THE EFFECT OF ISOTONIC NASAL SALINE IRRIGATION ON CHRONIC RHINOSINUSITIS SYMPTOMS IN ADULT PATIENTS AT THE KENYATTA NATIONAL HOSPITAL

DR. MEIMUNA WARE ADAN

H58/69409/2013

Masters of Medicine in Otorhinolaryngology, Head and Neck Surgery,

Department of Surgery,

The University of Nairobi

A dissertation submitted in partial fulfillment of the requirement for the Degree of Masters of Medicine Otorhinolaryngology, Head and Neck Surgery, University of Nairobi

STUDENT'S DECLARATION

This dissertation is my original work and has not been presented for the award of a degree at any other university.

Dr. Meimuna Ware Adan

Postgraduate student, M.Med (Otorhinolaryngology Head and Neck Surgery)

University of Nairobi,

Signature: …… Date: ……..……..……

SUPERVISORS' APPROVAL

This dissertation has been submitted with our approval as supervisors:

Prof. Isaac M. Macharia

Professor and consultant ENT- Head and Neck Surgeon,

Department of Surgery,

The University of Nairobi

Signature: …… Date: ……..…….……

Dr. Mwanisa Omutsani M.

Consultant ENT-Head and Neck Surgeon,

Kenyatta National Hospital

Signature: …… Date: …….……

DECLARATION OF ORIGINALITY FORM

(THE UNIVERSITY OF NAIROBI)

Name of Student: Dr. Meimuna Ware Adan

Registration Number: H58/69409/2013

College: Health Sciences

Faculty/School: School of Medicine and Surgery

Department: ENT thematic unit

Course Name: Otorhinolaryngology, Head and Neck Surgery

Title of work: "THE EFFECT OF ISOTONIC NASAL SALINE IRRIGATION ON CHRONIC RHINOSINUSITIS SYMPTOMS IN ADULT PATIENTS AT THE KENYATTA NATIONAL HOSPITAL"

Declaration

1. I understand what plagiarism is and I am aware of the University's policy in this regard.
2. I declare that this dissertation is my original work and has not been submitted elsewhere for examination, award of a degree or publication. Where other people's work or my initial work has been used, this has properly been acknowledged in accordance with the University of Nairobi's requirements.
3. I have not sought or used the services of any professional agencies to produce this work.
4. I have not allowed, and shall not allow anyone to copy my work with the intention of passing it off as his/her own work.
5. I understand that any false claim in respect of this work shall result in disciplinary action, in accordance with the University Plagiarism Policy.

Signature: ..... Date: .....

ACKNOWLEDGEMENT

I am grateful to my supervisors, lecturers, consultants, staff at the KNH, and all my colleagues for their support and guidance through this journey.

DEDICATION

I dedicate this thesis to my family for their immense support, patience and sacrifices. I look forward to spending quality time with you. Thank you**.**

SUBMISSION OF DISSERTATION

This dissertation has been submitted to the Department of Surgery, University of Nairobi.

Signature……...Date…….....

The Chairman,

Department of Surgery,

School of Medicine,

University of Nairobi.

TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

List of Figures

List of Tables

ACRONYMS AND ABBREVIATIONS

AAO-HNS -American Academy of Otorhinolaryngology Head and Neck Surgery

CI -Confidence Interval

CRS -Chronic Rhinosinusitis

ENT -Ear Nose and Throat

HSNI -Hypotonic saline nasal irrigation

IQR -Interquartile range

KNH -Kenyatta National Hospital

MLS -Milliliters

NPIF -Nasal peak inspiratory flow

NS -Normal saline

NSI -Normal saline irrigation

OMC -Ostiomeatal complex

OR -Odds ratio

P -p value

PH -Potential of hydrogen

RDI -Rhinitis disability index

RS -Rhinosinusitis

RSDI -Rhinosinusitis disability index

SIA -Single item sinus symptom severity score.

SNOT-20 -Sinonasal outcome test-20

SPSS -Statistical Package for social sciences

β -Standard deviation coefficient.

ABSTRACT

Background: Chronic rhinosinusitis (CRS) is inflammation of the sinonasal tract for longer than 12 weeks. Patients present with nasal blockage, facial pain, nasal secretions, and malaise. Nasal saline has been used as an adjunct therapy to relieve these symptoms.

Main Objective: To determine the effect of saline nasal irrigation in patients with CRS as an adjunct treatment among patients at Kenyatta National Hospital.

Study Design: Randomized controlled trial.

Study Population: Patients 18 years and above who have been diagnosed with CRS without polyps.

Study Setting: The Ear Nose and Throat clinic at The Kenyatta National Hospital.

Study duration: Between March 2019 to September 2019.

Methodology: A total of 50 patients diagnosed with CRS who satisfied the inclusion criteria were recruited and randomized using research randomizer into 25 control and 25 study group. Both groups continued using fluticasone furoate nasal spray and filled in the SNOT 20 questionnaire at the beginning and the end of the study. The study group self-administered nasal saline irrigation at high volume and low positive pressure twice daily for 28 days while the control group only used the nasal spray for the 28days. The study group, in addition filled a compliance diary and side effects questionnaire which was submitted on the 28^{th} day.

Data management and analysis: Data was entered into SPSS version 22, verified and analyzed. Descriptive statistics such as mean and median was used for normal and skewed variables respectively. The two groups were compared using independent t-test and paired sample t-test analysis. A p-value of ≤ 0.05 indicated statistical significance.

Results: Study population had 44 participants with 6 previously lost to follow up, therefore 22 controls and 22 cases. The improvement in SNOT-20 scores over the 28 days from baseline was 21.1 ± 14.7($P<0.001$) for the study and 13.0 ± 12.7 ($P=0.02$) for control groups. The Cohen's coefficient was 0.63.

Median compliance was at 96% and the most common side effect was nasal drainage.

Conclusion: Adjunct saline irrigation had marked improvement compared to those who used intranasal steroid sprays only. It has good compliance with minor side effect.

1.0 CHAPTER ONE: INTRODUCTION

Chronic rhinosinusitis (CRS) is the inflammation of the nose and the paranasal sinus mucosa for longer than 12 weeks(1). This disease causes signs and symptoms of nasal blockage, facial pain, generalized malaise, and nasal secretions that drain anteriorly and posteriorly.

Nasal saline irrigation (NSI) is the washing or flushing of saline solution into the nose and paranasal sinuses so as to remove debris and mucus. NSI has been used for hundreds of years by the Indian community that practiced Hatha Yoga to attain a higher state of meditation and general physical and spiritual wellbeing. As time went by, nasal saline irrigation became more popular and spread to the Western world. In 1938, Furstenberg encouraged its use in the treatment of acute nasal accessory sinus disease (2). Currently, it is widely used after sinonasal surgeries in the prevention of formation of the synechiae.

Prevalence of CRS was noted to be 12.5% of the United States of America population while in North West Nigeria, Iseh et al found 11.7% new cases of rhinosinusitis (RS) during a 2-year study at Usmanu Danfodiyo university teaching hospital, with CRS being 83.6% of the total(3,4). In Kenya, a study conducted by Gathiru et al at the Kenya medical training college showed a prevalence of 13.7% of that population suffered from allergic rhinitis(5). CRS is becoming a significant problem with the increase in the frequency of allergic rhinitis. This has resulted in a large financial burden in society (6).

Many guidelines on the management of CRS encourage the use of Saline nasal irrigation despite the paucity of studies supporting its efficacy. The South African guideline encourages its use as a preventive measure despite this fact(7)**.**

1.1 Background

1.1.1 Anatomy of the Nose and the Paranasal Sinuses

Anatomy of the sinonasal tract is of great importance in understanding CRS and its management. The nose is made up of two nasal cavities that are separated by the nasal septum. Anteriorly it has the vestibule that opens into the environment and posteriorly it opens into the nasopharynx via the choana. Each nasal cavity proper has a floor, roof, medial and lateral walls. The lateral wall consists of 3 or sometimes 4 bony projections covered by mucous membrane. The spaces between the turbinates are called meatus.

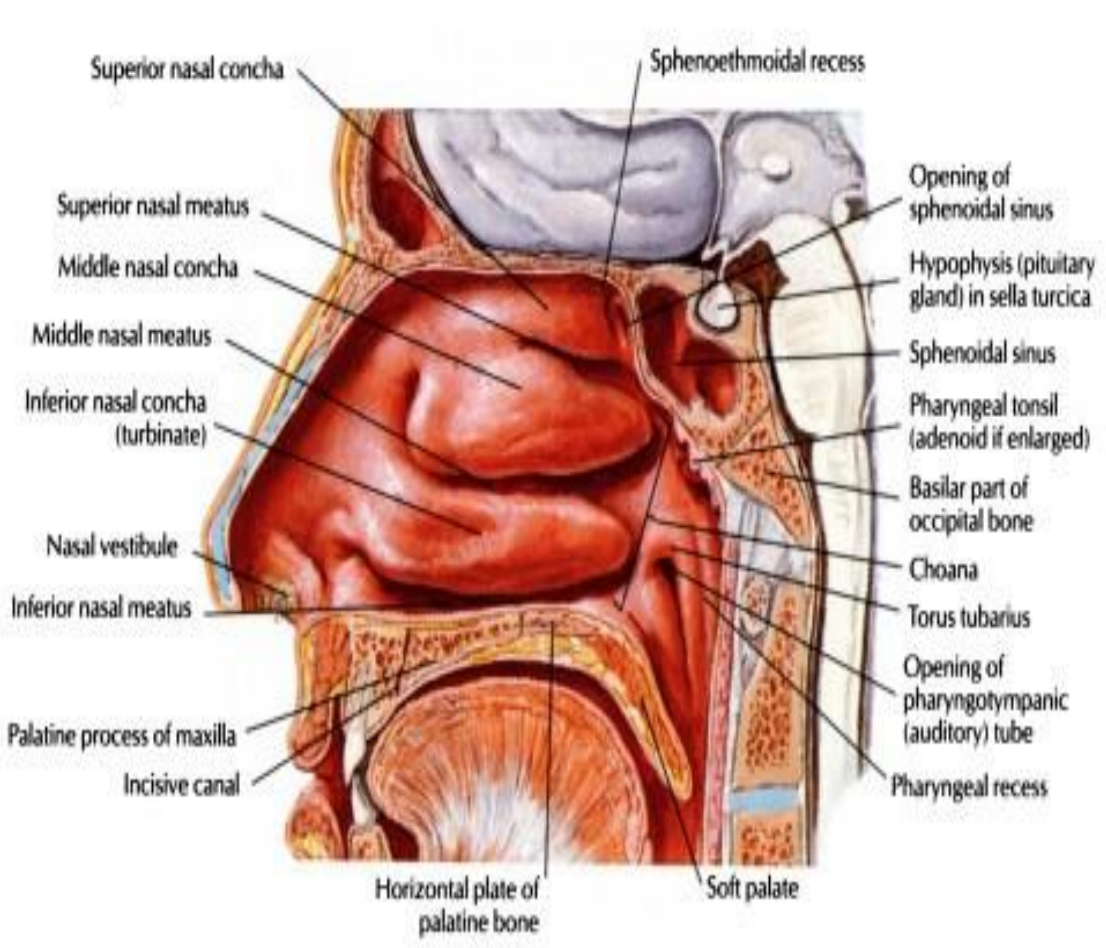


Figure 1: Anatomy of the lateral wall (8)

The paranasal sinuses are 4 paired mucus membrane lined air-filled cavities within the skull bone. The maxillary sinuses are located just beneath the eyes, thus maxillary sinusitis leads to pain or pressure over the cheek that radiates to the frontal region or teeth, increasing with strain or bending. Frontal paranasal sinuses are located just above the eyes, thus frontal sinusitis leads to facial pain around the eyes and forehead. The ethmoid sinuses are discrete air cells located between the eyes and the nasal cavity, thus ethmoid sinusitis leads to pain between the eyes and tenderness over the nasal bridge while the sphenoid sinuses are located posterior to the nose thus inflammation leads to ear pain, neck pain, pain at the vertex, the sides of the head and the occipital region.

