

**THE EFFECT OF BENZYDAMINE HYDROCHLORIDE ON POST
TONSILLECTOMY PAIN IN PAEDIATRIC PATIENTS AT
KENYATTA NATIONAL HOSPITAL (KNH) - A CLINICAL TRIAL**

BY

DR. NDUATI JAMES MWANGI

DEPARTMENT OF ENT- HN SURGERY

**A THESIS FOR DISSERTATION AS PARTIAL FULFILLMENT OF
REQUIREMENTS OF THE UNIVERSITY OF NAIROBI, FOR THE
AWARD OF THE DEGREE OF MASTER OF MEDICINE IN ENT,
HEAD AND NECK SURGERY**

2015

DECLARATION

I declare that this thesis is my original work and has not been presented for the award of a degree in any other university.

Signed

Date

Dr. Nduati James Mwangi

MBCh.B (UoN)

H58/7896/2006

CERTIFICATE OF APPROVAL

This research study was submitted to the Kenyatta National Hospital and University of Nairobi research and ethics committee for approval through the permission of the following supervisors.

Signed

Date

Professor I. M. Macharia, MBCh.B, MMED

Ear Nose and Throat-Head and Neck Surgery

Associate Professor ENT-Head and Neck Surgery

Department of Surgery

University of Nairobi

Signed:

Date

Dr. M. M. Omutsani, MBCh.B, M.MED

ENT-Head and Neck Surgery,

Consultant ENT Surgeon, ENT Department

Kenyatta National Hospital

ACKNOWLEDGMENTS

I would like to thank my supervisors Prof. I. M. Macharia and Dr M. M. Omutsani for their continued assistance, guidance and encouragements during this study. My appreciation also extends to all my teachers at the University of Nairobi and Kenyatta National Hospital for their contributions and constant encouragements.

Special thanks go to all the staff we worked with in the ENT satellite theatre, ward 5C staff, senior and junior colleagues. You all made this possible.

Thanks to the entire ENT/HN fraternity of KNH and beyond for their assistance and constant encouragements. I highly appreciate.

DEDICATION

I dedicate this work to:

God for his mercies and continued blessings.

My parents Mr. Josphat Njau Nduati and Mrs. Esther Njeri Nduati and all my siblings for their support, love, and constant support during all these time.

TABLE OF CONTENTS

DECLARATION	ii
ACKNOWLEDGMENTS	iii
DEDICATION	iv
TABLE OF CONTENTS.....	v
LIST OF TABLES AND FIGURES.....	vii
ACRONYMS AND ABBREVIATIONS	viii
ABSTRACT.....	ix
INTRODUCTION	1
LITERATURE REVIEW	5
RESEARCH QUESTION:.....	7
METHODOLOGY	9
ETHICAL CONSIDERATIONS.....	16
BUDGET	17
RESULTS	18
DISCUSSION.....	25
CONCLUSIONS.....	26
RECOMMENDATIONS	26
REFERENCES	27

APPENDICES	30
APPENDIX IA : GENERAL PATIENT INFORMATION AND CONSENT FORM.....	30
APPENDIX IIA : CONSENT AND ASSENT FORM	33
APPENDIX IB: MAELEZO YA UTAFITI	34
APPENDIX IIB: KIBALI CHA UTAFITI.....	36
APPENDIX III: PRE-OPERATIVE PROFILE.....	37
APPENDIX IV: OPERATIVE DETAILS.....	38
APPENDIX V: POST OPERATIVE PROFILE.....	39
APPENDIX VI: ANAESTHESIOLOGIST/ANAESTHETIST INFORMATION SHEET....	40
APPENDIX VII: APPROVAL LETTER	41

LIST OF TABLES AND FIGURES

TABLES

Table 1: Demographic characteristics.....	18
Table 2: Clinical presentations.....	19
Table 3: Effect on PTP (post tonsillectomy pain).....	23
Table 4: Effect on dietary intake	24

FIGURES

Figure 1: Surgical indication and management	20
Figure 2: Operation time.....	21
Figure 3: Hemoglobin level	21
Figure 4: Effect on PTP (post tonsillectomy pain)	22

ACRONYMS AND ABBREVIATIONS

BHCL	-	Benzydamine Hydrochloride
ENT-HN	-	Ear, Nose and Throat-Head and Neck
GA	-	General Anaesthesia
KEBS	-	Kenya Bureau Of Standards
KNH	-	Kenyatta National Hospital
NSAID	-	Non-Steroidal Anti-inflammatory Drug
PI	-	Principal Investigator
PTP	-	Post Tonsillectomy Pain

ABSTRACT

Background: Tonsillectomy is one of the commonest operations in most ENT centers including Kenyatta National Hospital (KNH). It involves removal of palatine tonsils which can be achieved through several surgical techniques. In KNH blunt dissection method is used in all patients. This leaves a raw tonsillar bed which is a source of post-operative pain which most of the time may be dismissed as trivial although it causes dysphagia, otalgia and inability to speak properly.

Benzydamine Hydrochloride is a locally acting non-steroidal anti-inflammatory drug (NSAID) with local anaesthetic, and analgesic properties for pain relief. It is used for inflammatory conditions of the mouth and throat. Although it is sometimes used during the post-tonsillectomy period, its effectiveness had not been studied in our patient population.

Research question: How effective is Benzydamine hydrochloride in controlling Post tonsillectomy pain (PTP) in paediatric patients?

Objective: The study determined the effectiveness of Benzydamine hydrochloride oral pharyngeal gargle in management of PTP in paediatric patients undergoing tonsillectomy at KNH.

Study methodology: The study was a randomised double blind clinical trial conducted in Kenyatta National Hospital (KNH)ENT-HN department, in Nairobi.106 patients aged between 4 and 12 years who were undergoing tonsillectomy for adenotonsillar hypertrophy or chronic recurrent tonsillitis were recruited via sequential random sampling and placed in any one of the two arms of the study. Informed consent was obtained from the parent/guardian. The perioperative profile forms were used to collect the patients' details and characteristics.

Information on pain control and dietary oral intake was obtained for one week post-operatively and recorded in the visual Analogue Scale and dietary intake forms.

Analysis of Results: Statistical analysis was done using SPSS statistical package version 18 upon export of cleaned and entered data in excel data base. Descriptive analysis was done. The independent Student T test and Chi square test were used to compare data from the two groups for significant differences.

Results: Benzydamine hydrochloride oral pharyngeal gargle was noted to have significant effect on reduction of PTP in all the days assessed. The greatest impact was on day 7 post operatively where 90.6% of patients in the test group had only mild pain compared to 49.1% of the control group (p-Value <0.001) . This effect of pain control impacted on the oral intake significantly from day 4 post operatively where 42 of the test group patients were on soft diet while only 26 of the control group were on it (p-value 0.001). On day 7, 52 of the test patients were on either usual or soft diet while 43 of the control group were on soft diet.(p-value 0.01)

Conclusion: Benzydamine hydrochloride oral pharyngeal gargle was found to be effective in management of PTP in paediatric patients four years and above. This effect on pain control was noted to be of beneficial effect on the patients in terms of early dietary oral intake.

INTRODUCTION

Background

Tonsillectomy is a common procedure in childhood performed by otolaryngologists that usually results in significant morbidity including pain.¹ It is often performed together with adenoidectomy especially in children with obstructive symptoms. The indications for tonsillectomy have remained controversial but one of the most widely accepted is recurrent tonsillitis. This is normally defined as six genuine attacks of tonsillitis per year for two years consecutively.² Other indications include but are not limited to peritonsillar abscess, sleep apnoea and upper airway obstruction especially when there is also adenoid hypertrophy.³

Tonsillectomy and adenoidectomy are relatively safe procedures but the associated morbidity and mortality should never be taken lightly. They include haemorrhage (both intraoperatively and postoperatively), post tonsillectomy pain (PTP), respiratory distress and airway obstruction, changes in speech that are usually temporary, sore throat, otalgia, fever, postoperative vomiting and wound infection.^{4,5} Trauma to the surrounding tissues can result in odynophagia with reduced food and fluid intake that can lead to dehydration. Others like nasopharyngeal stenosis and velopharyngeal insufficiency, atlantoaxial subluxation, meningitis, depression, and death are extremely rare.⁶

Anatomy

The tonsil usually refers to the palatine tonsils laterally located in the oropharynx on either side. They occupy the tonsillar fossa (sinus) between the palatoglossal and palatopharyngeal arches.⁷ The tonsillar floor is covered by fascia, an extension of the pharyngobassillar fascia. This forms the tonsillar capsule which is loosely attached to the muscular wall of the pharynx consisting of the superior constrictor and the styloglossus muscles. The capsule is firmly

attached to the side of the tongue antero-inferiorly in front of the insertion of palatoglossus and palatopharyngeus muscles. There is a loose pseudocapsule formed of loose areolar tissue enabling the tonsil to be easily enucleated during tonsillectomy.⁸

The lateral relation (tonsillar bed) is formed by the superior constrictor muscle. Superiorly is the soft palate while anteriorly and posteriorly are the palatoglossal and palatopharyngeus muscles respectively.⁷ These structures can be injured during dissection and in case of excessive coagulation. These resultant raw areas are exposed in the postoperative period to food and drinks leading to significant postoperative morbidity including pain and delayed healing.

