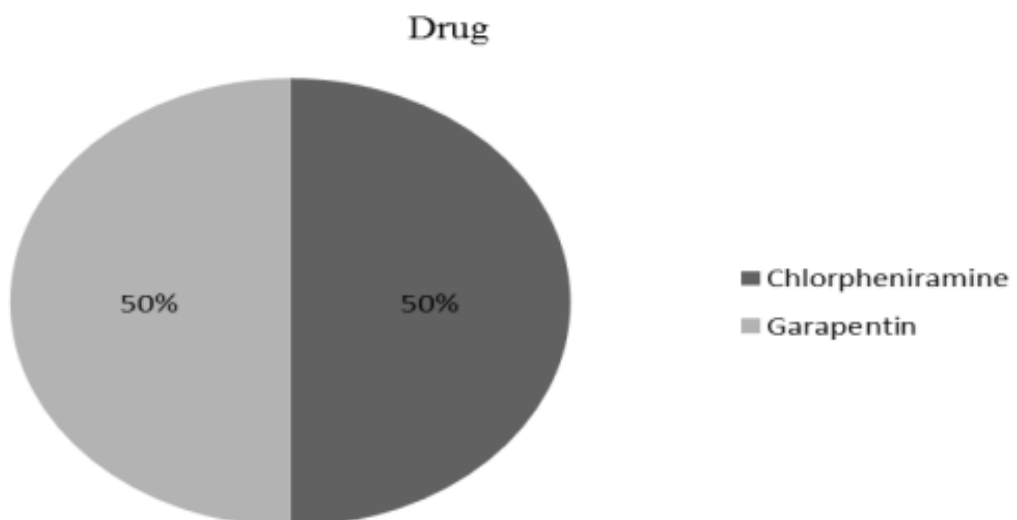
64% (32 patients) of the respondents had second degree burns as compared to 22%(11 patients)who had second degree superficial and deep burns while 14% (7 patients) had both second and third degree burns.

FIGURE 5: area of most intense pruritus



Most 33(66%) of the respondents had area of most intense pruritus being trunk; 31(62%) had most pruritus in lower limbs; 17(34%) upper limbs; 6(12%) neck; 3(6%) face while 1(2%) each had area most affected by postburn pruritus being scalp and abdomen

FIGURE 6: pie chart illustrating drugs administered



During the period of the study (4 weeks), 25(50%) of the respondents were administered Chlorpheniramine and 25(50%) respondents were administered Gabapentin.

Patients in the chlorpheniramine arm were all started at a dose of 4mg twice a day but due to poor response their frequency of administration was increased to 4mg thrice a day for 8 of the 25(32%) patients in that arm.

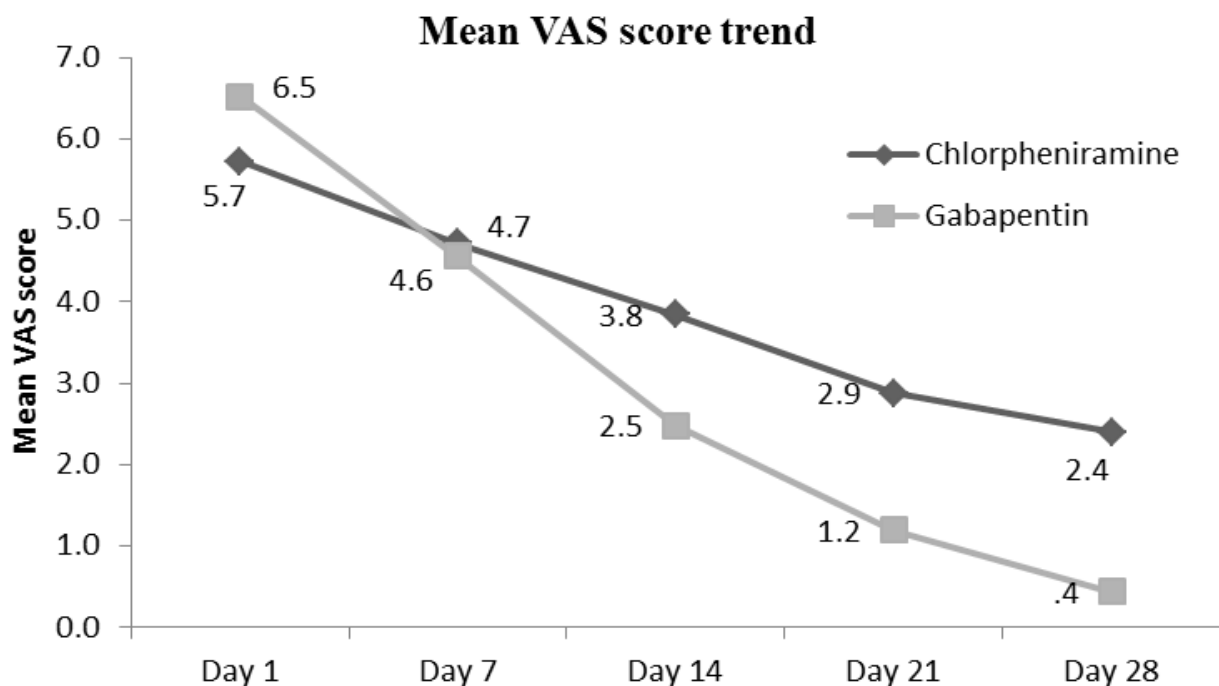
Patients in the gabapentin arm were all started off at a dosage of 300mg once daily and none of them required adjustment of dosage or frequency of administration.