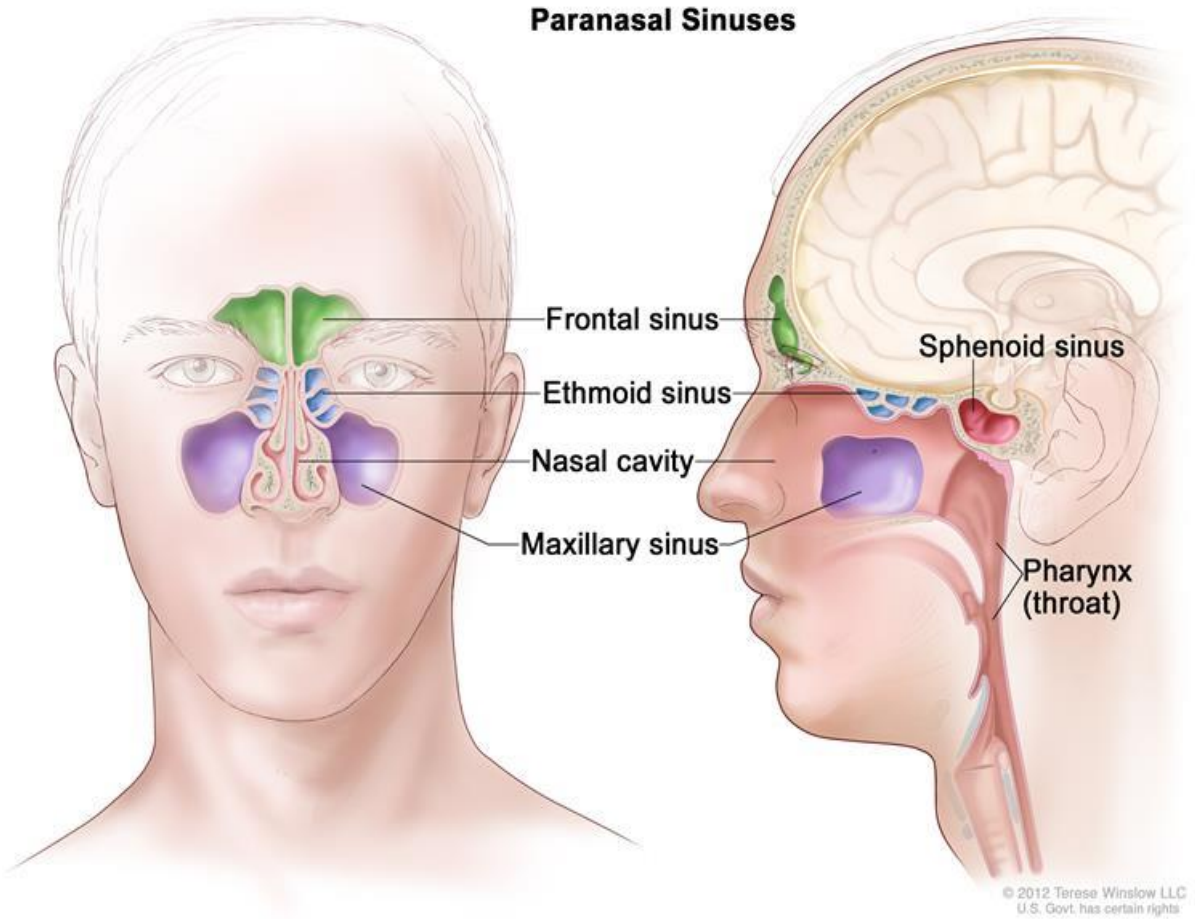


Figure 2: Paranasal Sinuses (9)

The inferior turbinate houses the inferior meatus where the nasolacrimal duct opens. Between the middle and inferior turbinate is the middle meatus which contains an area with common channels that link the frontal sinus, anterior and middle ethmoid sinuses and the maxillary sinuses known as the ostiomeatal complex (OMC). This allows air flow and mucociliary drainage and is functionally significant as it is anatomically constricted thus blockage can easily occur leading to sinusitis. The blockage of this complex in CRS is frequently used as one of the indications for surgical treatment of CRS. Between the superior and middle turbinate is the superior meatus where the posterior ethmoid and sphenoid sinus openings are located.

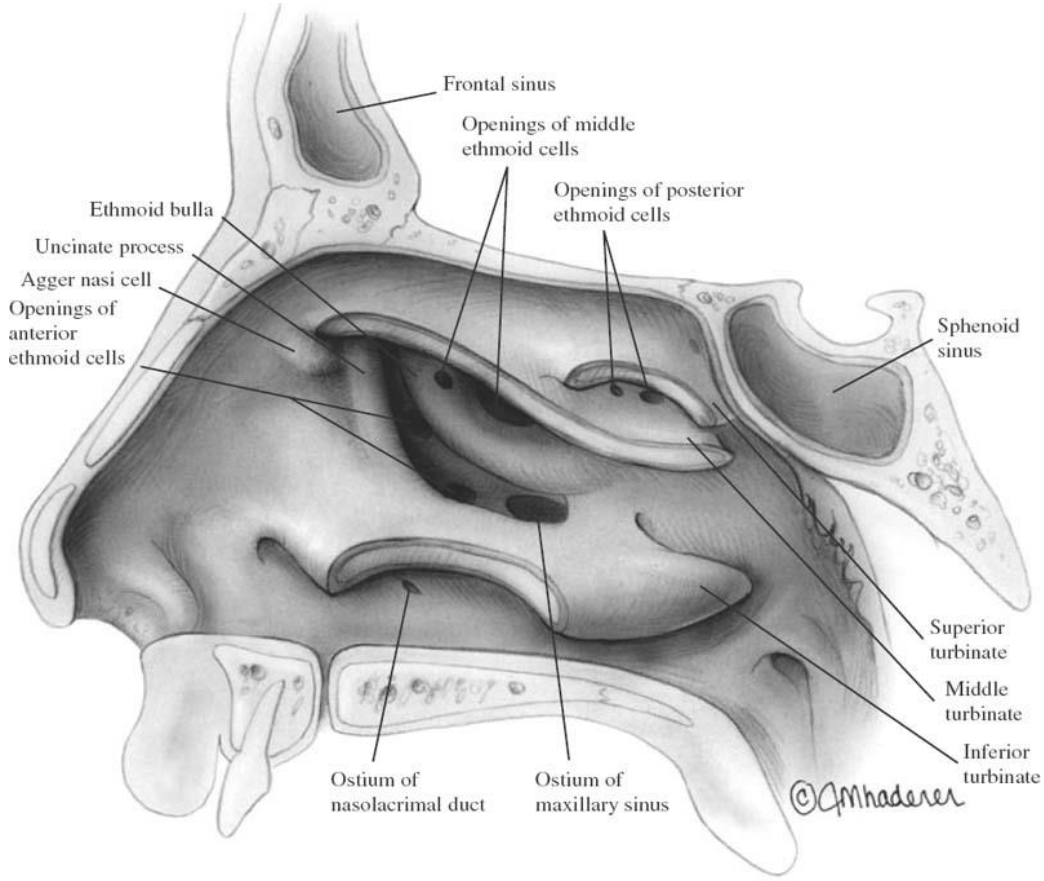


Figure 3: Anatomy of the sinus drainage (10).

The medial wall of the nasal cavity proper is made of the nasal septum, the floor is made of the palatine process of the maxilla in its anterior three quarters and the horizontal process of the palatine bone in its posterior quarter while the roof is made up of body of sphenoid in its posterior slopping part the nasal bones in its anterior slopping part and the cribriform plate in its middle horizontal part.

The vestibule of the nose is lined by stratified squamous epithelium with hair follicles and sebaceous glands which when infected leads to folliculitis. The olfactory epithelium is located in the upper posterior aspect of the nose and is essential for the perception of smell. Infection or inflammation of this area leads to anosmia (inability to perceive odors) which may be permanent if the disease persists. The rest of the nasal cavity and paranasal sinuses are covered by the respiratory epithelium which is pseudostratified columnar ciliated epithelia with goblet cells and sebaceous glands.

1.1.2 Function of the Nose and Paranasal Sinuses.

The nose and the paranasal sinuses have various physiologic functions which include aiding in respiration, conditioning of inspired air, protection of lower respiratory tract, olfaction, nasal reflex, vocal resonance and gives the face its structure and shape.

1.1.3 Mucociliary Escalator

The mucosa contains sebaceous glands which secrete sebum that is known to be water repellant at the same time contains immune cells and goblet cells interspersed among the epithelial cells.

The respiratory epithelium has a surface liquid that is formed from goblet cells, epithelium, and submucosal glands secretions. It has 2 layers which are the sol layer and a more superficial gel layer. The gel layer is made of high molecular weight glycoprotein (mucin) linked with proteins and lipids with a high water content of about 95%. It is viscous, elastic and adhesive. Due to difficulty in collection of the sol layer, its physical and biochemical properties have not yet been discerned.

The surface liquid contains macrophages which engulf particles and antimicrobial proteins like lysozymes and lactoferrins and peptides like defensin which prevent bacterial colonization. The surface mucus traps debris for transport towards the nasopharynx.