Surgical Procedure

Tonsillectomy can be performed via several methods. A range of surgical techniques continue to be used; these include 'cold' cutting, dissection and snaring, electrocautery, laser tonsil ablation (LTA), harmonic (ultrasonic) scalpel, monopolar radiofrequency ablation, bipolar radiofrequency ablation (coblation), thermal welding and micro-debriding.⁹ At KNH, for this study, cold blunt dissection was used. Hemostasis was achieved by use of pressure packing and cautery.¹ Thus good surgical technique was imperative in reducing complications that would have led to morbidity and mortality.

Morbidity and management

Despite the fact that tonsillectomy is considered a fairly minor procedure, it is often associated with significant postoperative morbidity including pain, bleeding, difficulty in swallowing, ear ache, fever, mouth odour, weight loss and reduced oral intake.¹⁰ Postoperative pain is the most common complication of tonsillectomy. Several validated pain measurement tools have been devised including visual analogue scale (VAS) that was

used in this study.^{11,12} At KNH, these had successfully been used in a study prior to this on effect of antibiotics use on post-operative morbidity following adenotonsillectomy, titled; “Single intra-operative intravenous co-amoxclav versus full post-operative course in prevention of post adenotonsillectomy morbidity at Kenyatta National Hospital, Nairobi, Kenya.¹³ Thus being a frequent complication, various techniques for reducing pain have been developed. These postoperative pain, ranging from mild to severe, may actually last from a few days to two weeks and does affect oral intake, sleeping pattern and ultimately the quality of life.¹⁴ It should be noted that severe pain has been reported in 20% to 50% of children and young adults who have undergone tonsillectomy.¹⁵

Several methods have been tried in management of PTP. Many studies have been conducted to determine the efficacy of steroids, local anesthetics, antibiotics, and oral analgesic preparations in pain control yet there still is no consensus on the optimum approach.¹⁶ The ideal postoperative tonsillectomy medication should provide an adequate reduction in morbidity while minimising side effects, therefore topical agents would seem to be an ideal, safe option. At KNH, the standard post tonsillectomy treatment includes a course of oral antibiotics and analgesics for 5-7 days. It does not usually include a locally acting mouth wash or gargle.

History

The use of mouthwash to control oral bacteria can be traced back almost 5000 years to the Chinese who recommended child's urine use for the control of gingivitis.¹⁷ Modern era of mouthwashes was introduced by the release of Listerine (a mixture of essential oils thymol, menthol, methyl salicylate, and eucalyptol with ethanol as the solvent) as an over-the-counter (OTC) remedy for bad breath in 1914.¹⁸

Mechanism of action

Benzydamine Hydrochloride (3-(1-(benzylindazol-3-yl)oxy) propyl-dimethyl-amine hydrochloride; C₁₉H₂₃N₃O₂·HCl) is an indolic non-steroidal anti-inflammatory drug (NSAID).¹⁹ Its exact mechanism of action is unknown but is thought to act by the following mechanisms. Benzydamine is lipophilic at pH 7.2, has an affinity for membranes and shows membrane stabilizing properties with local anaesthetic effects. Unlike other NSAIDs, Benzydamine does not inhibit the cyclo- nor the lipoxygenase enzyme systems but slightly inhibits Phospholipase A₂ as well as the lysophosphatide-acyltransferase.²⁰ It enhances Macrophage PGE₂ synthesis, and effectively inhibits the production of reactive oxygen species by phagocytes, their degranulation and aggregation.²¹ Its strongest in vitro effect is the inhibition of leukocyte adhesion to vascular endothelium. Thus Benzydamine's anti-inflammatory effect is considered to be by preventing vessel wall damage from activated, adhering and emigrating leukocytes hence being vaso-protective.²⁰

Thus Benzydamine is used topically as a non-steroidal anti-inflammatory drug that has also analgesic, anesthetic, antipyretic, antimicrobial, and anti-inflammatory effects.²² It is used as an adjuvant therapy in reducing pain, hyperemia, and edema as it specifically acts on the local mechanisms of inflammation.

LITERATURE REVIEW

Several studies have been undertaken on the use of topical agents in managing post tonsillectomy pain. Majority of the them show that indeed they are effective though some are equivocal.

Young et al ²³ did a study on Benzydamine Hydrochloride pump spray as a post-operative analgesic in children undergoing tonsillectomy in a double-blind trial in 56 subjects compared to a placebo in 1987. The raw tonsil bed was sprayed and assessment of post-operative pain was done on the soreness of the throat by the child, parent and surgeon; together with the degree of referred earache, the ability of the child to swallow without discomfort, and the macroscopic appearance of the healing tonsillar bed. Results showed that the Benzydamine spray was more effective than placebo in the control of post-operative pain.

The efficacy of Benzydamine Hydrochloride (Difflam) spray in relieving pain post-operatively following tonsillectomy was assessed by Valijan A et al ²⁴ two years later. They had 29 patients (17 years and above) and they were assessed only in the first 24 hours following the procedure and showed equivocal results.

Earlier in 1984 Giacomelli et al ²⁵ had done studies with Benzydamine nebulizers and had positive results on their efficacy in post tonsillectomy patients.

Mahmut Özkırıs et al ²⁶ did a study in 2010 on the effects of post-operative topical chlorhexidine gluconate and Benzydamine Hydrochloride spray (Farhex) on post-operative pain and oral intake in tonsillectomized patients. A total of eighty patients (40 patients in the Farhex group and 40 patients in the control group) were included in the study. They found out that the use of topical Farhex oral spray remarkably reduced post-operative pain in

tonsillectomized patients, especially at 18 hours post-operatively as the mean pain score was significantly lower in the Farhex group compared to the control group ($p < 0.01$).

A study was done in a tertiary care hospital in Pakistan in 2011 by Habib-Ur-Rehman et al²⁷ on the efficacy of Benzydamine Hydrochloride in treatment of post-tonsillectomy patients. 100 patients were included 50 in each arm (study and placebo group) and followed for six weeks. At 1st week the pain relief was almost equal in both groups while at 6th week pain was better controlled in study group. They also noted faster healing in study group using Benzydamine Hydrochloride thus concluding that the use of Benzydamine Hydrochloride (0.15%) reduces the intensity and duration of post-tonsillectomy pain and helps in improving early healing of wound.

In 2004 a single-blind, randomized clinical trial was done comparing Benzydamine Hydrochloride and *Salvia officinalis*(SO), a topically applied herbal preparation frequently used for the same indication; as an adjuvant local treatment to systemic Nonsteroidal Anti-Inflammatory Drug in controlling pain after tonsillectomy, adenoidectomy, or both by Sinisa Lalicevic et al²⁸. They found that Benzydamine, as an adjuvant to an NSAID, was more effective than SO in controlling postoperative pain and infection. The pain-reducing effect of Benzydamine was noted to be of quick onset and persisted for 1 week after surgery. They had enrolled a total of 420 patients that comprised of 217 females and 203 males; of which children were 278 and adults 142.