POSTBURN PRURITUS

There was general decrease in the mean VAS score for Chlorpheniramine and Gabapentin from day one to day 28, that is, 6.5 to 0.4 for Gabapentin and 5.7 to 2.4 for Chlorpheniramine respectively.

Mann Whitney U test indicated that there was insignificant difference in VAS scores on Day 1(p-value = .071) and Day 7 (p-value = .905) but thereafter patients administered Chlorpheniramine had significant higher VAS score as compared to patient administered Gabapentin (Day 14 p-value = .002, Day 21 p-value < .001 and Day 28 p-value < .001).

FIGURE 7: trend of reduction of vas



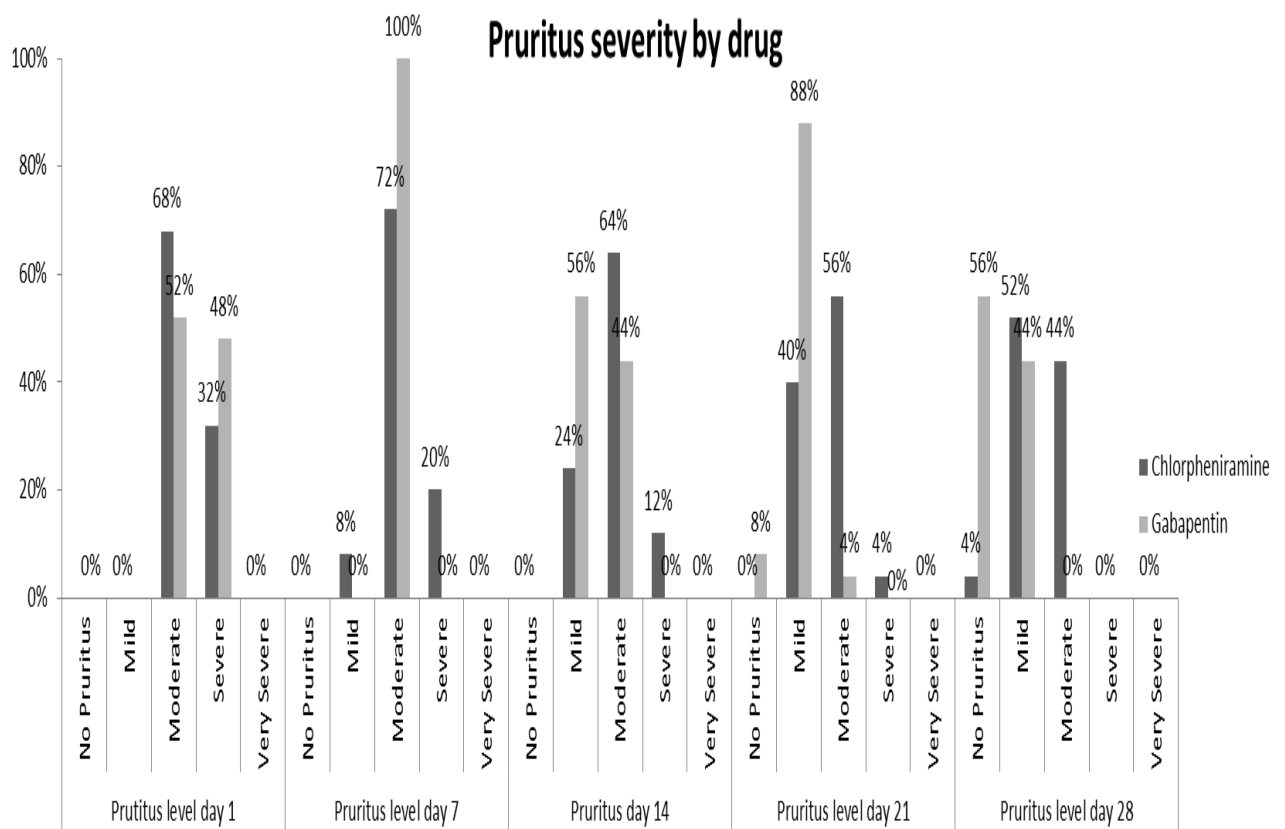
To determine the pruritus severity, the VAS scores were recorded as follows:

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.

The outcome (number of respondents), were as indicated in figure 8 below. At the end of the study period 14(56%) of patients using Gabapentin had no pruritus as compared to 1(4%) of patients who were on chlorpheniramine.

FIGURE 8: severity of pruritus from day 1 to 28

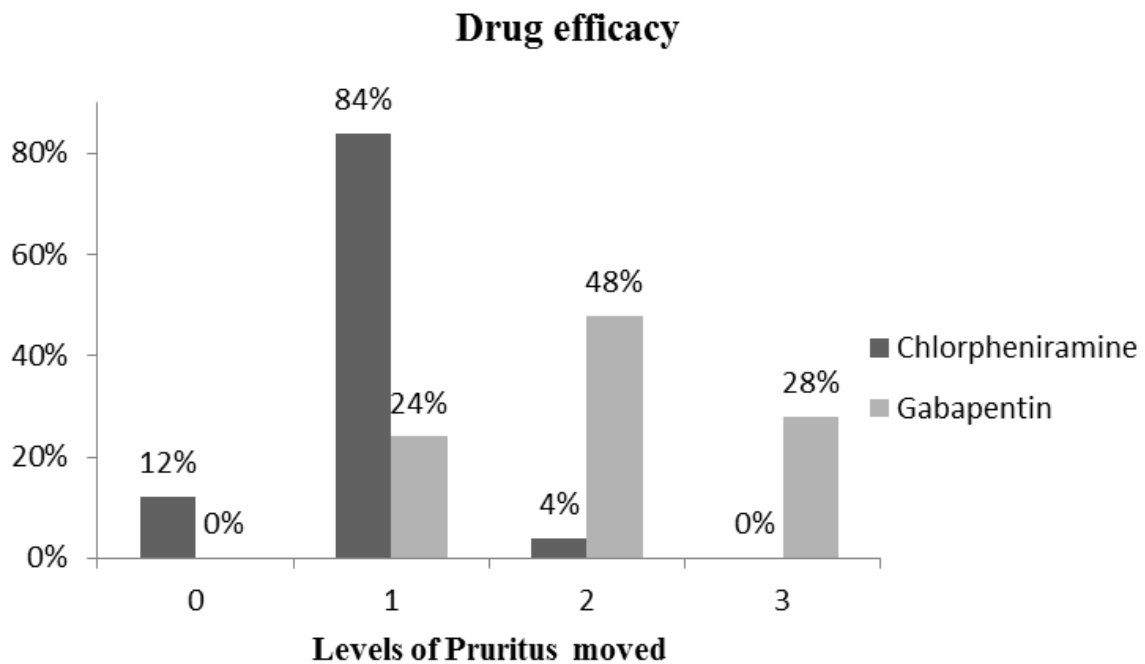


To assess the efficacy of the two drugs in dealing with pruritus, the progress of patients from one level to another during the study was considered with a patient who moved from one level of pruritus to another awarded a score of 1 while a patient who stagnated was awarded a score of 0(zero) during the successive measurement period.

Since there was no respondent with very severe pruritus, the maximum score was 3 (moved patient from severe pruritus at day 1 to no pruritus at day 28) and the minimum score was 0 (the pruritus level of the patient remained constant throughout the study period).

The scores were then summed up to get the efficacy score as indicated in the figure 9 below. Majority 21(84%) of the respondents who were administered Chlorpheniramine moved 1 level of pruritus while 12(48%) patients who were administered Gabapentin moved 2 levels of pruritus. Mann Whitney U test revealed that Gabapentin is more effective than Chlorpheniramine (p-value < .001).