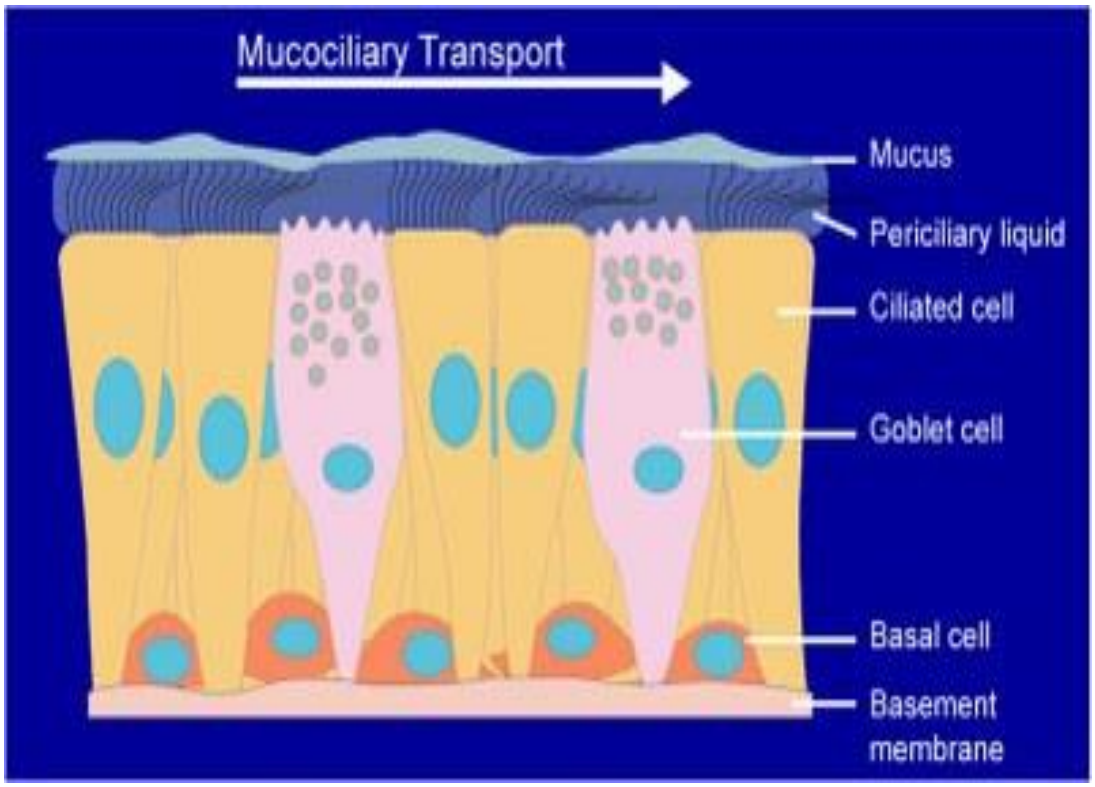


Figure 4: Mucociliary Escalator (11).

Periciliary or aqueous sol layer is approximately 7 micrometers thick while the mucus or gel layer is of variable thickness. The ciliary tip extends to the mucus layer and the Cilia beat within the sol layer in one direction. This forms the mucociliary escalator which is very important in the normal functioning of the nose as it removes particles of 0.5 to 5 microns.
Only the cilia tip extends into the mucus layer for an efficient beat, with each beat having 2

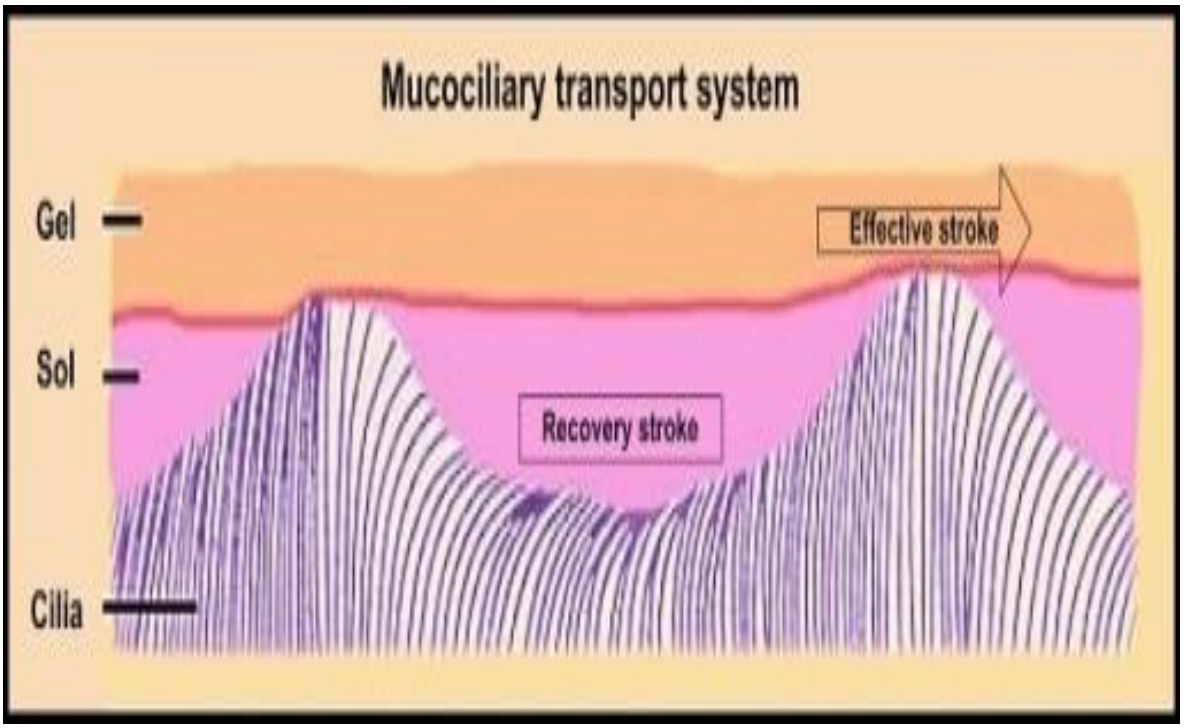


Figure 5: Mucociliary Escalator ciliary Beat (12)

phases. The first phase is the active or effective stroke that moves the mucus posteriorly, and the second phase is the recovery or passive phase that occurs entirely within the sol layer moving the cilia to the resting position where it remains for a while before restarting this cycle over and over again.
There is active chloride secretion into the surface liquid and with it goes water from the serous cells thus expanding its height. Apical cells have sodium channels while the basolateral membrane of the epithelia has sodium/potassium pumps that actively pump out sodium.
Ciliary beat depends on Ph. tonicity and viscosity of the surface liquid. For optimal mucociliary function, the ph. should be between 7 and 9, with intact epithelium, a temperature of 23 degrees centigrade and moderate viscosity.

1.1.4 Diagnosis of CRS.

According to the 2015 American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS) guidelines, CRS diagnosis depends on the presence of mucopurulent drainage, nasal obstruction or congestion, facial pain, pressure fullness and a decreased sense of smell. There should also be documented proof of inflammation via findings of purulent mucous or edema in the middle meatus or ethmoid region, polyps in the nasal cavity or middle meatus via use of anterior rhinoscopy or nasal endoscopy or alternatively radiographic image evidence of inflammation of the paranasal sinuses (**Appendix I**) which include thickening of the sinonasal mucosa, presence of fluid levels and blockage of the ostiomeatal complex.

The sinonasal out-come test 20 (SNOT 20 (**Appendix IV**)) is a measuring tool for quality of life assessment and has been validated in several countries Like America, and Portugal. Its main purpose is to measure the quality of life impact of interventions on a patient with rhinosinusitis (13,14). It is a multiple choice 20 item test that is usually scored with a single summary score of 0 to 5 without domains or subscales. It assesses a wide range of health-related quality of life issues like the physical, functional, and emotional impact of rhinosinusitis and its interventions in the form of a nasal, ear, facial, sleep, and psychological symptoms. There are 4 main domains that have been validated i.e. the Psychological, Rhinologic, ear and face domain and lastly sleep domain. Two symptoms did not fit into any of these domains i.e. cough and waking up tired. The Rhinologic domain entails 5 symptoms which are, need to blow the nose, sneezing, runny nose, postnasal drip and thick nasal discharge. The ear and facial symptoms domain has 4 symptoms i.e. ear fullness, dizziness, ear pain and facial pressure or pain. The psychological domain has 6 symptoms which are fatigue, reduced concentration, reduced productivity, frustration/restlessness/irritability sadness and embarrassment. The sleep domain has 3 symptoms i.e. difficulty falling asleep, waking up at night and lack of a good night sleep (13). SNOT-20 is simple to understand and easy to administer, even more so when using the domains to summarize the symptoms.

1.1.5 Management of CRS

CRS has potential predisposing factors that contribute to illness persistence and or recurrence. Some of these conditions are cystic fibrosis, anatomical variance, ciliary dyskinesia, allergic rhinitis, immunocompromised state, gastroesophageal reflux disease, and smoking. Ideally, these causes should be identified, managed and treatment tailored to individual patient presentation.

The principle of medical management of CRS is to improve drainage, aeration, ventilation, eradicate infection and reduce mucosal edema. Symptoms are relieved by the use of topical decongestants, topical steroids, antibiotics, topical cromolyn, mucolytic, and nasal saline irrigation.

According to the AAO-HNS 2015 update on criteria on diagnosis and management of CRS, the diagnosis between acute exacerbation of CRS and acute recurrent rhinosinusitis must be distinguished from acute bacterial rhinosinusitis. Furthermore, the acute exacerbation should be managed according to cause either bacterial or viral with an antibiotic where appropriate.

Patients initially receive daily nasal saline irrigation for a duration of 4 weeks with or without topical intranasal steroid. CRS with nasal polyposis, in addition, is treated with oral glucocorticoids i.e. prednisolone daily, that is tapered over several days.

Patients diagnosed with allergic rhinitis who have sneezing and itching of the nose are treated with Antihistamines to relieve these symptoms. Those with aspirin allergies or asthma are managed with leukotriene inhibitors as it is an effective adjunct to a steroid. CRS due to gastroesophageal reflux disease should be treated with proton pump inhibitors.