STUDY JUSTIFICATION

Post tonsillectomy pain though usually brushed aside as trivial, can range from mild to severe and may last a few days to weeks. This happens despite optimal systemic analgesic dosages, as almost all patients still experience local pain, a problem noted also at KNH. This is usually demonstrable by the odynodysphagia especially in the immediate post-operative period. This affects oral intake which eventually lead to complications like dehydration. Several studies had shown that the use of Benzydamine Hydrochloride in addition to the usual systemic analgesics reduces post tonsillectomy pain thus leading to early return to normal diet. At KNH, the standard post tonsillectomy treatment does not include any topical pain agent. It includes antibiotics and standard oral analgesics. There was therefore a need to determine whether addition of Benzydamine Hydrochloride would reduce post-tonsillectomy pain in our patient population as had been found elsewhere.

RESEARCH QUESTION:

How effective is Benzydamine Hydrochloride oral pharyngeal gargle in controlling PTP?

HYPOTHESIS

Null Hypothesis:

There is no difference between Benzydamine Hydrochloride and placebo when used locally as an oral pharyngeal gargle in controlling post tonsillectomy pain.

Alternate Hypothesis:

Benzydamine Hydrochloride is better than placebo when used locally as an oropharyngeal gargle in controlling post tonsillectomy pain.

AIMS AND OBJECTIVES

Broad Objective

To determine the efficacy of Benzydamine Hydrochloride oral pharyngeal gargle in management of PTP in paediatric patients undergoing tonsillectomy at KNH.

Specific Objectives

1. To determine the effect of Benzydamine Hydrochloride oral pharyngeal gargle in post tonsillectomy pain management in paediatric patients.
2. To determine the effect of post tonsillectomy pain control on oral intake with the use of Benzydamine Hydrochloride oral pharyngeal gargle in paediatric patients.

METHODOLOGY

Study Design

The study was a double-blind hospital based randomized clinical trial.

Study area

It was carried out at Kenyatta National Hospital ENT-HN department (ward and theatre).

Study population

It targeted patients aged between four and twelve years who underwent adenotonsillectomy or tonsillectomy during the study period.

Inclusion criteria Exclusion criteria

It included patients between four and twelve years of age who underwent adenotonsillectomy (or tonsillectomy) during the study period and whose parents or guardians consented to the study. Those patients of non-consenting parents/guardians or with any co-morbid conditions like malnutrition, anaemia, diabetes, known allergy to drug or medication that were used during the study were excluded.

Sampling Method

Consecutive sampling of the patients who met the inclusion criteria during the study period was done until the desired number of 106 patients was reached.

Sample size determination.

Sample size necessary to detect statistically significant difference between test and control groups in reduction of morbidity with Power of 90% and 5% significant level was calculated using the formula by Lwanga et al ²⁹ as follows;

Detected difference $d = 0.25$ (detected difference size)

Proportions of two groups $\pi_1 = 0.10$ and $\pi_2 = 0.35$

Power=90% which implies $\beta = 0.90$ and therefore $Z_\beta = 1.282$

Significance level $\alpha = 0.05$ implying $Z_\alpha = 1.96$

Therefore, the Sample Size under individual randomization (equal groups)

$$n_t = 2\sigma^2 \left[\frac{(Z_\alpha + Z_\beta)^2}{d^2} \right]$$

Where $\sigma^2 \approx \frac{1}{2} [\pi_1(1-\pi_1) + \pi_2(1-\pi_2)]$

Therefore $\sigma^2 = \frac{1}{2} [(0.10 \times 0.90) + (0.35 \times 0.65)] = 0.15875$

therefore the sample size under individual randomization (per arm) was

$$n_t = 2 \times 0.15875 \left[\frac{(1.282 + 1.96)^2}{0.25^2} \right] = 53.39$$

The total sample size for the study was 106. Each arm had 53 patients.

Procedure

Screening of the patients included in the study was done in ward 5C by the PI. Gurgling dress rehearsal were done and demonstrations done in the ward by the PI and the ward nurses using clean water. The patients who met the inclusion criteria and beat the exclusion criteria were consecutively recruited into the study and were given research numbers 1-106 .The PI reviewed and examined the patients and filled their bio data /details in the preoperative profile sheet. (Appendix 3).The parents /guardians were then introduced to the visual analogue scale that was used to record the pain levels at these point by the PI. Preoperative review of the patients was done by both the surgeon (PI) and the anaesthetist scheduled to perform the operation, with starving of the patients six hours prior to surgery.

The patients were taken to the operating room the following day. Efforts to make GA induction, maintenance and reversal similar in all the recruited patients, with same standard intraoperative analgesia were done. This included fentanyl -2micogrammes/kg, tramadol-1mg/kg body weight, and paracetamol -10mg/kg body weight (125mg, 250mg, 500mg suppositories). Antibiotics (IV co-amoxclav,25mg/kg body weight) and dexamethasone (0.2mg/kg body weight) were given at induction.

Tonsillectomy was done by blunt dissection while adenoidectomy by sharp curettage (for those undergoing adenotonsillectomy). Pressure packing and monopolar diathermy were used to achieve haemostasis. Intraoperative details were entered appropriately in the operative detail forms (Appendix 4).

Patients post-operatively on reversal were taken to the ward. Similar medications were prescribed (antibiotics -oral co-amoxiclav at 25mg/kg; analgesics –both paracetamol-10mg/kg body weight and ibuprofen-20mg/kg body weight) post operatively from day 0.

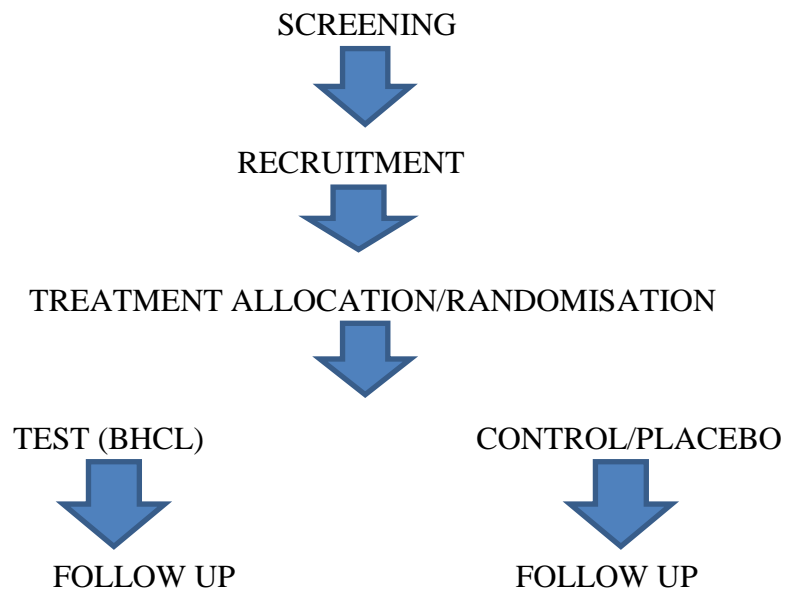
Allocation to any one of the two arms (test or control) was done during issuance of the medication from KNH 5th floor pharmacy. This was done using coded numbers that had previously been securely computer generated by the statistician and delivered by email to the pharmacist in charge of KNH 5th floor pharmacy. The pharmacist was alerted of the recruited study patients through a treatment sheet prescription of the study material by the PI. The allocated coded number was indicated on the T-sheet which was used at the end of the study to reveal the code and thus which arm of the study each patient was in.

Patients started the mouth rinses (test and control) on the evening of the operation after being fully awake and thereafter three times (15mls each time for at least thirty seconds) in a day; prior to taking their meals. This was done under supervision from their parents/ guardians/ ward nurse.

The test and control medications were availed in similar containers. No commercial labels were put on the containers. Each patient received two bottles of each for one week use. They gurgled about 15mls each time, three times a day. The patients (parents/guardians) and the researcher were blinded to the medication given to the patient. The placebo used as control consisted of distilled water with added food colouring (approved by KEBS) similar in colour to the the test medication. Its safety and quality was confirmed by the KEBS approval document. This was prepared by the pharmacist.

Majority of the patients were discharged on day 1 postoperatively. Those noted to be in excessive pain were retained for another day. Whenever possible the principal investigator reviewed the patients on Day 1, 4 and 7 post operatively and recorded the findings in the data collection sheets in terms of the pain experienced, and the status of oral dietary intake. Otherwise cell phone contacts of all the parents/guardians were obtained and these facilitated information collection via phone interviews and consultations.

FLOW CHART



Outcomes Measures

Comparison between the two groups was done using the information gathered from the parents/guardians that was recorded regarding the severity of pain and level of oral dietary intake.