FIGURE 9: comparison of drug efficacy



SEDATION

Sedation was graded as mild, moderate or severe. Both chlorpheniramine and gabapentin had side effects of sedation but with varying degrees depending on the dosage and frequency of administration. 64% of patients administered Gabapentin had moderate degree of sedation on day 21 and day 28 while all (25/100%) patients administered Chlorpheniramine had only mild degree sedation on day 7 and day 14. There was an increase in number of patients who experienced moderate sedation with chlorpheniramine from day 14 to 28 when the dosage of chlorpheniramine was increased from 4 mg twice daily to 4 mg thrice a day.

TABLE 1: drug by degree of sedation

Drug	Degree of Sedation							
	Day 7		Day 14		Day 21		Day 28	
	Mild	Moderate	Mild	Moderate	Mild	Moderate	Mild	Moderate
Chlorpheniramine	25	0	25	0	19	6	19	6
Gabapentin	11	14	9	16	9	16	9	16

5.0 DISCUSSION

5.1 Introduction

This study sought to evaluate one of the more common drugs used to treat post burn pruritus (chlorpheniramine) and to compare it with a newer drug (gabapentin) in terms of their efficacy in treating this condition.

5.2 Pruritus

Most of the participants in this study had 2nd degree deep burns (64%) , while 22% of the participants had 2nd degree both superficial and deep. 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 8 on the visual analogue scale (VAS) and the lowest being 3. 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 on the VAS. This is in keeping with the results of a study by Ioannis Goutos and Peter Dziejewski^[2] in 2009 that found that most patients with postburn pruritus experienced more itchiness in the lower limbs and especially at night.

5.3 Medications to treat postburn pruritus

Chlorpheniramine was started at a dose of 4mg twice a day and with weekly measurements of pruritus using the VAS, dose adjustments were made depending on the response of the patient. Those who were noted not to have improvement had their dosage increased to 4mg thrice a day.

Patients who were assigned to the gabapentin group were noted to respond to the initial dose of 300mg once daily and none of them required increment of their dosage throughout the course of the study.

5.4 Response to treatment

Gabapentin was found to be more effective in 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).

While there was no significant difference in the first week, at the end of the study there was a significant difference in the reduction of VAS scores from the Mann-Whitney U test with a p value of less than 0.001.

While assessing the efficacy of the two drugs in treating postburn pruritus, an efficacy score was assigned based on movement from one level of pruritus to another, i.e from severe to moderate or mild. The difference from one level to the next was assigned a value of 1.

The 2 arms were then analyzed once again using the Mann-Whitney U test Gabapentin was found to be more effective than chlorpheniramine with majority of the patients administered gabapentin moving 2 levels down while those administered chlorpheniramine moved down by only 1 level. The difference was significant with a p-value of less than 0.001.

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 initial dose of 300mg is sufficient without the need to increase the dosage or frequency of administration.

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 and colleagues^[21] where they 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, several patients were able to reach itch free status i.e VAS scores of 0-1. 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.

5.5 Sedation

Both chlorpheniramine and gabapentin caused sedation. Gabapentin had more participants experiencing moderate sedation compared with chlorpheniramine.

The patients who were in the chlorpheniramine arm initially had mild sedation, however, those in whom the frequency of administration of the medication was

increased experienced a corresponding increment of sedation levels from mild to moderate. Other studies which have evaluated the use of gabapentin for treatment of various forms of pruritus such as the one by Yesudian and colleagues in 2005^[15] have found the main adverse effect to be sedation as found in this study.

However, none of the participants' sedation in both arms necessitated stopping of the medication or withdrawal from the study.

6.0 CONCLUSION AND RECOMMENDATIONS

Postburn pruritus is a common and distressing complication of burn wounds and its adequate management is important in the care of burns patients. This study sought to compare chlorpheniramine, (commonly used drug for this condition though not with very satisfactory results), with gabapentin (which more recently has been found to be more effective) .

This study has demonstrated the superiority of gabapentin over chlorpheniramine in the management of postburn pruritus without serious adverse effects.

Gabapentin is therefore recommended in the management of postburn pruritus as it has demonstrated the ability to not only significantly reduce the severity of pruritus but also assist patients in achieving an itch free status. This is in tandem with the recommendation by Zachariah J R and colleagues^[7] in their study in 2012 where while reviewing current treatment options for postburn pruritus recommended use of gabapentin for patients who do not respond to antihistamines or emollients.