Cystic fibrosis being an autosomal recessive disease causes severe and refractive sinonasal diseases. CRS due to cystic fibrosis is mostly associated with nasal polyps therefore in addition to the steroid nasal spray, oral steroids, and hypertonic saline irrigation, surgery may be indicated to relieve the nasal blockage. Surgery e.g. functional endoscopic sinus surgery is also used in patients with an anatomic obstruction or those who have failed to improve on medical therapy. Patients with CRS should not be treated with topical or systemic antifungal therapy.

1.1.6 Nasal Saline Irrigation

Saline is a mixture of sodium chloride and water, which is available in several different, strengths Isotonic or normal saline which is 0.9% sodium chloride, hypertonic saline which is 3%, 5%, 7% and 23.4% sodium chloride, hypotonic saline 0.45% and 0.22% sodium chloride. In saline, sodium and chloride compounds are at a ratio of 1:1, therefore every 100grams of sodium chloride contains 39.34grams of sodium and 60.66grams of chloride. Sodium chloride is responsible for the salinity of seawater and extracellular fluid found in multicellular organisms. Normal saline (NS) or physiological saline was also known as indifferent fluid as it has a similar freezing point as human serum and did not cause visible erythrocyte lysis. NS has a higher chloride content of up to 50% and higher sodium content of 10% more than that of serum. It also has a low pH of approximately 5.4 making it acidic.

Saline may be delivered to the nose via different methods such as irrigation, sprays, nebulization, and drops. These preparations are available in varying tonicity from isotonic to hypertonic solutions that may be either premixed or need the user to mix the preparations themselves for each use. There have been many additives to the saline irrigation that have been described over the years. Some of these additions include steroids e.g. budesonide, antibiotics, baby shampoo, manuka honey, and bicarbonate.

Saline nasal irrigation fluids may be delivered to nose either by positive or negative pressure. In negative pressure saline nasal irrigation, the user sniffs the fluid into their nose while positive pressure the user squirts the fluid into the nose. The positive pressure method has been shown to be more effective as there is a uniform distribution of the fluid within the sinuses as compared to the negative pressure method (15). Therefore, most physicians prescribe positive pressure nasal irrigation. In addition, the positive pressure irrigation may be either high volume (generally accepted as 100ml or more of fluid to each nostril), or low volume (less than 100ml to each nostril) with pressure not less than 12000 Pascal for an effective rinse.

Positive pressure nasal irrigation is performed by pumping warm freshly prepared saline (by using a syringe, squeeze bottle, neti pot, bulb syringe, and motorized irrigators) into the nasal cavity as cold water irritates the mucosa and causes an exaggerated gag reflex. It is also preferred to use distilled water, sterile or boiled and cooled, due to the risk of bacterial contamination. One may also include a small amount of bicarbonate as a buffering agent to adjust the solution's pH to the human body ph. and for more comfort. The general mechanism of action of saline solutions is softening nasal secretions and facilitating clearance of possible allergens (pollens, house dust mites, mold spores, animal dander, etc.) from nasal mucosa. In addition to this role, it causes vasoconstriction, hence reducing nasal obstruction. It also appears to have an anti-inflammatory effect, therefore reducing mediators and cells involved in allergic inflammation (histamine, prostaglandins, leukotrienes, and eosinophils). The use of nasal saline irrigations before the administration of anti-allergic sprays increase their effectiveness, prevent mucus crusts formation, and allow mucus drainage. It also reduces mucosal edema by its osmotic effect and improves mucociliary clearance.

Due to its chemical constitution normal saline, nasal saline irrigation has been known to cause transient symptoms like nasal irritation, nasal burning, nasal drainage, headache, tearing, nose bleeds, ear fullness, ear pain, and dizziness. Nasal saline irrigation side effects rarely cause a need to discontinue treatment.

2.0 CHAPTER TWO: LITERATURE REVIEW

Saline nasal irrigation has gained popularity in the management of rhinosinusitis. This is partly due to the emergence of evidence that it causes clinically significant improvement in symptoms in patients with CRS. In 2007, Pynnone et al did a community based randomized controlled study on 127 patients with chronic sinonasal symptoms (16). Although they compared high volume, low positive pressure hypertonic nasal irrigation with hypertonic saline spray, they were able to find clinically significant improvement on symptom with severity scores to be 4.4 points lower at 2 weeks, 8.2 points lower at 4 weeks, and 6.4 points lower at 8 weeks in the irrigation group than the spray group. In 2005, Rabago et al in 2005 published a study with an outcome that concurred with the above conclusion (17). They found significant improvement in the quality of life score in 54 patients diagnosed with either acute or chronic rhinosinusitis. In this study hypertonic saline was used over a 6 month period in the first phase. Although their sample size was small at 40 patients Nguyen et al found a statistically significant decrease in quality of life scores in patients with allergic rhinitis who used isotonic saline as an adjunct to intranasal corticosteroids (18). Furthermore, Sosheyov et al found that after irrigating the nose of children for 4 weeks with either normal saline or hypertonic saline the postnasal drip symptoms improved significantly (19). This status was maintained a month after the irrigation had been stopped.

Despite the positive outcomes that have been noted in these studies, the effect of saline on the nasal mucosa is still a subject of debate. Bonnomet et al measured ciliary beat frequency and wound repair speed in cultured nasal ciliated cells that were exposed to non-diluted sea water, diluted seawater, and normal saline (20). Saline was noted to induce ciliary death after 30 minutes. 5 of the 10 cultures incubated with normal saline exhibited no viable cells. It was also noted to inhibit physiological wound healing. This is thought to be due to the acidic nature of saline which had a pH of 5.2. The diluted seawater, on the other hand, had better outcomes this is thought to be due to the minerals contained therein that enhance ciliary function. The best outcome was found in undiluted seawater which had a higher pH (7.9) and more minerals compared to the other two. Contradicting these outcomes Inanli et al in 2002 found no significant difference on effects of topical agents i.e. fluticasone propionate, oxymetazoline, 3% and 0.9% saline on mucociliary clearance on acute bacterial rhinosinusitis [(21)].

Saline nasal irrigation is noted to have few and tolerable side effects in adults. Rabago et al reported 10 out of 44 participants (23%) experienced nasal irritation, burning sensation, tearing, nasal discharge, headaches, and nosebleeds after nasal irrigation with buffered hypertonic saline of 2-3.5% concentration of which they reported to be "not significant", with 4% of them reporting nasal burning sensation, and headaches that was significant during the 6-month period (22). The participants who experienced side effects diluted the solution further by 50% to reduce or completely eradicate the side effects while some altered the irrigation dates temporarily. He also had an outcome of 3 patients who reported using the irrigation on 50% or fewer days and 31 subjects who reported using the irrigation for 91% of the days and more. Hong SD et al found that 63.6% of the children studied had good compliance while 36.4% had poor compliance (23). The main reason for the poor compliance was difficulty in the administration of the irrigation as they found it cumbersome, only 2 out of 28 patients complained of otalgia and ear fullness.

2.1 Study Justification.

The use of saline nasal irrigation is recommended in guidelines from various parts of the world for the treatment of CRS despite a paucity of studies on its efficacy. The few studies done are from developed countries, whose environmental and socio-demographic profiles differ from those in developing countries. This study was an attempt at determining the effect of this simple adjunctive treatment for CRS in a population with lower income, different cultural practices and weather conditions. The findings from this study will add to the body of evidence on the efficacy or otherwise of nasal saline irrigation used in patients with chronic rhinosinusitis, more so in the Kenyan population. The findings of this study will contribute to the development of guidelines for the management of CRS in Kenya.

3.0 CHAPTER THREE: STUDY METHODOLOGY

3.1 Research Question

What is the effect of isotonic nasal saline irrigation on the symptomatology of adult patients with CRS at Kenyatta National Hospital?

3.2 Study Objectives

3.2.1 Main Objective

The main objective of this study was to determine the effect of nasal saline irrigation in patients with CRS as an adjunct treatment.

3.2.2 Specific Objectives

a) To determine the change of symptoms in patients with CRS on NSI using SNOT-20 questionnaire.
b) To determine compliance of patients with CRS to NSI.
c) To determine the side effects of NSI.

3.3 Study Design

This was a randomized controlled trial.

3.4 Setting

This study was undertaken at the Ear Nose and Throat clinic at The Kenyatta National Hospital.

3.5 Study Population

The study population was patients who were 18years and above, who had been diagnosed with CRS without polyps according to the AAO-HNS criteria (**Appendix I**).

3.6 Inclusion Criteria for the Control and Study Groups

a) Patients who had been diagnosed with CRS according to AAO-HNS criteria.
b) Patients 18 years and above who were able to self-report.
c) Patients who had not had antibiotics treatment at least one week prior to recruitment.
d) Patients who gave informed consent.

3.7 Exclusion Criteria for the Control and Study Groups

a) Patients who had nasal polyps.
b) Patients who had bleeding disorders and those on anticoagulant medication.
c) Patients who had sinonasal surgery less than 6 months prior to recruitment.
d) Those who had used the study intervention 2 weeks prior.
e) Patients who had other sinonasal pathology apart from CRS without polyps.
f) Patients who were not able to read and write.

3.8 Sample Size

Sample size calculation was based on the primary outcome of the study. Data was collected from SNOT 20 which has a range of 0 to 100 with 0 being the best outcome and 100 being the worst outcome. Mean averages and the formula for continuous variable or outcome for randomized control trial were used (24).

n = the sample size in each of the groups.

m^1 = population mean in group 1 = 37 (16)

m^2 = population mean in group 2 = 32

$m^1 - m^2$ = difference the investigator wishes to detect = 5

SD = population variance or standard deviation = 7 (16)

a = conventional multiplier for alpha =0.05 = 1.96

b = conventional multiplier for power or beta= 0.80 = 0.84

$$\mathbf{n = 2\left\{\frac{(a+b)^2\ sd}{(m^1-m^2)^2}\right\}} \quad (24)$$

$$\mathbf{n = 2\left\{\frac{(1.96+0.84)^2 x 7^2}{(37-31)^2}\right\} = \frac{768.32}{36} = 21.34}$$

Total minimum sample size required was **21.34 x 2 = 42.68**

15% loss to follow-up was added: **(0.15 x 42.68) + 42.68 = 49.08**

Total sample size was rounded off to the nearest even number i.e. **50 participants**.

Thus 25 patients in the test group and 25 patients in the control group.

3.9 Sampling Procedure

3.9.1 Randomization

Participants were assigned to either the study group (NSI group) or control group (non-NSI group) according to block randomization method. The randomization was done using a research randomizer computer programme before participant selection (25). Research randomizer uses the Math.random method within the Javascript programming language as the core to generate random numbers. The Math.random function returns a floating point, pseudorandom number in the range of 0-1 (inclusive of 0 but not 1) with approximately uniform distribution over that range (26). Therefore, there were 50 sets of 1, with each set having a possibility of being in either the study or control group. Each set was allocated a random number between 1 and 50 which represented the participants. The first 25 sets were allocated to the study group and the last 25 sets were allocated to the control group.