1.The visual analogue scale (appendix V) was used to record estimated pain level

No pain.

Very severe pain.

1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	----

on a scale of 0-10. The parents or guardians estimated the amount of pain they thought their children (patients) were experiencing on day 1, 4,7 post operatively.

2. Dietary oral intake was assessed by the consistency of the diet taken (tolerated) by the patient on day 0,1,4 &7 postoperatively. The consistency included liquids, soft diet, or their usual diet.

Quality Control

The proforma forms were pretested before commencement of data collection and appropriate modifications made. The PI did all the operations for consistency. The patient's history, physical examination and assessment of pain and return to normal diet was mainly done by the principal investigator to maintain consistency and avoid inter-observer errors especially for day 4 and 7.

Data Entry, Analysis, Presentation

Data was collected using the pretested structured data collection sheet. The collected data was then cleaned, checked for any inconsistencies and entered into Microsoft Excel data base. Both continuous/numerical and categorical data was collected. These were then exported to SPSS Statistical Package version 18 for statistical analysis. Descriptive statistics was done to determine mean, median, frequencies and proportions of the various variables. Comparison of continuous/numerical data was done using the independent t-test while comparison of categorical data was done using the Chi-square test. Comparison of grades of pain in control and study groups at 1st, 4th and 7th post-operative days was done using Chi-square test. Comparison of the duration of time (number of days) to normal diet after surgery in control and study groups was done using the independent t-test. An alpha level of 0.05 was used for significance test where applicable. The results are presented in form of tables, graphs, and figures together with their descriptions.

Study Limitations

1. It was difficult getting the exact taste between test and control.
2. There was the possibility of unreported self-medications(use of alternative medications) at home.
3. There were limited variations in the way different parents/guardians estimated the pain level experienced by their children.

Study Period

The study was carried-out in September and October 2014 upon approval in August.

MATERIALS AND EQUIPMENT

Gloves.

Face masks.

Tongue depressors.

Head light.

Benzydamine Hydrochloride preparation.

Distilled water.

Food colouring approved by KEBS (same colour as the BHCL preparation).

Similar containers for medication and the placebo. (Similar packaging).

15ml cups/containers (container tops).

ETHICAL CONSIDERATIONS

1. The study was carried out after approval by The Ethics and Research Committee of Kenyatta National Hospital and University of Nairobi.
2. Informed written consent was given by the parent or guardian of the patients recruited into the study. Assent forms were signed by the children 8 years and above.
3. Parents/ guardians did not incur any extra financial costs and their confidentiality was maintained at all times.
4. Participants had the right to withdraw from the study at any time without any penalty.
5. No mismanagement resulted from parents or guardian/patient declining to consent/assent to the study. Participation was purely voluntary.
6. There was no monetary gain by the primary investigator from the study.
7. Results will be published for the benefit of other health practitioners and the medical fraternity at large.

BUDGET

CONSIDERATION	UNIT	QUANTIY	UNIT COST(Ksh)	TOTAL COST(Ksh)
Benzydamine HCL		110	800	88,000/=
Food colouring/containers		2/212	70	15,000/=
Pharmacist				20,000/=
Biostatician				25,000/=
KNH/UoN-ERC charges				2,000/=
Printing paper/stationery		25	400	10,000/=
Printing charges				10,000/=
Phone credit charges				5,000/=
Contingency(Other)				10,000/=
Total				185,000/=

RESULTS

In this study, 106 patients were recruited and operated on during the study period. The test and control group each had 53 patients. The demographic characteristics and distribution in clinical presentation are as shown in the table below.

Demographic characteristics:

Table 1: Demographic characteristics of paediatric patients randomized to Benzydamine hydrochloride and control treatment for management of post tonsillectomy pain:

	Treatment N = 53	Control N = 53	P value
Sex			
Male	31(58.5%)	29(54.7%)	0.695†
Female	22(41.5%)	24(45.3%)	
Mean age in years (SD)	6.1 (1.6)	5.7 (1.8)	0.269‡
Mean weight in Kg (SD)	21.8 (6.4)	20.2 (6.3)	0.21‡
Residence			
Within Nairobi County	45(84.9%)	43(81.1%)	0.605†
Outside Nairobi County	8(15.1%)	10 (18.9%)	

† Chi square test; ‡ t-test

- The sex distribution among the treatment and the control groups were not statistically significant(p=0.695)
- Mean age in years in the 2 groups was comparable.(p=0.269)
- Mean weight in Kilograms between the two groups was comparable (p=0.21)
- Most of the patients in either the group were from Nairobi County.

Clinical presentation:

In terms of the clinical presentation the main complaints among majority of the patients were snoring, mouth breathing, nasal blockage, and recurrent sore throats. The duration of these symptoms was also recorded accordingly. On examination they were noted to have tonsillar hypertrophy that was graded according to their size. (Grade 1-4). The distribution of these characteristics among the test and control group was as shown in the following table.

Table 2: Clinical presentation of patients randomized to Benzydamine hydrochloride and control treatment for management of post tonsillectomy pain:

	Treatment N = 53	Control N = 53	P value
Duration of snoring (in months)			
< 36	19 (35.8%)	21 (39.6%)	0.897
36-47	18 (34%)	16 (30.2%)	
48 and above	16 (30.2%)	16 (30.2%)	

Duration of mouth breathing (in months)			
< 36	24 (48.3%)	21 (39.6%)	0.766
36-47	17 (32.1%)	17 (32.1%)	
48 and above	12 (22.6%)	15 (28.3%)	
Duration of nasal blockage (in months)			
< 36	26 (49.1%)	21 (39.6%)	0.541
36-47	17 (32.1%)	18 (34%)	
48 and above	10 (18.9%)	14 (26.4%)	
Duration of recurrent sore throat (in months)			
< 36	16 (30.2%)	20 (37.7%)	0.112
36-47	15 (28.3%)	21 (39.6%)	
48 and above	22 (41.5%)	12 (22.6%)	
Tonsil grade			
2	6 (11.3%)	3 (5.7%)	0.130
3	19 (35.8%)	29 (54.7%)	
4	28 (52.8%)	21 (39.6%)	

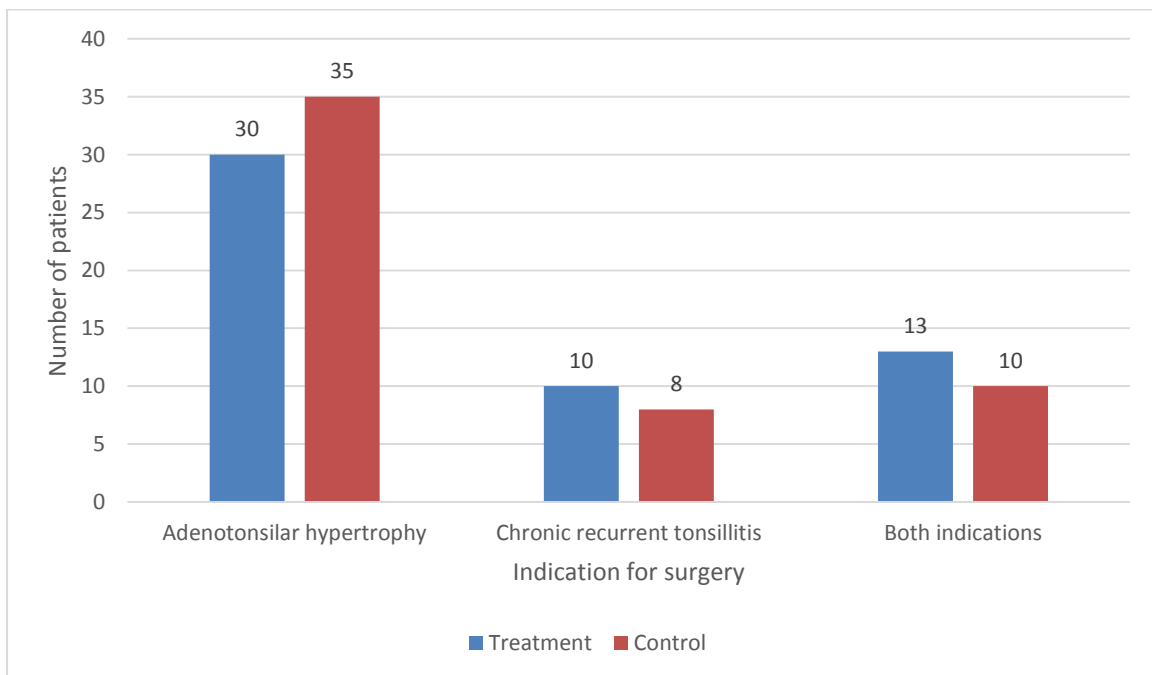
† Chi square test;

- The duration of symptomatology in either of the two groups was not statistically significant.
- The distribution of these characteristics in each of the study group was comparable.