It is also recommended to first grade the degree of pruritus using a tool such as the visual analogue scale so as to help decide the medication to use, the dosage and frequency of administration guided by the severity of pruritus.

Mild severity of pruritus may be adequately managed by chlorpheniramine but for better relief in moderate to severe pruritus, gabapentin is indicated.

The study also lays ground for further studies to evaluate the two drugs in combination to see if there is an even better patient response as far as reduction of postburn pruritus is concerned.

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APPENDICES

APPENDIX I: DATA COLLECTION FORM

PATIENT NUMBER			
AGE , SEX AND WEIGHT			
BURN SURFACE AREA AND DEPTH			
AREA OF BODY MOST AFFECTED BY PRURITUS			
DRUG ADMINISTERED			
DOSAGE			
DAY 1			
DAY 7			
DAY 14			
DAY 21			
DAY 28			
VISUAL ANALOGUE SCALE SCORES	<p> mild itch: 0.1 – 2.9 moderate itch: 3.0 – 6.9 severe itch: 7.0 – 8.9 very severe itch: 9.0 – 10.0 </p> <p>0 1 2 3 4 5 6 7 8 9 10</p>		
DAY 1			
DAY 7			
DAY 14			
DAY 21			
DAY 28			
DEGREE OF SEDATION	MILD	MODERATE	SEVERE

APPENDIX 2

GENERAL PATIENT INFORMATION AND CONSENT FORM

English version

This is an informed consent form for persons aged 18 years and above as well as those below the age of 18 whose guardians/ next of kin/ parents allow to be included in the study whose title is

‘Comparative study of gabapentin and chlorpheniramine in the management of post-burn pruritus at Kenyatta National Hospital.’

Principal investigator: Dr. Kenneth Mbira Ngunju

Institution : School of Medicine, Department of surgery, University of Nairobi

Supervisors: Dr. Nang’ole Wanjala, Dr. Mark Awori.

This informed consent has three parts

1. The Information sheet that seeks to give you details about the study
2. The certificate of consent to append your signature if you agree to take part
3. Statement by the principal researcher

A copy of the consent form shall be availed to you in full.

Part 1: Information sheet

My name is Dr. Kenneth Mbira Ngunju , a Postgraduate student at the School of medicine, University of Nairobi. I am conducting a research study titled ‘Comparison of gabapentin and chlorpheniramine in management of post-burn pruritus in patients at Kenyatta National Hospital’.

Postburn pruritus is a common complication affecting patients suffering from burns and especially those whose wounds take more than three weeks to heal. Management has included use of antihistamines such as chlorpheniramine with unsatisfactory results. There is need to evaluate other pharmacologic agents which have been found to be more effective. This study aims to evaluate one such agent; gabapentin and compare it with chlorpheniramine to determine whether gabapentin is more effective or not. Using the information derived from this study, conclusions will be drawn which may influence treatment practices locally.

I would like to invite you to take part in this study. Participation is purely voluntary and you are allowed to consent either immediately after getting this information or after a period of consultation.

You are free to ask questions at any time regarding this study, or to seek any clarification from either myself or my research assistant. If you consent to participate in the study, some personal details as well as information concerning your condition will be sought.

You will then be randomly assigned a number between one(1) and fifty(50) recruited into one of the two arms of the study depending on whether the number assigned to you is even or odd. Once assigned to either of the two groups(chlorpheniramine or gabapentin), the respective medication will be administered. At regular intervals information will be sought from you regarding the effect of the medication on pruritus as well as any side effects that you may experience.

There will be no difference in the quality of care between the two groups and neither are there any risks of being assigned to either arm.

You are guaranteed that all the information taken from you will be kept strictly confidential and will not be accessed by anyone other than the researchers and any other person authorised by the KNH/UON Ethics and research committee. This information will be coded with numbers such that only the researchers can identify you.

Participation in this study will be through a clinical interview and a clinical examination. Withdrawal from this study can be done at any stage and will not affect your treatment at this hospital.

This proposal has been reviewed and approved by the KNH/UON ERC which is a body that ensures the protection of persons like yourself that take part in research studies.

This approval has been granted after submission of the study proposal to the committee by the Chairman of the Department of Surgery, School of Medicine, University of Nairobi with the approval of a University supervisor.