Results of the randomization was as follows:-

Group A (control group):

28, 31, 42, 38, 40, 9, 43, 20, 15, 34, 6, 17, 35, 26, 16, 50, 14, 39, 13, 3, 47, 36, 21, 27, 7,

Group B (study group):

37, 33, 11, 49, 45, 12, 29, 22, 48, 19, 8, 5, 32, 2, 46, 25, 24, 41, 44, 23, 1, 4, 10, 18, 30

https://www.randomizer.org/

The SNOT-20 questionnaires was then allocated the randomized participant number and arranged according to the sequence of the set numbers. Each questionnaire was sealed in a numbered opaque envelope together with a consent form. The study group envelope contained an additional questionnaire on side effects and a compliance diary.

3.9.2 Recruitment and Consent

Patients who were on follow up at the ENT clinic at KNH with a diagnosis of CRS were informed about the study and verbal consent for re-evaluation was sought by the primary investigator. Re-evaluation was done via history taking and physical examination, including an anterior rhinoscopy examination using a headlight and a thudicum nasal speculum to confirm diagnosis according to the AAO-HNS criteria (**Appendix I/VIII**). Once the inclusions were satisfied the consent form was explained and they were allowed to ask questions. Those who agreed to participate in the study were recruited and subsequently picked the topmost sealed opaque envelopes previously prepared. They then filled the consent form (**Appendix II/III**) and the SNOT-20 questionnaire (**Appendix IV**). Both the study and control groups continued or were started on fluticasone furoate as part of normal CRS management throughout the study duration. Those who did not consent continued with the clinic follow-up.

3.9.3 Data Collection

The study participants filled the questionnaire which was a quality of life measure i.e. SNOT-20 on day 0. The study group in addition received a booklet containing the NSI side effects questionnaire and compliance diary which they filled at home on a daily basis for the duration of the study (28 days) while the control group did not receive the booklet. On the 28^{th} day, all the participants presented to the ENT clinic to fill in a SNOT-20 questionnaire and the study group in addition, submitted the booklet.

3.9.4 Materials

The items required for the study participants were as follows-

a) Informed consent form.

b) Warm normal saline solution (0.9%) manufactured by the same manufacturer.

c) Two 20cc syringes,

d) Quality of life questionnaire i.e. SNOT-20 (**Appendix IV**)

e) Compliance diary (**Appendix V**).

f) Side-effects questionnaire (**Appendix VI**).

3.9.5 Procedure

The principal investigator demonstrated how NSI was to be done. The study participants withdrew 20ml of the saline solution into the syringe leaned over a basin or sink, then squirted it into one nostril while directing the fluid along the floor of the nostril and angulating the syringe laterally. The solution was to flow out either through the mouth or the other nostril. Once this was achieved they were asked to repeat the procedure 4 more times in each nostril. NSI was done twice daily (morning and evening) for the duration of the study, which was 28 days. They received irrigation supplies together with written instructions to the same including criteria of discontinuing the treatment which was severe epistaxis or unbearable pain caused by the NSI. The study group was required to fill in the reason and date of discontinuing treatment.

The study group received a weekly telephone call from the principal investigator during the 28 days so as to know their progress and address any concerns that they may have had. The principal investigator first introduced themselves then asked the following questions.

a) Do you have time to respond to my questions, if not when will you be available to answer a few questions?

b) How many bottles of saline are remaining?

c) Do you still have the syringes?

d) What challenges and queries do you have with the procedure?

3.9.6 Measuring Tools

a) SNOT 20 (**Appendix IV**)

b) Questionnaire on side effects (**Appendix VI**).

c) Adherence to the NSI will be assessed using compliance diary (A**ppendix V**).

3.10 Quality Control and Quality Assurance

Patients who had been diagnosed with CRS were sent to the principal investigator for confirmation of the diagnosis through history taking, physical examination and the use of a thudicum nasal speculum for anterior rhinoscopy. All study patients were provided with the same brand of saline for irrigation and two 20 cc syringes. Apart from being shown how to do the irrigation, they were also provided with written instructions. They also received a weekly call to see how they were progressing and any concerns they may have had were addressed. Data collection was done using a validated tool i.e. The SNOT-20 (**Appendix IV**). All the questionnaires were self-administered with the SNOT-20 questionnaire being administered at the clinic in the presence of the principal investigator in case of any clarifications and assistance they may have needed.

3.11 Data Management

Data was collected using case report forms based on the study questionnaires (**Appendix IV, V and VI**). The case report forms were inspected for completeness prior to data entry. Each complete form was entered into the study database designed in MS Office Access (2013). Data was stored in a numeric coded format for continuous variables and categorical data, and in text format for open-ended questions. To ensure data quality assurance the database contained range and validity checks to identify outliers and invalid values. Data was transferred from Access databases to SPSS for data verification and analysis. During data cleaning each variable field was inspected to identify outlier values, and invalid entries. Cross-tabulation was used to check consistency between related variable fields. Any inconsistency between the questionnaire and data contained in the database was resolved by checking case report forms and re-entering the data contained in the forms.

3.12 Data Analysis

Data was analyzed using SPSS (version 21). For the descriptive analysis, every single variable was analyzed according to the randomization (study or control) group. Analysis of continuous variables e.g. age, involved calculating mean and standard deviation for normally distributed variables and median and interquartile range for skewed variables i.e. compliance. Fisher's exact test was used to analyze gender in the various groups. Categorical variables e.g. most common symptoms in patients with CRS was analyzed using percentages of patients that presented with each symptom separately for the normal saline and control group. The primary outcome was the symptom severity for CRS assessed using quality of life index based on SNOT-20. The mean index score was compared between the patients randomized to

saline irrigation and the control using independent sample t-test. Paired sample t-test was used to compare the mean improvement within the study and control groups. The mean difference in SNOT-20 score was reported along with the corresponding 95% confidence interval and p value. A percentage of patients with side effects of nasal irrigation was calculated. Comparison of the prevalence of side effects at the baseline and end of study was done using chi square test. Compliance data was used for the treatment group as a description of treatment uptake, and linear regression was used to determine relationship between compliance and improvement.

3.13 Study Limitations

The study limitations are as follows.

1. Controlling environmental factors e.g. Allergens, smoke.
2. Could not ascertain honesty in filling the compliance and side effects questionnaires.
3. Could not ascertain compliance with the procedure of nasal irrigation.
4. Could not ascertain the temperature of normal saline for all the participants.
5. Did not collect data on side effects of the control groups.

3.14 Ethical Considerations

The ethical considerations were as follows.

a) This study was started after the approval from the KNH – UON ETHICS AND RESEARCH COMMITTEE. Reference number- P401/06/2018.

b) Confidentiality was maintained by the use of anonymous biodata with numbers and individual files locked and secured.

c) No extra cost was incurred by the participants.

d) Consent was sought from the patients and controls and those who did not consent were not discriminated against as they continued to receive regular treatment and follow-up at the ENT clinic.

e) Participants found to have other ENT diseases apart from CRS without polyps and other comorbidities were referred to the ENT clinic at KNH for further management.

f) Participants were allowed to withdraw at any time without penalties during the study.

g) The results of this study is available to the medical fraternity and the public via medical journals, conferences.

h) There was no conflict of interest in the part of the patient, author or institution.

4.0 CHAPTER FOUR: RESULTS

4.1 Overview

There were 50 participants who were successfully randomized into 25 study and 25 control groups. Out of these, six were lost to follow-up, three in the control and three in the study group, therefore, data at the twenty eighth day was not obtained and intention to treat analysis was deemed unsuitable for this study, as outcomes would not portray the effect of saline irrigation if they were included.

4.2 Baseline and demographic measurements.

A total of 44 participants were included in the analysis, 22 were study and 22 were controls.

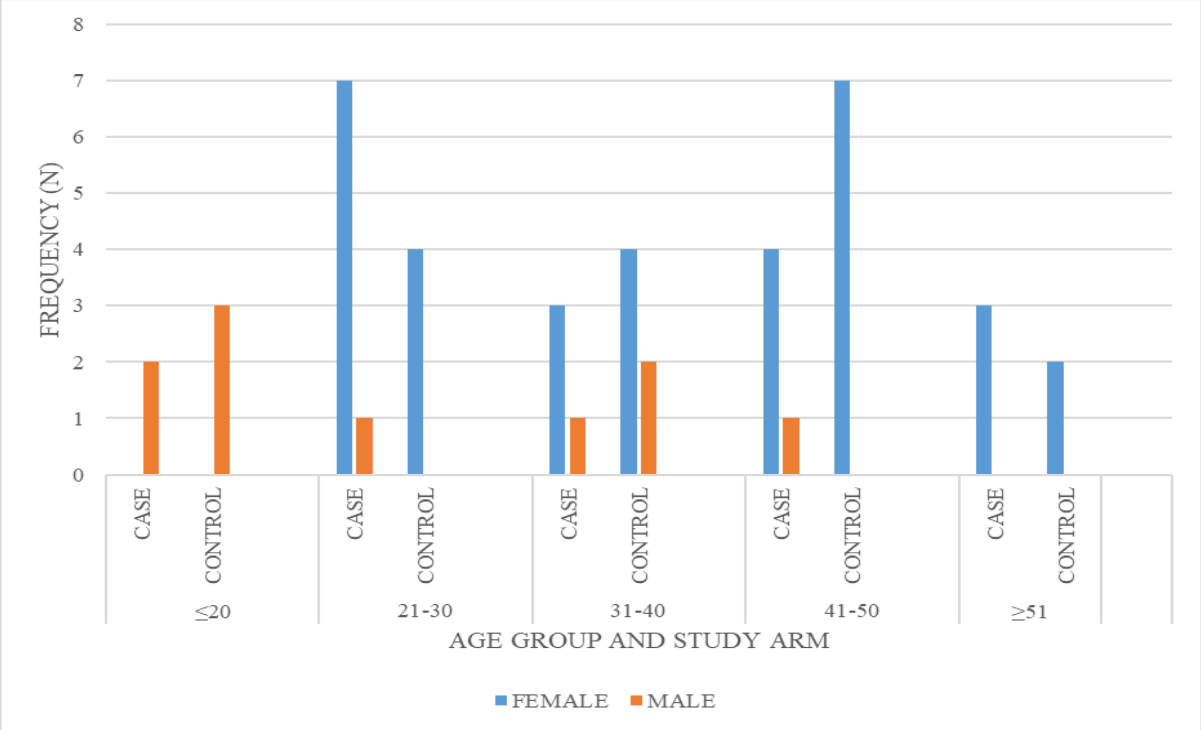


Figure 6: Age and gender distribution graph of both the study and control groups

The study population consisted of 10(22.7%) males and 34(77.3%) females with a male to female ratio of 1:3.4 which is consistent with findings in other studies. There was no significant difference in terms of sex distribution between the study and control arms with 5 males and 17 females in each of the groups.