Surgical indication and management

The indications for surgery included adenotonsillar hypertrophy, chronic recurrent tonsillitis or both. Among the test group, the patients with above indications were 30, 10 and 13 respectively. In the control group they were 35, 8, and 10 respectively. The operations done were either adenotonsillectomy or tonsillectomy. 43(81.1%) patients in the test group underwent adenotonsillectomy and 10(18.9%) underwent tonsillectomy. In the control group those done the former operations were 45(84.9%) and the later were 8(15.1%). This is shown in the graph below:

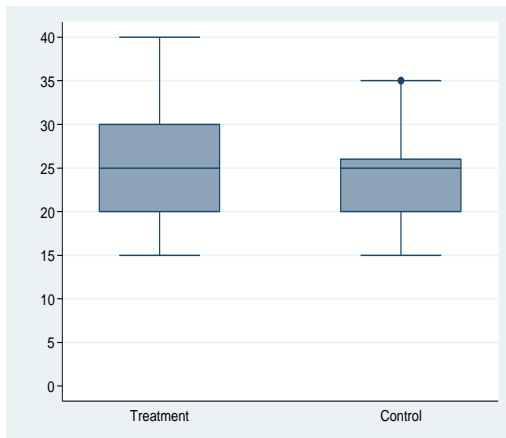
Figure 1: Surgical procedure adenotonsillectomy 43 (81.1%) versus 45 (84.9%), p = 0.605; the remaining patients underwent tonsillectomy:



- The number of patients done either adenotonsillectomy or tonsillectomy in either arm of the study was not statistically significant.

Figure 2: Operation time

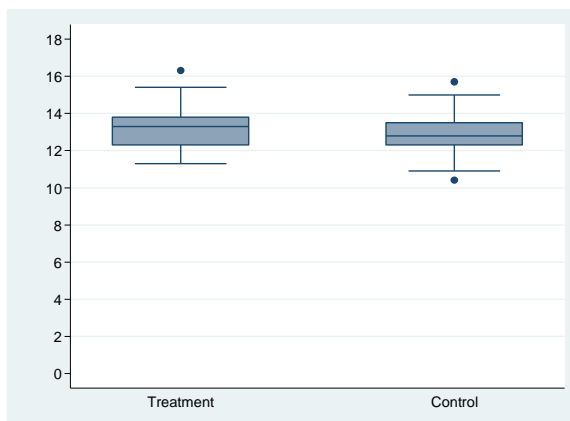
For the time taken to do the operations, the range was between 15 and 40 minutes for all the cases. The diagram below represents the comparison between the two groups.



The median time for the operations done was 25 minutes in each group. The operation times are comparable in the two groups.

Figure 3: Hemoglobin level

The hemoglobin levels of the patients in both groups were also compared as shown here below:

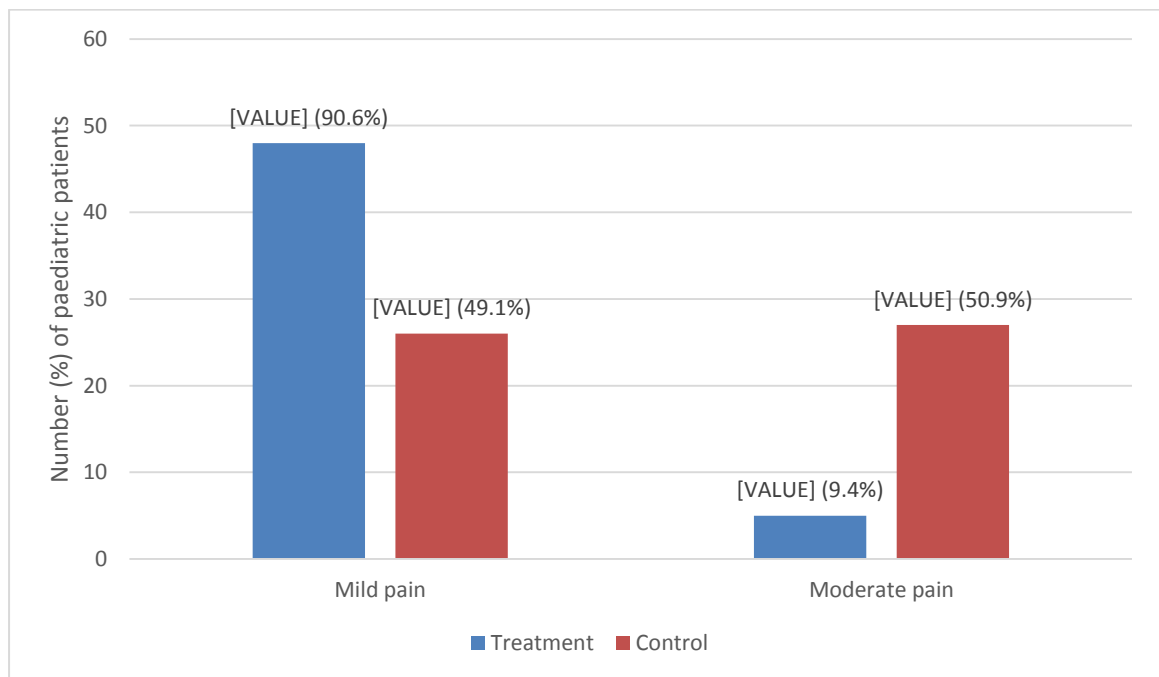


- The median hemoglobin levels in the two arms are comparable with majority being around the 13.0g/dl level.

Effect on PTP (post tonsillectomy pain):

The effect that Benzydamine hydrochloride had on post tonsillectomy in terms of the pain levels as recorded in the VAS (Visual Analogue Scale) on day 1, 4 and 7 Post operatively; the greatest effect was noted on day 7.

Figure 4: Effect of Benzydamine hydrochloride in post tonsillectomy pain management on day 7.



Benzydamine treatment was associated with a statistically significant reduction in pain on day 7 post operation. In both groups patients reported both mild or moderate pain and no severe or very severe pain. Patients in the treatment group were more likely to report mild pain (48, 90.6%) compared to the patients in the control group (26, 49.1%), p value < 0.001.

The effect observed on day 1 and 4 is shown below

Table 3: Effect of Benzydamine hydrochloride in post tonsillectomy pain management on day 1 and day 4.

	Treatment N = 53	Control N = 53	P value
Pain severity on day 1			
Moderate	7 (13.2%)	2 (3.8%)	0.032
Severe	42 (79.2%)	39 (73.6%)	
Very severe	4 (7.6%)	12 (22.6%)	
Pain severity on day 4			
Mild	34 (64.1%)	6 (11.3%)	<0.001
Moderate	17 (32.1%)	42 (79.2%)	
Severe	2 (3.8%)	5 (9.4%)	

On day 1, no one was in mild pain in either group. Majority of the patients in either arm were in severe pain. But the difference is still significant.

On day 4, there was a statistically significant difference in severity of pain experienced by the patients with the majority in control group being in mild or moderate (P value<0.001). No one had very severe pain.

Effect on dietary intake:

In terms of dietary intake the greatest impact of the Benzydamine hydrochloride PTP control was noted on day 4 and 7 postoperatively as shown below:

Table 4: Effect of Benzydamine hydrochloride PTP control on dietary intake day 4 and day 7.

	Treatment N = 53	Control N = 53	P value
Day 4 diet			
Liquid	11 (20.7%)	27 (50.9%)	0.001
Soft diet	42 (79.3%)	26 (49.1%)	
Day 7 diet			
Liquid	1 (1.9%)	6 (11.3%)	<0.001
Soft diet	14 (26.4%)	43 (81.1%)	
Usual diet	38 (71.7%)	4 (7.6%)	

On day one all patients were on liquid diet except 2 who happened to be in the test group.