In the event that you require any additional information or for any other purpose regarding this study, relevant contact details are listed below:

1. Dr Kenneth Mbira

Department of Surgery

School of Medicine

University of Nairobi

P.O. Box 19676-00202

KNH, Nairobi

Tel:0717710570

2. The Secretary

KNH/UON Ethics and Research Committee (ERC)

Tel no: +2542726300-19 Ext.44102

P O BOX 20723-00202, Nairobi, Kenya

Email: uonknh_erc@uonbi.ac.ke

3. Dr. Nang'ole Wanjala / Dr. Mark Awori

Department of Surgery

School of Medicine,

University of Nairobi

Tel:020-2726300

Part 2: Consent certificate

I.....freely give consent of myself /my proxy..... to take part in the research study carried out by Dr Kenneth Mbira Ngunju, the nature of which he has explained to me. I understand that my participation in the study is purely voluntary and that I am free to withdraw this consent at any time. I also understand that withdrawing my consent will not affect the quality of care given to myself/my proxy at the Kenyatta National Hospital.

Signature of participant/Guardian/Next of kin.....

Date.....

I certify that the above consent has been freely given in my presence

Witness Name.....

Witness Signature.....

Date.....

Left thumbprint if participant illiterate (witness to countersign)

Part 3: Statement by the researcher

I confirm that the information relating to this study as contained in the information sheet has been accurately read to the participant. I confirm that I have ensured the understanding of its contents by the participant who understands that:

1. Declining to give consent or otherwise participate in this study will not affect the quality of care given at this institution
2. All information provided by the participant will be kept strictly confidential
3. The conclusions from this study may be used to influence local clinical practice

I further confirm that the participant has been allowed to seek clarification of all aspects of this study and that he/she has freely and willingly given consent. The participant has also been provided with a copy of the Informed consent form.

Name of researcher

Signature.....

Date.....

Kiswahili version

Sehemu ya kwanza: Maelezo

Jina langu ni Dr. Kenneth Mbira Ngunju, mwanafunzi katika Kitivo cha masomo ya Udaktari, Chuo kikuu cha Nairobi. Ninafanya utafiti kuhusu 'kulinganisha dawa aina ya chlorpheniramine na ile ya gabapentin katika kutibu kujikuna baada ya kuchomeka katika wagonjwa katika hospital kuu ya Kenyatta.'

Kujikuna baada ya kuchomeka ni adhari inayowakumba wagonjwa wengi hasa wale ambao majeraha yao yanachukua zaidi ya wiki tatu kupona. Kwa kawaida matibabu ya shida hii ya kujikuna yamekuwa kutumia dawa za aina ya antihistamine kama vile chlorpheniramine ambayo matokeo yake hayajakuwa ya kuridhisha sana.

Kwa hivyo kuna hamu ya kupata dawa ambazo zina tibu vyema zaidi. Dawa kama hii ni kama gabapentin ambayo italinganishwa na chlorpheniramine ili kuona kama ina manufaa zaidi kuliko ile ya chlorpheniramine. Matokeo ya utafiti huu yataweza kubadilisha na kuboresha matibabu ya shida hii ya kujikuna baada ya majeraha ya kuchomeka.

Ningependa kukualika kujumuishwa kwenye utafiti huu. Kujumuishwa kwako ni kwa hiari na unayo haki kujiondoa kwenye utafiti huu wakati wowote. Idhini yako ya kujumuika unaweza kuipa maramoja baada ya kusoma nakala hii ama baada ya muda wa kufikiria. Unao uhuru wa kuuliza maswali yoyote kuhusu utafiti huu kutoka kwangu.

Baada ya kukubali kujumuishwa katika utafiti huu, utapewa nambari kati ya moja(1) na hamsini(50), kisha kulingana na nambari uliopata utawekwa katika kitengo cha kupewa dawa ya chlorpheniramine au kitengo cha kupewa dawa ya gabapentin. Kisha utakuwa ukiulizwa jinsi kujikuna kunavyopungua katika muda wa mwezi mmoja.

Hakuna tofauti yoyote katika hali ya matibabu katika vitengo vyote viwili katika utafiti huu. Unaweza kujitoa katika utafiti huu wakati wowote bila kuadhiri matibabu yako.

Ukikubali kujumuishwa kwenye utafiti maelezo yako binafsi pamoja na maelezo ya ugonjwa wako yatachukuliwa.