Most of the participants were between the ages of 21-30 years at 28.9% followed by 41-50 years at 26.7%, 31-40 year at 22.2%, ≤20 years and ≥50 years at 11.1%.

Table 1: Baseline of individual domain SNOT scores of study and control groups.

DOMAIN	STUDY (n=22)	CONTROLS (n=22)	P-VALUE
Rhinologic	13.0	11.1	0.24
Ear and face	7.1	5.9	0.35
Psychological	16.5	10.4	**0.03**
Sleep dysfunction	7.0	3.6	**0.03**
Cough	2.0	1.3	0.14
Wake up tired	3.1	1.7	**0.004**
Duration of follow-up(days)	28	28	1.00

For individual domains psychological, sleep and waking up at night had a statistically significant difference at base-line between the study and control groups.

Table 2: Post-treatment characteristics as per individual domains.

DOMAIN	MEAN SCORE		P-VALUE
	STUDY	CONTROLS	
Rhinologic	7.8	6.7	0.46
Ear and face	5.1	4.0	0.34
Psychological	8.2	5.8	0.22
Sleep dysfunction	3.7	2.0	0.07
Cough	1.2	1.0	0.71
Wake up tired	1.6	1.1	0.25

There was no statistically significant difference at the end of the study in the individual domains between the controls and cases.

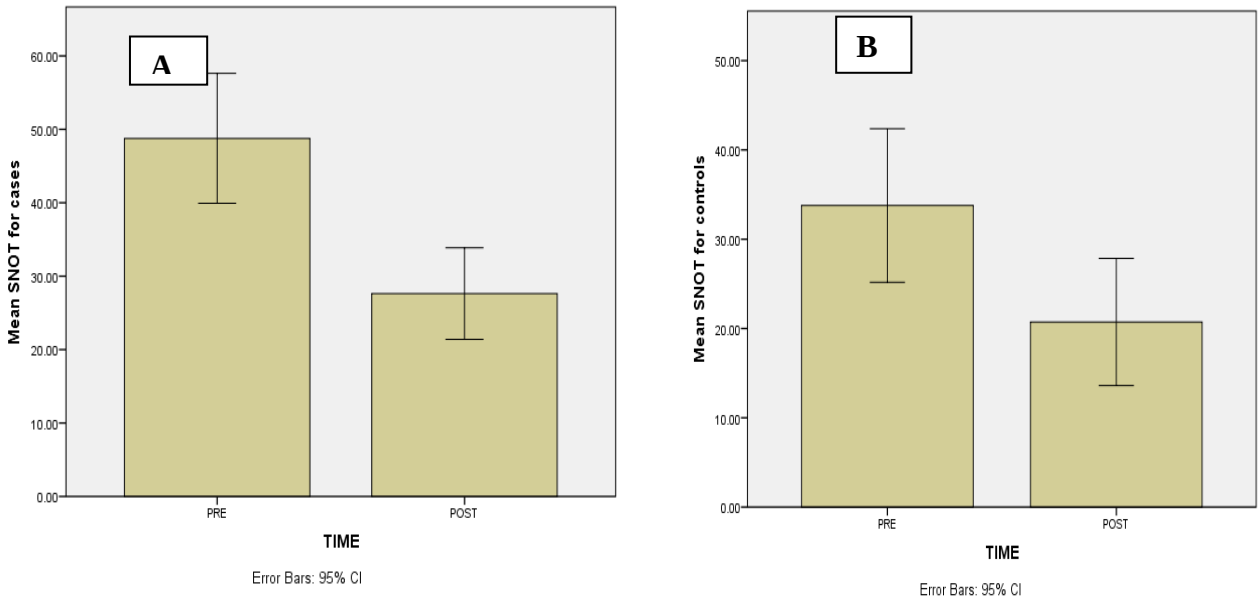


Figure 7: Baseline and post-treatment snot scores for study and control groups.

SNOT score at baseline for the study group had a mean score of 48.8±20 while SNOT at baseline for controls had a mean score of 33.2±19.5.The SNOT scores were significantly different between the study and control groups at baseline P=0.02.

For both the study and control groups, the mean SNOT scores at the end of the 28days were lower than at the beginning at 27.6±14.1 and 20.27±16.1 respectively, However, the difference was not significant, p=0.14 .

When SNOT-20 scores over the 28 day period were modeled, the time-averaged decrease (improvement) in SNOT-20 scores from baseline was 21.1 ± 14.7(CI: 10.6 to 31.6, P<0.001) for the study and 13.0 ± 12.7 (CI: 2.2 to 23.9, P=0.02) for control groups with a difference of 8.1 (p=0.04). The magnitude of treatment effect quantified by Cohen coefficient was 0.63.

Table 3: **The mean improvement in individual domains from baseline in the control and study groups**

DOMAINS	MEAN IMPROVEMENT		P-VALUE
	STUDY	CONTROL	
Rhinologic	5.2	4.4	0.53
Ear and face	2.0	1.9	0.9
Psychological	8.3	4.4	0.06
Sleep dysfunction	3.2	1.6	1.12
Cough	0.9	0.3	0.13
Wake up tired	1.5	0.6	**0.02**

The mean improvement from baseline in the groups who woke up tired was of statistical significance in both the study and control groups.

4.3 Compliance

The median compliance was 96.4% (IQR: 88.4 to 99.1). Most of our study group were compliant to their nasal irrigation. However, upon linear regression analysis, no significant linear relationship was found between compliance and SNOT scores after 28 days (P=0.052, β=0.43).

4.4 Side Effects of Treatment in the Study Group.

Table 4: Baseline and post-treatment Side effects in the study group

SIDE EFFECTS	BASELINE	POST-TREATMENT	X^2	0r	95% CI	P-VALUE
Burning sensation	0(0.0%)	5(22.7%)	5.64	----	----------	0.05
Dizziness	0(0.0%)	2(9.1%)	2.10	-----	----------	0.49
Tearing	1(4.5%)	2(9.1%)	0.36	2.1	0.18-25.01	1.00
Nasal bleeding	0(0.0%)	1(4.5%)	1.02	-----	----------	1.00
Nasal Irritation	0(0.0%)	5(22.7%)	5.64	----	----------	0.05
Headache	6(27.3%)	8(36.4%)	0.49	1.52	0.42-5.47	0.75
Nasal drainage	8(36.4%)	19(86.4%)	11.60	11.08	2.48-49.06	**0.002**

When comparing a group of known side effects at baseline and post-treatment, nasal drainage was the only statistically significant side-effect that was noted.

5.0 CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

The aim of this study was to determine the effect of nasal saline irrigation in patients with CRS as an adjunct treatment. This study shows an improvement of the total SNOT-20 scores at the end of the study in both groups i.e. 48.8 ± 20 to 27.6 ± 14.1 in the study and 33.2 ± 19.5 to 20.27 ± 16.6 in the control arm. This shows that in both groups the intervention given was appropriate for the disease. On analysis of the extent of improvement of total SNOT-20 scores from baseline to the end of the study, both the study and control groups had shown statistically significant improvement of 21.1 and 13.0 respectively though the study group had improved more compared to the controls $p<0.001$ and $p=0.02$ respectively. Due to the statistically significant difference between the baseline values, the cohen coefficient was used to check the magnitude of treatment effect.

The magnitude of effect of saline was noted to be of moderate impact. These findings are in keeping with a community based randomized control trial on nasal saline irrigation for chronic sinonasal symptoms done by Pynnonen comparing isotonic saline nasal irrigation to saline nasal spray [(16)]. They found an improvement of 8.2 points that was statistically significant ($p= 0.001$) at 4 weeks on using saline irrigation. These results are also in keeping with the study done by Nguyen on participants with allergic rhinitis using isotonic saline for 4 weeks in which mini-rhinoconjuctivitis quality of life questionnaire was used to collect data and found a decrease from 36.7 ± 20.48 to 14.9 ± 11.03 at 4 weeks with a p value of 0.001 [(18)]. Nguyen's study however was prospective cross-sectional study whereby the patients were initially treated with 30 day intranasal corticosteroid then those who did not improve were started on isotonic saline irrigation and the intranasal steroids. Rabago in 2002 did a randomized controlled trail on the use of hypertonic buffered nasal saline irrigation over a 6 month period [(17)].

They used Rhinosinusitis disability index (RSDI) and single item sinus symptom severity assessment (SIA) to collect the data. Despite showing improvement at the 1.5month point the participants did not have statistically significant improvement. On comparing the extent of improvement of the individual domains from baseline to the 28th day, both the study and control groups had clinically significant improvement with the study group having a more marked improvement which was in keeping with the improvement in the total scores. The wake up tired group though had a statistically significant difference with the study group

being more marked. This may be due to the use of NSI in the evening as it is known to help wash out debris, reduce inflammation, cause vasoconstriction and its osmotic effect on the nasal mucosa thus reducing the edema and clearing out the secretion and debris that may cause crusting and so increase airflow during sleep. This is supported by a randomized control trial, double blinded done by Hauptman et al who found improved mucociliary clearance from 178 to 128 seconds, and an increased nasal patency on instilling (physiologic) isotonic saline drops [27].

This study reports a higher compliance of 96.4% to the saline irrigation as compared to the findings by Rabago et al of 87% during the 6 month period of the study and the findings of Pynnonen et al of 81% over the 4 week period [16,22]. Hong did a prospective study on nasal lavage of pediatric patients and found a good compliance rate of 67% despite the complaints of the procedure being cumbersome and the age of the participants [23]. Despite the high compliance noted in this study, there was no demonstrable relationship between the good compliance and symptom improvement across the board, therefore no comparison could be made.

A group of the most common side-effects previously reported by various studies was used in our analysis. On comparing before and after irrigation, nasal drainage was found to have increased significantly after the use of saline with an Odds ratio of 11.08 (CI 2.48-49.06).Therefore nasal drainage can be fully attributed to the saline irrigation. This is in keeping with the findings by Pynnonen et al [16]. Despite the side effects experienced by the participant none of them discontinued the NSI which is a finding in keeping with other clinical trials done to assess the same. It can therefore be concluded that the side effects were not very serious.