On day 4, majority (42) of the test group were on soft diet with only about half (26) of the control on soft diet. (p value=0.001)

On day 7, nearly all (52) in test group were on either soft or usual diet compared those in control (43) who were still on soft diet. (p value= <0.001).

DISCUSSION

A total of 106 paediatric patients were recruited into the study, each arm having 53 patients. The test group had 31 males and 22 females while the control group had 29 males and 24 females. This shows they were evenly distributed among the groups with p-value of 0.695. In terms of age the mean ages were 6.1 years and 5.7 years respectively. This was not statistically significant (p-value 0.269). The mean weight was 21.8 Kgs and 20.2 Kgs with p-value of 0.21. Majority of the patients were from Nairobi County (45 Vs 13) with a p-value of 0.605. It is therefore clear that these demographic characteristics did not contribute any bias towards the results.

The clinical complaints and findings the patients presented with mostly included snoring, mouth breathing, nasal blockage, recurrent sore throats and tonsillar hypertrophy. In terms of duration of these signs and symptoms the range from 12 to 72 months. When these characteristics and their duration were subjected to statistical analysis, no statistically significant difference was noted between the test and control groups. Thus no bias could have amounted from these.

Indications for surgery were either adenotonsillar hypertrophy, chronic recurrent tonsillitis or a combination of the two. In the test group these comprised of 30, 10 and 13 patients respectively while in the control they were 35, 8, and 10 respectively. In terms of surgeries done adenotonsillectomies were 43(81.1%) and 45(84.9%) in each group respectively and the rest were tonsillectomies. These were well distributed among the two groups of the study.

The median hemoglobin level of the patients in either group was 13.0g/dl. Other levels were distributed evenly around this point. In terms of the time taken to do the operation the median time was equal in both groups. Hence these two factors would not have had a significant effect on the final results.

A significant outcome of this study was the effect Benzylamine hydrochloride oral pharyngeal gargle had on post-tonsillectomy pain especially on day 7 postoperatively. It was associated with a statistically significant reduction in pain. In both groups patients reported both mild or moderate pain and no severe or very severe pain. Patients in the treatment group were more likely to report mild pain-48(90.6%) compared to the patients in the control group-26 (49.1%), p value < 0.001. On day 1, no one was in mild pain in either group. Majority of the patients in either arm were in severe pain (42 vs. 39). But when this result was statistically analysed the difference was noted to be significant (p-value 0.032). Thus it still has an effect on day 1. This is comparable to a study done in 2010 by Mahmut Özkırıs et al²⁶ where they showed remarkable pain reduction especially at 18 hours postoperatively. A total of 80 patients were involved.

On day 4, there was a statistically significant difference in severity of pain experienced by the patients with the majority in control group being in mild or moderate pain.(p-value 0.001) No one had very severe pain.

These results are comparable to the results of a study done by Sinisa Lalicevic et al²⁸ in 2004 on Benzydamine hydrochloride versus a herbal preparation in controlling post-tonsillectomy pain. Its pain-reducing effect was of quick onset and persisted for 1 week after surgery. In this study, 278 of the 420 patients involved were paediatric patients.

A similar study was done in 2011 by Habib-Ur-Rehman et al²⁷ in a group of 100 patients (study and placebo group) and were followed for six weeks. They noted almost equal pain relief in both groups at 1st week though it was better controlled for the test group at 6 weeks. Thus though the number recruited was almost equal, the follow up was longer.

In terms of oral dietary intake, the effect of post tonsillectomy pain control by Benzydamine hydrochloride was noted to have a positive impact at day 4 and day 7. At day 4, 42(79.3%) patients in the test group were on soft diet compared to 26(49.1%) in the control (p-value of 0.001). On day 7, 38 patients in test group were on usual diet with 14 on soft diet compared to 43 in the control who were on soft diet (p -value of < 0.001). No study was found which showed the effect of this post-tonsillectomy pain control on dietary intact.

Conclusions

Benzydamine hydrochloride oral pharyngeal gargle was found to be effective in management of PTP in paediatric patients especially most significantly on day 7 postoperatively. This effect was also noted on day 4 and on day 1 postoperatively. The effect of PTP control by using Benzydamine hydrochloride oral pharyngeal gargle on oral intake does not have an impact on day one. Its positive effects are seen on day 4 and day 7 as in improves on early oral intake post tonsillectomy.

Recommendations

Paediatric patients four years and above should be put on Benzydamine hydrochloride oral pharyngeal mouth gargle post tonsillectomy or adenotonsillectomy for at least one week.

REFERENCES

1. Mutune M.H. The effect of Amoxicillin on morbidity after paediatric adenotonsillectomy at Kenyatta National Hospital, Nairobi, Kenya. M. Med ENT H&N Surgery thesis. University of Nairobi. 2004: 5-45.
2. Alan G.K. Scott-Brown's Otolaryngology, sixth edition. Butterworth-Heinemann International Editions. 1997: pg 6/18/8.
3. Charles W.G and Scott E.H. Tonsil and Adenoids. Paediatrics in review. 2000; volume 3;21:75-78.
4. Wiatrak B J, Myer CM III, Andrews TM. Complications of adenotonsillectomy children under 3 years of age. Am J Otolaryngol. 1991;12:170-172.
5. Handler SD, Miller L, Richmond KH, Baranak CC. Post-tonsillectomy hemorrhage: Incidence, prevention and management. Laryngoscope. 1986;96:1243-1247.
6. Singer JI. Evaluation of the patient with neck complications following tonsillectomy or adenoidectomy. Pediatr Emerg Care. 1992;8:276-279.
7. Chummy S N. Lasts Anatomy : Regional and Applied, Churchill Livingstone Medical Division Copyright 2006 11th edition; pgs 401-402
8. Paradise JL . Tonsillectomy and Adenoidectomy . Pediatric otolaryngology(1983) : 122–6.
9. Koempel JA, Solares CA, Koltai PJ. The evolution of tonsil surgery and rethinking the surgical approach to obstructive sleep-disordered breathing in children. J Laryngol Otol 120 (12): 993–1000.
10. Mann EA, Blair EA, Levy AJ, Chang A. Effect of topical antibiotic therapy on recovery after tonsillectomy in adults. Otolaryngology - Head and Neck Surgery 1999;121(3):277–82.
11. McGrath PJ, Unruh AM. Measurement assessment of paediatric pain. In: Wall ED, Melzack R, editors. Textbook of pain. 4th ed.. Edinburgh: Churchill Livingstone; 1999. p. 371–94.
12. Kaygusuz I, Susaman N. The effects of dexamethasone, bupivacaine and topical lidocaine spray on pain after tonsillectomy. International Journal of Pediatric Otorhinolaryngology 2003;67(7):737–42.
13. Single intra-operative intravenous co-amoxclav versus full post-operative course in prevention of post adenotonsillectomy morbidity at Kenyatta National Hospital, Nairobi, Kenya. M. Med ENT H&N Surgery thesis. University of Nairobi. 2008: 6-32.
14. Chacra ZA, Manoukian JJ, Al-Qahtani K, Al-Eisa M, Balys R, Hagr A, et al. Hydrogen peroxide mouth rinse: an analgesic post-tonsillectomy. Journal of Otolaryngology 2005;34(3):178–82.