Utapatiwa hakikisho ya kwamba maelezo yote utakayotoa yatawekwa siri wala hakuna atakayeona maelezo haya isipokuwa watafiti na watu waliokubaliwa na kamati ya uadilifu

ya Hospitali kuu ya Kenyatta ikishirikiana na Chuo kikuu cha Nairobi. Nambari zitatumiwa badala ya majina ili kukinga maelezo yako.

Maelezo yatachukuliwa kwa njia ya maswali . Kujiondoa kwako hakutaadhiri kiwango cha matibabu utakachopatiwa katika hospitali hii.

Ruhusa ya kufanya utafiti huu umepatiwa kutoka Kamati ya Uadilifu wa Utafiti ya Hospitali kuu ya Kenyatta ikishirikiana na Chuo Kikuu cha Nairobi, kupitia Mwenyekiti wa Idara ya Upasuaji, Kitivo cha Masomo ya Udaktari, Chuo Kikuu cha Nairobi.

Ikiwa unahitaji maelezo zaidi kuhusu utafiti huu, tafadhali wasiliana na wafuatao:

1. Dr Kenneth Mbira

Department of Surgery

School of Medicine

University of Nairobi

SLP: 19676-00202

KNH, Nairobi

Simu :0717710570

2. Katibu

KNH/UON Ethics and Research Committee (ERC)

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Barua pepe: uonknh_erc@uonbi.ac.ke

3. Dr. Nang'ole Wanjala / Dr. Mark Awori

Department of Surgery

School of Medicine,

University of Nairobi

Simu: 020-2726300

Sehemu ya pili: Idhini

Mimi.....nimekubali kwa hiari yangu/hiari ya
mgonjwa niliyemsimamia.....kujumuishwa
kwenye utafiti unaoendeshwa na Dr Kenneth Mbira, baada ya kupewa maelezo kamili na
yeye. Ninaelewa kuwa kujumuika kwangu ni kwa hiari na nina uhuru wa kujiondoa wakati
wowote. Naelewa kwamba kujiondoa kwangu hakutaathiri kwa vyovyote kiwango cha
huduma nitakayopokea katika Hospitali Kuu ya Kenyatta.

Jina la mgonjwa/Msimamizi wa mgonjwa.....

Sahihi.....

..

Tarehe.....

Nimeshuhudia ya kwamba idhini ya mhusika imetolewa kwa hiari yake mwenyewe

Jina la shahidi.....

Sahihi ya shahidi.....

Tarehe.....

**Alama ya kidole gumba cha
kushoto**(mgonjwa asiyejua kuandika – sharti
shahidi kutia sahihi kando)

Sehemu ya tatu: Idhibati ya Mtafiti mkuu

Ninatoa idhibati ya kwamba maelezo kuhusu utafiti huu yametolewa kikamilifu kwa mhusika, na kwamba nimemsaidia kuelewa kwamba:

1. Kutotoa idhini ama kujiondoa kwenye utafiti huu hautaathiri kwa vyovyote kiwango cha matibabu atakayopata katika hospitali hii.
2. Maelezo yote yatakayotolewa yatawekwa siri.
3. Matokeo ya utafiti huu yanaweza kutumiwa katika kuchangia ujuzi wa kubaini ugonjwa unaochunguzwa.

Ninatoa idhibati pia ya kuwa mhusika amekubaliwa kuuliza maswali yoyote kuhusu utafiti huu na kwamba ametoa idhini kwa hiari bila kulazimishwa. Mhusika pia amepewa nakala ya stakabadhi ya idhini.

Jina la mtafiti

Sahihi.....

Tarehe.....



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Ref: KNH-ERC/A/30

2nd February, 2015

Dr. Kenneth Mbira Ngunju
Dept of Surgery
School of Medicine
University of Nairobi

Dear Dr. Kenneth

Research Proposal: Comparative Study of Gabapentin and Chlorpheniramine in the management of post-burn pruritus at Kenyatta National Hospital (653/11/2014)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and approved your above proposal. The approval periods are 2nd February 2015 to 2nd February 2016.

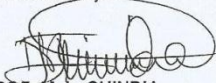
This approval is subject to compliance with the following requirements:

- a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
- b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
- c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
- d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
- e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
- f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
- g) Submission of an *executive summary* report within 90 days upon completion of the study
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website www.erc.uonbi.ac.ke

Protect to discover

Yours sincerely



PROF. M. L. CHINDIA
SECRETARY, KNH/UON-ERC

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