5.2 Conclusion

Nasal saline irrigation is an important adjunct in the care of patients with chronic rhinosinusitis, improving symptoms more than the use of intranasal steroid only. It is safe with minimal side effects and well tolerated.

5.3 Recommendations

Clinicians should encourage regular use of isotonic nasal saline irrigation at high volume and low pressures as adjunct treatment in the management of chronic rhinosinusitis.

TIMELINE

PERIOD	ACTIVITY
July to December 2017	Proposal writing
January to May 2018	Proposal presentation
June to March 2019	Ethical approval and corrections
April 2019 to September 2019	Data collection and analysis
October 2019 to December 2019	Thesis write up
March 2020	Result presentation

BUDGET

This study was financed by the primary investigator.

	ITEM	UNIT NUMBER	COST (Kenyan Shillings)	TOTAL COST (Kenyan Shilling)
1.	20 CC Syringe	50	20	500
2.	500ml normal saline	450	70	31,500
3.	Compliance diary	25	50	2,600
4.	Envelopes	50	5	250
5.	Printing	700	10	7000
6.	Carrier bags	25	300	7500
7.	Statistician			25,000
	Total			**74,350**

REFERENCES

1. Huntzinger A. Guidelines for the diagnosis and management of rhinosinusitis in adults. Am Fam Physician. 2007;76(11):1718-1724.
2. Anand V K. Epidemiology and economic impact of rhinosinusitis. The Annals of otology, rhinology & laryngology Supplement. 2004;193:3-5.
3. Iseh K R and Makusidi M. Rhinosinusitis: a retrospective analysis of clinical pattern and outcome in Northwestern Nigeria. Annals of African medicine. 2010;9(1):20-26.
4. Charles G. The prevalence of allergic rhinitis in college students at Kenya Medical College Nairobi [Dessertation]: University of Nairobi; 2006.
5. Thomas M, Yawn B P, Price D, et al. EPOS Primary Care Guidelines: European Position Paper on the Primary Care Diagnosis and Management of Rhinosinusitis and Nasal Polyps 2007 - a summary. Primary care respiratory journal: journal of the General Practice Airways Group. 2008;17(2):79-89.
6. Furatenberg W M. The treatment of acute nasal accessory Sinus disease. Annals of Otology, Rhinology & Laryngology. 1938;4(47):902-909.
7. Lubbe D. Rhinosinusitis: Management guidelines in South Africa. Africa Journal online. 2009, vol.27(8)
8. http://pedimedicine.com/anatomy-nose-nasal-paranasal-sinus/ (accessed on 10/09/2017)
9. https://www.cancer.gov/types/head-and-neck/patient/adult/paranasal-sinus-treatment-pdq (accessed on 10/09/2017)
10. https://entokey.com/surgical-anatomy-of-the-paranasal-sinus/ (accessed 5/01/2020)
11. http://www.med.unc.edu/cemalb/mucociliaryclearance/images/RetentionGraph.jpg/@@images/311c8f3d-de26-4198-a724-6a8d0063445c.jpeg (accessed on 12/2/2017)
12. https://openi.nlm.nih.gov/imgs/512/217/3199796/PMC3199796_CTO-03-02-g-006.png. (12/10/2017)
13. Pynnonen M A, Kim H M, Terrell J E. Validation of the Sino-Nasal Outcome Test 20 (SNOT-20) domains in nonsurgical patients. American journal of rhinology & allergy. 2009;23(1):40-45.
14. Bezerra T F, Piccirillo J F, Fornazieri M A, et al. Cross-Cultural Adaptation and Validation of SNOT-20 in Portuguese. International journal of otolaryngology. 2011;2011:306529.

15. Olson D E, Rasgon B M, Hilsinger R L. Radiographic comparison of three methods for nasal saline irrigation. The Laryngoscope. 2002;112(8 Pt 1):1394-1398.
16. Pynnonen M A, Mukerji S S, Kim H M, et al. Nasal saline for chronic sinonasal symptoms: a randomized controlled trial. Archives of otolaryngology-Head & neck surgery. 2007;133(11):1115-1120.
17. Rabago D, Pasic T, Zgierska A, et al. The efficacy of hypertonic saline nasal irrigation for chronic sinonasal symptoms. Otolaryngology-Head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2005;133(1):3-8.
18. Nguyen S A, Psaltis A J, Schlosser R J. Isotonic saline nasal irrigation is an effective adjunctive therapy to intranasal corticosteroid spray in allergic rhinitis. American journal of rhinology & allergy. 2014;28(4):308-311.
19. Shoseyov D, Bibi H, Shai P, et al. Treatment with hypertonic saline versus normal saline nasal wash of pediatric chronic sinusitis. The Journal of allergy and clinical immunology. 1998;101(5):602-605.
20. Bonnomet A, Luczka E, Coraux C, et al. Non-diluted seawater enhances nasal ciliary beat frequency and wound repair speed compared to diluted seawater and normal saline. International forum of allergy & Rhinology. 2016;6(10):1062-1068.
21. Inanli S, Ozturk O, Korkmaz M, et al. The effects of topical agents of fluticasone propionate, oxymetazoline, and 3% and 0.9% sodium chloride solutions on mucociliary clearance in the therapy of acute bacterial rhinosinusitis in vivo. The Laryngoscope. 2002;112(2):320-325.
22. Rabago D, Zgierska A, Mundt M, et al. Efficacy of daily hypertonic saline nasal irrigation among patients with sinusitis: a randomized controlled trial. The Journal of family practice. 2002;51(12):1049-1055.
23. Hong S D, Kim J H, Kim H Y, et al. Compliance and efficacy of saline irrigation in pediatric chronic rhinosinusitis. Auris, nasus, larynx. 2014;41(1):46-49.
24. Marlies N, Giovanni T, Frido W D et al. Sample size calculations: basic principles and common pitfalls. Nephrol Dial Transplant. 2010 25:1388-1396
25. https://www.randomizer.org/about/ (Accessed 15/2/2018)
26. https://developer.mozilla.org/en-S/ docs /Web / JavaScript / Reference /Global_Objects / Math / random (Accessed on 15/2/2018)

27. Hauptman G, Ryan M. The effect of saline solutions on nasal patency and mucociliary clearance in rhinosinusitis patients. Otolaryngology-Head and neck surgery.2007;137(5):815-821.

APPENDICES

Appendix I: American Association of Otorhinolaryngology Head and Neck Surgeons; Diagnosis of Chronic Rhinosinusitis

CHRONIC RHINOSINUSITIS (CRS)	**Twelve weeks or longer of two or more of the following signs and symptoms**
	• *mucopurulent drainage (anterior, posterior, or both),*
	• *nasal obstruction (congestion),*
	• *facial pain-pressure-fullness, or*
	• *Decreased sense of smell.*
	And inflammation is documented by one or more of the following findings:
	• *Purulent (not clear) mucus or edema in the middle meatus or anterior ethmoid region*
	• *Polyps in the nasal cavity or in middle meatus, and or*
	• *Radiographic imaging showing inflammation of the paranasal sinuses.*

Appendix II: Consent form (English version)

General Patient Information

Participant Study number:

Study Title: THE ROLE OF NASAL SALINE IRRIGATION ON CHRONIC RHINOSINUSITIS IN ADULT PATIENTS AT KENYATTA NATIONAL HOSPITAL.

Principal Investigator: Dr. Meimuna.W. Adan (Postgraduate student in Ear Nose and Throat Surgery, University of Nairobi)

Supervisors: - Prof. Isaac M. Macharia

-Dr. Mwanisa Omutsani M

Introduction

Chronic Rhinosinusitis is a very common nasal disease and is associated with social and economic burden. Many parts of the world are currently using Nasal saline irrigation as part of the treatment of this disease to control its symptoms.

You are requested to participate in a research study that seeks to determine whether the use of saline irrigation has an effect on both the patient and the symptoms of the disease in the Kenyan setting.

We ask that you read this form and ask any questions that you may have before agreeing to participate in this study.

Purpose of the Study

The purpose of this study is to determine whether the use of saline nasal irrigation has any effect on both the patient and on the symptoms of chronic rhinosinusitis in patients that attend the ENT clinic at Kenyatta national hospital. The results of this study will be used to guide medical management of patients with this disease.

Description of the Study

Once you have accepted to participate in this study, you will be allowed to ask any questions in regards to the study and raise any concerns you may have. Once you are satisfied with the answers you have received you will select an opaque envelope that contains a consent form which you will sign. The opaque envelope also contains a randomly pre-assigned group which you will belong to for the purposes of this study. You may be in the study group which means you will need to do nasal irrigation twice a day for 28days (the procedure is described in the booklet) in addition to using your normal treatment and you will also need to fill in the provided booklet on a daily basis preferably. Alternatively, you may be in the control group, which means you will only continue with your normal treatment. On the 28th day, you will all

be required to come back to the clinic to fill in another questionnaire and submit the booklet if you were in the study group. You will be expected to avail information about your disease and take the prescribed treatment.

Risks involved

Saline nasal irrigation has been shown to have minimal side effects if any. As such it is safe to use. You may experience some nasal discomfort that will resolve after continued use. Very rarely may one develop severe bleeding from the nose that may need medical attention.

Benefit of participating

Information from this study will shed light on how to manage this disease in Kenya and lay a foundation for further studies to better control symptoms of the disease.

Confidentiality

All the information we obtain from you will be kept confidential.

Payments

As a participant, you will not bear the cost of any materials needed for the study. Since saline nasal irrigation is part of standard management of chronic rhinosinusitis and is in the guidelines for management of this disease in other parts of the world, you will be expected to bear the financial burden of the side effects experienced if any.

Use of Information (data) collected.

Like any other scientific information, we will seek to share our findings with other doctors in Kenya and the rest of the world.

Rights as a Participant

Participation in the study is voluntary. Once inducted in the study, you can choose to discontinue at any time without being penalized. Your care will continue as usual.

You may ask any questions about this study at any given time. Feel free to contact the principal investigator using the contact details provided.

Investigators Declaration

I as the principal investigator declare that no financial payments were received by the principal investigator, supervisor nor Kenyatta National Hospital from any pharmaceutical companies or any other quarter to finance this study.

Principal Investigator

Dr. Meimuna.W. Adan

ENT resident

Phone number0721-596 644

Email: munmun.adan@gmail.com

Supervisors

Prof; Isaac M. Macharia.

Professor and Consultant ENT-Head and Neck surgeon,

Department of Surgery, University of Nairobi.