15. Romsing J, Ostergaard D, Drozdiewicz D, Schultz P, Ravn G. Diclofenac or acetaminophen for analgesia in paediatric tonsillectomy outpatients. *Acta Anaesthesiologica Scandinavica* 2000;44(3):291-5.
16. Kountakis SE. Effectiveness of perioperative bupivacaine infiltration in tonsillectomy patients. *Am J Otolaryngol.* 2002;23:76-80.
17. Schubert MM, Newton RE. The use of benzydamine HCl for the management of cancer therapy-induced mucositis: preliminary report of a multicentre study. *Int J Tissue React.* 1987; 9:99-103.
18. Madan Kumar PD, Sequeira PS, Shenoy K, Shetty J. The effect of three mouthwashes on radiation-induced oral mucositis in patients with head and neck malignancies: A randomized control trial. *J Can Res Ther* 2008; 4:3-8.
19. Müller-Peddinghaus R. New pharmacologic and biochemical findings on the mechanism of action of the non-steroidal antiphlogistic, benzydamine. A synopsis. *Arzneimittelforschung.* 1987 May;37(5A):635-45
20. Segre G, Hammarström S. Aspects of the mechanisms of action of benzydamine. *Int J Tiss React.* 1985;7:187-93.
21. Baggiolini M, Mauderli P, Catanese B. Effect of benzydamine on exocytosis and respiratory burst in human neutrophils and mononuclear phagocytes. *Agents Actions.* 1985; 16:346-52.
22. Turnbull RS. Benzydamine hydrochloride (Tantum) in the management of oral inflammatory conditions. *J Can Dent Assoc* 1995;61:127-34
23. Young JR. A comparative study of benzydamine hydrochloride ('Difflam' pump spray) and placebo as analgesics following tonsillectomy. *International Journal of Tissue Reactions* 1987;9(2):131-3.
24. Valijan A. Pain relief after tonsillectomy. Effect of benzydamine hydrochloride spray on postoperative pain relief after tonsillectomy. *Anaesthesia* 1989;44(12):990-1.
25. Giacomelli F, Pastore F, Zangari M, Marchiori C, Soranzo GP. Tonsillectomies: postoperative therapy using 'Tantum Verde' spray *Gazzetta Medica Italiana* 1984;143(7-8):639-44.
26. Mahmut Özkırıs , Cemil Mutlu The effects of post-operative topical chlorhexidine gluconate and benzydamine HCL spray (farhex) on post-operative pain and oral intake in tonsillectomied patients. *Journals of Medicine and Medical Sciences* October 2011 Vol. 2(10) pp. 1143-1146 .
27. Habib-Ur-Rehman, Fazal-I-Wahid, Muhammad Javaid, Adil Khan, Iftikhar Ahmad Khan. Efficacy of benzydamine hydrochloride in treatment of post-tonsillectomy patients in

a tertiary care hospital. Gujarat Journal of Otorhinolaryngology and head and neck surgery 2012 ; 9(1):8-10.

28.Sinica L, Ivan D .Comparison of Benzydamine Hydrochloride and Salvia Officinalisas an adjuvant local treatment to systemic nonsteroidal anti-inflammatory drug in controlling pain after tonsillectomy, adenoidectomy, or both: An open-label, single-blind, Randomized Clinical Trial. Current therapeutic research 2004; 65(4):360-372.

29.Lwanga SK, Lemeshow S. Sample size determination in health studies - A practical manual. 1st ed. Geneva: World Health Organization; 1991.

APPENDICES

APPENDIX IA : GENERAL PATIENT INFORMATION AND CONSENT FORM

Title: The effect of Benzydamine Hydrochloride on Post Tonsillectomy Pain in paediatric patients at Kenyatta National Hospital (KNH)- A clinical trial.

Principal Investigator: Dr Nduati J.Mwangi Resident ENT Head and Neck Surgery, University of Nairobi. Contact: 0722459553; email: jmknduati@yahoo.com P.O.Box 19697-0202, KNH

KNH/ UON-ERC: Prof. CHINDIA Email: uonknh_erc@uonbi.ac.ke

Introduction

My name is Dr Nduati J. Mwangi. I am the principal investigator in this study and a post graduate student at the university of Nairobi, ENT,H&N department under department of Surgery. Participation in this study is voluntary. We aim to find out the effect of the drug Benzydamine Hydrochloride on postoperative pain management and oral intake compared to those who don't use it. Your child will get either the medicine being studied or a control medication .Both the medications will be similar in appearance and neither you or the researcher will know who will get which medication. We will only know after the study is finished as the records will be kept by the hospital pharmacist.

How to participate

1. We will ask you questions seeking to know the complaints the child has to warrant the surgery planned and what surgery the child will be undergoing. The findings and the child's details will be recorded. The study has two groups(the test and control group) and the child will be put in any randomly. The child will be required to

rinse/gurgle the medication from the first day up to one week postoperatively three times a day just before meals. You will be reporting on the pain levels the child experience(s) using a scale of 1-10 which you will be shown how to use. If no complications arise, the child will be discharged on the day following the surgery and will be seen in the ENT clinic on day 4 and day 7 following the operation. The findings will be recorded.

2. Similar procedure will be carried out on all the participants recruited.
3. How does your participation affect you / or your child ?

Participation or lack of it in this study will not in any way adversely affect you/ your child in any way in terms of the care you receive because:

1. You/the child will receive the same treatment as others even without participating in the study only that the child won't use the medications being studied.
2. The medication being studied is not a new medicine and has been used without any adverse effects for many years.
3. All information given by you will be accorded confidential treatment.
4. You are free to withdraw your child from the study whenever you wish.

Are there any hidden dangers?

1. There are no hidden dangers
2. Refusing to consent will not affect the management and handling of you / your child ..

How does your participation help us?

1. The findings in the study will help us confirm the effectiveness of the medication being investigated on management of post tonsillectomy pain.

2. We shall share the findings of the study with other professional colleagues elsewhere. Thus the findings can be published in scientific journals or be presented at scientific conferences without divulging any specific patient information.
3. You are free to discuss this with family members and we shall be ready to answer any questions raised.
4. If you have any concern during the study, you can contact the above named.

KNH/UoN Ethics Research Committee is the body that is mandated with the authority of reviewing all the research proposals for any research to be undertaken in the institutions (Kenyatta National hospital and University of Nairobi). They ensure that they are up to international standards and safe to all those candidates that will be enrolled to participate after which they give approval. The contacts of the Committee are the following:

KNH/UON-ERC,
P.O. Box 20723 Code 00202
NAIROBI
[Tel:726300-9](tel:726300-9)
Fax:725272
Telegrams:MEDSUP,Nairobi

KNH/UON-ERC
Email:uonknh_erc@uonbi.ac.ke
Website:www.uonbi.ac.ke
Link:www.uonbi.ac.ke/activities/KNHUoN

3 If you understand everything said and have accepted it then please fill in and sign the consent form provided. If your child is between ages 8years and 17years, he or she will sign an assent form.

APPENDIX IIA : CONSENT FORM

Study number.....

I Mr/Mrs./Ms.....the parent/guardian of

master/miss..... agree to enroll him/her into

the study as explained to me by **Dr. Nduati J. Mwangi**. My signature is confirmation that I have understood the nature of the study and that whatever information that I give will remain confidential. I also confirm that no monetary or material gains have been promised or given to me for participating in the study.

Signed.....(Parent/guardian) Relationship.....

Date:.....

ASSENT FORM

I voluntarily agree to participate in the research having had the information read to me and understood the nature of the study and that whatever information I give will remain confidential.

Sign your name here (Minor)..... Date

Signature of principal investigator..... Date:.....

APPENDIX IB: MAELEZO YA UTAFITI

KIELELEZO KWA MZAZI WA MGONJWA JINSI YA KUSHIRIKI.

Jina langu ni Daktari Nduati J. Mwangi. Mimi ndiye naongoza utafiti huyu ni mimi ni mwanafunzi katika chuo kikuu cha Nairobi utengo wa upasuaji haswa kitengo wa ENT-HN ;yaani kitengo cha upasuaji wa masikio, mapua, koo, kichwa na shingo. Kushiriki katika utafiti huu ni kwa hiari yako. Sisi tuna lengo la kujua ufanisi wa dawa ‘Benzydamine Hydrochloride’ kwa kuzuia maumivu na hivyo kuwezesha ulaji kwa mdomo baada ya upasuaji ikilinganishwa na wale ambao hawatumii dawa hii. Mtoto wako atapata dawa hii yenye tunafanyia utafiti ama yenye haina dawa hii ndani yake. Dawa zitakuwa rangi sawa na ndani ya chupa sawa. Kati ya Mtafiti na wewe hakuna atakayejua chupa gani iko na dawa gani ndani yake. Hii itajulikana baada ya utafiti kumalizika. Daktari mwingine Mfamasia ndiye ataweka rekodi na kuonyeshana baada ya utafiti kumalizika.

Jinsi ya kushiriki.

1. Tutauliza wewe maswali ili tujue malalamiko ya mtoto wako yanayomfanya apasuliwe.Hii maelezo yote yatarekodiwa. Utafiti utakuwa na makundi mawili (kundi la kujaribiwa na la kudhibiti) na mtoto anaweza ingia kwa kundi lolote lile. Mtoto atastahili kutumia dawa kutoka siku ya kwanza mpaka wiki moja baada ya upasuaji mara tatu kwa siku kabla ya mlo. Utakuwa unarekodi kiwango cha maumivu mtoto atakuwa anahisi kwa kutumia kiwango cha 1-10 ambacho utakuwa umeonyeshwa jinsi ya kutumia . Kama hakutakuwa na matatizo yeyote, mtoto ataruhusiwa kwenda nyumbani siku yenye itakayofuata ile ya upasuaji. Ataonekana katika kliniki ya ENT siku ya 4 na ya 7 baada ya operesheni. Matokeo yatarekodiwa.
- 2.Utaratibu sawa utafuatwa kwa kila ya mshiriki

Ushiriki wangu na mtoto wangu utatuathiri vipi ?

Hakuna athari zozote kwako au kwa mtoto kwa sababu:

1. Mtapokea matibabu sawa bila kushiriki katika utafiti ila tu mtoto hatatumia dawa zenye zafanyiwa utafiti.
2. Dawa inayofanyiwa utafiti sio mpya na imetumika kwa miaka mingi bila madhara yoyote kuripotiwa..
3. Habari yote utakayopatia itakuwa siri.
4. Uko na uhuru wa kuondoa mtoto wako kutoka kwa utafiti huu wakati wowote utakapo .

Je, kuna hatari yoyote iliyojificha?

1. Hakuna hatari yoyote iliyojificha.
2. Kukataa kushiriki kwa utafiti huu hakuta athiri matibabu yenye mtoto wako atakayopokea.

Kushiriki kwako na mtoto wako kutatusaidia aje?

1. Matokeo ya utafiti huu yatusaidia sisi kuthibitisha ufanisi wa dawa hii katika kuzuia maumivu baada ya upasuaji huu.
2. Tutagawana matokeo ya utafiti na madaktari na waugizi wenzetu wote popote walipo na matokeo kuchapishwa katika majarida ya kisayansi.
3. Uko na uhuru wa kujadili suala hili na familia yako na tuko tayari kujibu maswali yoyote yale yatakayojili.

Kama kuna suala (au swari) lolote ungetaka kuelezewa wakati wa utafiti , unaweza kuwasiliana na yeyote kati ya hawa kwa hizi namba:

1 .Dr. Nduati J.M. Simu: 0722-459 553,Saduku la posta 19697-0202 KNH, Barua pepe, jmknduati@yahoo.com

2 .Katibu wa Kamati ya utafiti, KNH/UoN-ERC; Prof Chindia Barua pepe, uonknh_erc.uonbi.ac.ke

Kamati ya utafiti, , KNH/UoN-ERC ndiyo ina wajibu wa kuhakikisha kwaba utafiti wowote unaofanyika katika hospitali kuu ya Kenyatta na chuo kikuu cha Nairobi uko wa hali ya juu ka mahali pengine popote duniani na kwaba hautadhuru yeyote atakayeshikirishwa kwa utafiti huo. Ukitaka kuwasiliana nao, nambari za mawasiliano ndizo hizi:

KNH/UON-ERC, P.O. Box 20723 Code 00202 NAIROBI Tel:726300-9 Fax:725272 Telegrams:MEDSUP,Nairobi

KNH/UON-ERC Email: uonknh_erc@uonbi.ac.ke Website: www.uonbi.ac.ke Link: www.uonbi.ac.ke/activities/KNHUoN

Kama umelewa hii maelezo na umekubali basi unaweza weka sahihi yako kwenye fomu ya kibali cha utafiti kifuatacho.

APPENDIX IIB: KIBALI CHA UTAFITI

Nambari ya utafiti.....

Mimi, Bi/Bwana Mzazi wa

Nimekubali kushiriki katika utafiti huu baada ya kuelezwa na daktari ...**Nduati J.Mwangi**....

Sahihi yangu ni thibitisho ya kwamba nimeelewa umuhimu wa utafiti huu na kwamba habari yoyote nitakayotoa itawekwa siri..Pia nathibitisha ya kwamba sijapewa au kuahadiwa pesa au chochote kile, kukubali kushiriki kwenye utafiti huu.

Sahihi UhusianoTarehe

Kibali cha mtoto (miaka 8-17)

Nimeelezwa kuhusu utafiti huu na daktari **Nduati J.Mwangi** na nimeelewa umuhimu wake. Sahihi yangu ni thibitisho ya kwamba nimekubali kushiriki katika utafiti huu.

Sahihi ya Mtafiti Tarehe

APPENDIX III: PRE-OPERATIVE PROFILE.

Study Number.....
 Age..... Group; A...../B.....
 County Sex.....

Presenting complains.	Yes	No	Duration of symptoms.[months]
Snoring.			
Mouth breathing.			
Nasal blockade.			
Recurrent sore throat.			

Clinical examination:

Body weight.....Kgs.

General condition; Good...Fair...Sick.....[tick where appropriate].

Throat; Tonsils grade;

Other findings.....

Indication for surgery.....

Planned operation.....

Laboratory investigations.

Urea and electrolytes;

Full hemogram;

APPENDIX IV: OPERATIVE DETAILS.

Research number

Date.....

Weight.....

Research number.....

Sex.....

Age..... Group; A.... / B...[tick]

Diagnosis..... Operation.....Time taken.....min

Drugs; 1. GA..... Induction..... Maintenance.....

Reversal.....

2. Analgesics (Tramadol.....mg.....Paracetamol.....mg

3. Antibiotics (IV co-amoxclav).....mg

4. Dexamethasone.....mg

.

Haemostasis achievement:

Diathermy	Packing
-----------	---------

Diathermy points...[nasopharynx...]

[Tonsillar fossa; right.../left....]

Constrictors involved...yes/...no.

Complications.....

.....

.....

APPENDIX V: POST OPERATIVE PROFILE.

Date.....

Study No.....

1.POST OPERATIVE PAIN.

Visual Analogue Scale.

Please indicate the severity of the pain your child is experiencing today according to your judgement.

No pain. Very severe pain.

Day 1

1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	----

Day 4.

1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	----

Day 7.

1	2	3	4	5	6	7	8	9	10
---	---	---	---	---	---	---	---	---	----

2.DIETARY INTAKE.

Consistency.	D0	D1	D4	D7
None.				
Liquids.				
Soft diet.				
Usual diet.				

APPENDIX VI: ANAESTHESIOLOGIST/ANAESTHETIST INFORMATION SHEET.

We are conducting a study on The effect of Benzydamine hydrochloride oral pharyngeal gargle on post tonsillectomy pain in paediatric patients. Thus uniform/standard intra op medications administration will be required on the recruited patients. The following medications will be used:

Analgesics

Fentanyl -2microgrammes/kg body weight.

Tramadol- 1mg/kg body weight.

Paracetamol- 10mg/kg body weight (125mg, 250mg, 500mg suppositories)

Antibiotics

IV co-amoxclav-25mg/kg body weight.

Others

Dexamethasone -0.2mg/kg body weight.

The IV medication should be administered at induction.

Your co-operation will be highly appreciated.

APPENDIX VII: APPROVAL LETTER



UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355

Ref: KNH-ERC/A/268



KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: www.uonbi.ac.ke

Link: www.uonbi.ac.ke/activities/KNHUoN



KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

14th August 2014

Dr. Nduati James Mwangi
Dept. of Surgery
School of Medicine
University of Nairobi

Dear Dr. Mwangi

**RESEARCH PROPOSAL: THE EFFECT OF BENZYLAMINE HYDROCHLORIDE ON POST
TONSILLECTOMY PAIN IN PAEDIATRIC PATIENTS AT KENYATTA NATIONAL HOSPITAL (KNH) –
A CLINICAL TRIAL (P124/03/2014)**

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 14th August 2014 to 13th August 2015.

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.uonbi.ac.ke/activities/KNHUoN.

Protect to Discover

Yours sincerely



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

- c.c. The Principal, College of Health Sciences, UoN
 The Deputy Director CS, KNH
 The Chairperson, KNH/UoN-ERC
 The Assistant Director, Health Information, KNH
 The Dean, School of Medicine, UoN
 The Chairman, Dept. of Surgery, UoN
 Supervisors: Prof. I.M. Macharia, Dr. M.M. Omutsani

Protect to Discover