Dr. Mwanisa Omutsani M.

Consultant ENT-Head and Neck surgeon (KNH)

If you have any questions on your rights as a participant contact the *Kenyatta National Hospital Ethics and Research Committee (KNH-ERC)* by calling *2726300 Ext. 44355.*

Consent Certificate

Your participation in this study is entirely voluntary

I…….. Participant study number…… do hereby consent to be included in this study on the effects of isotonic nasal saline irrigation on chronic rhinosinusitis symptoms in adult patients at Kenyatta national hospital.

The nature of the study has been fully explained to me by Dr ……...…….

I have not been promised any material gain to participate.

Signed……..……. (Self) Date……

Appendix III: Fomu ya Idhini (Consent form- Swahili Version)

Maelezo ya utafiti

Maada: Athari ya umwagiliaji wa maji ya chumvi kwa ugonjwa wa sinus kufura kwa wagonjwa wa hospitali kuu ya Kenyatta.

Mtafiti: Dr. Meimuna .W. Adan, resident in ENT head and neck surgery.

Kianzilishi:

"Chronic rhinosinusitis" ugonjwa unaojulikana wa "rhinologic" na unahusishwa na mzigo wa kiuchumi na kijamii. Ningependa ushiriki katika utafiti wa kubaini adhari ya matumizi ya umwagiliaji wa maji ya chumvi kwa mgonjwa na kwa dalili za ugonjwa huo. Taifa nyingi zinatumia mbinu ya maji ya chumvi kutibu ugonjwa huu.

Tunakuomba usome fomu hii na uulize maswali yoyote ambayo unaweza kuwa nayo kabla ya kukubali kushiriki katika utafiti huu.

Madhumuni ya utafiti:

Kusudi la utafiti huu ni kuthibitisha matokeo ya umwagiliaji wa maji ya chumvi katika hali ya sinusitis ya muda mrefu kwa wagonjwa ambao huhudhuria kliniki ya ENT katika Hospitali ya Taifa ya Kenyatta. Majibu ya utafiti huu utasaidia katika mwelekeo bora wa kutibu wagonjwa hawa.

Ufafanuzi na mbinu za utafiti huu:

Pindi utakapokubali kuhusika katika utafiti huu, utakubaliwa kuuliza maswali yoyote kuhusu utafiti huu. Ukikubali kuhusika katika utafiti huu, utachagua bahasha itakayokuwa na fomu la kukubalu kushiriki. Itabidi ujaze hilo fomu. Bahasha pia itakutenga katika tengo aina mbili. Tengo moja itakuhitaji kusafisha pua na maji la chumvi mara mbili kwa siku kwa kipindi cha siku 28. Katika huo mud utatakikana kujaza kitabu cha kuonyesha unaosha pua. Pia utaendelea kutumia matibabu yako ya kawaida ya kutibu ugonjwa huu. Katika tengo la pili utajaza tu fomu la kukubali kushiriki na fomu la kwanza. Vitengo vyote viwili vitatakikana kirudi cliniki katika siku la 28 na kujaza fomu la mwisho na kurudisha kitabu ulichopewa. Utafiti utakuwa kwa muda wa siku 28.

Hatari zinazohusika:

Umwagiliaji wa maji ya chumvi katika pua umeonekana kuwa salama kutumika. Lakini unaeza pata mwasho katika pua ambayo huisha ukiendelea kutumia maji hili. Athara kubwa ambayo ni kuvuja damu katika pua ni nadra sana.

Faida za kuhusika katika utafiti huu:

Matokeo ya utafiti huu utatumika kuboresha matabibu ya ugonjwa huu wa "chronic rhinosinusitis". Huu utafiti pia utatumika kama msingi wa utafiti zitakazofanyika siku za usoni**.**

Hali ya usiri:

Maelezo yote kuhusu mgonjwa yatawekwa katika hali ya siri.

Malipo:

Hakuna malipo utakayotakikana kutoa ya utafiti huu. Kwa sababu maji ya chumvi hutumika katika ugonjwa huu, malipo ya hospitali kwa tiba la athara kubwa itakuwa kwako.

Unahaki ya kukataa na pia kujiaondoa katika kushiriki. Uamuzi kushiriki katika utafiti huu ni wako. Kukataa kwako kushiriki haina athari zozote, na matibabu yako yataendelea kama kawaida**.**

Hali ya kuuliza maswali:

Unahaki ya kuuliza maswali yoyote yale wakati wowote kuhusu utafiti huu na utajibiwa na mtafiti mkuu. Waweza kuwasiliana nami kupitia anwani za mawasiliano yaliyopewa.

Kibali cha Utafiti

Sahihi yako itaonyesha ya kuwa umekubali kushiriki katika utafiti huu kwa hiari yako na kuwa umesoma na kuelewa maelezo uliyopewa hapo juu.

Tamko

Mtafiti mkuu wa huu utafiti, wahusika na Hospitali kuu cha Kenyatta haijapewa pesa au mali yoyote na waundaji wala wauzaji wa madawa yeyote.

Mtafiti mkuu.

Dr. Meimuna.W. Adan

ENT resident

Phone number 0721-596 644

Email: munmun.adan@gmail.com

Wasimamizi

Prof; Isaac.M. Macharia.

Professor and Consultant ENT-Head and Neck surgeon,

Department of Surgery, University of Nairobi.

Dr. Mwanisa Omutsani.M.

Consultant ENT-Head and Neck surgeon,

Kenyatta National Hospital.

Ukiwa na swali yoyote waweza kuuliza wakati wowote *Kenyatta National Hospital Ethics and Research Committee (KNH-ERC)* kupitia nambari *2726300 Ext. 44355.*

Cheti cha Idhini:

Mimi (Jina la mshiriki) ……..…

Kutoka …….nimekubali kushiriki katika utafiti huu. Nimeelezewa kwa ubayana kinachohusu utafiti huu na Daktari…….

Sahihi ya mgonjwa…….…….. Tarehe……

Sahihi ya mtafiti……... Tarehe……

Appendix IV: Sino Nasal Outcome Test (SNOT-20)

Study participant no: ……..

I.D.:_____ **SINO-NASAL OUTCOME TEST (SNOT-20)** DATE:_____

Below you will find a list of symptoms and social/emotional consequences of your rhinosinusitis. We would like to know more about these problems and would appreciate your answering the following questions to the best of your ability. There are no right or wrong answers, and only you can provide us with this information. Please rate your problems as they have been over the past two weeks. Thank you for your participation. Do not hesitate to ask for assistance if necessary.

1. Considering how severe the problem is when you experience it and how frequently it happens, please rate each item below on how "bad" it is by circling the number that corresponds with how you feel using this scale: →	No problem	Very mild problem	Mild or slight problem	Moderate Problem	Severe Problem	Problem as bad as it can be	5 Most Important Items
1. Need to blow nose	0	1	2	3	4	5	○
2. Sneezing	0	1	2	3	4	5	○
3. Runny nose	0	1	2	3	4	5	○
4. Cough	0	1	2	3	4	5	○
5. Post-nasal discharge	0	1	2	3	4	5	○
6. Thick nasal discharge	0	1	2	3	4	5	○
7. Ear fullness	0	1	2	3	4	5	○
8. Dizziness	0	1	2	3	4	5	○
9. Ear pain	0	1	2	3	4	5	○
10. Facial pain/pressure	0	1	2	3	4	5	○
11. Difficulty falling asleep	0	1	2	3	4	5	○
12. Wake up at night	0	1	2	3	4	5	○
13. Lack of a good night's sleep	0	1	2	3	4	5	○
14. Wake up tired	0	1	2	3	4	5	○
15. Fatigue	0	1	2	3	4	5	○
16. Reduced productivity	0	1	2	3	4	5	○
17. Reduced concentration	0	1	2	3	4	5	○
18. Frustrated/restless/irritable	0	1	2	3	4	5	○
19. Sad	0	1	2	3	4	5	○
20. Embarrassed	0	1	2	3	4	5	○

2. Please mark the most important items affecting your health (maximum of 5 items)_____ ↑

PROCEDURE:

1. Wash your hand with clean water and soap.
2. Ensure the saline solution is of clear fluid with no particles and unopened then Pour half of the content of the saline solution into the clean bowl. This will be the portion used for the day.
3. Store the remainder of the saline in a clean place. One bottle of saline to be used in two (2) days.
4. Divide the saline in the bowl in 2 using one portion in the morning and the other in the evening.
5. Withdraw 20ml of saline with the 20cc syringe.
6. Either in a bathroom standing or standing near a sink with your head tilted to the opposite side squirts the saline into one nostril at one go.
7. Make sure the tip of the syringe is inside your nostril, angulated toward the middle outer nose and downwards.
8. Make a 'kkkkk' sound during the procedure to avoid saline going onto your throat.
9. Repeat this process 5 times in each nostril. Total of 100ml of solution.
10. Discard the remaining fluid in the bowl.
11. You may take a break in-between the irrigation for a few seconds to minutes if you feel dizzy or tired during the procedure.
12. Repeat this process (5 to 11) twice daily i.e. in the morning and evening.

NB:

a) The solution should be warmed to approximately body temperature by putting the bottle in preheated water and leaving it for a few minutes before use.

b) Any remaining saline should be stored in a clean, dry place.

c) After use, the syringe should be washed with utensil detergent rinsed thoroughly with clean water and stored in a clean dry container stored for the next use.

d) Please note the saline solution is harmless to your health, swallowing the fluid should not give you adverse effects. If you are hypertensive due to the salt content avoid swallowing the fluid. You may experience some burning sensation in the nose and throat, and dripping of the fluid from the back of your throat or the front. Mild staining with blood may also occur. These sensations usually subside within a few days of doing the procedure. Please do not be alarmed. In case of severe unbearable pain or severe bleeding from the nose discontinue the procedure, note the date of

discontinuation on the compliance diary and the reason for stopping treatment and contact the principal investigator using telephone number below as soon as possible.

e) For any clarifications or concerns please call the number provided.

Thank you.

Contact Information:

Dr. Meimuna. W. Adan

Tel; 0721596744, **Email**: munmun.adan@gmaol.com

Compliance Questionnaire

Please write the date you do the procedure in the box provided. Put a tick✓ **in** the box provided if the procedure is done and ✕ if not done. In case you are unable to continue the treatment please indicate the date last procedure was done and the reason for discontinuing treatment.

Tafadhali weka alama ya ✓ unapotumia maji ya chumvi katika pua na alama ya ✕ unapokosa kutumia maji ya chumvi katika sanduku mwafaka ya hiyo siku.

DATE OF IRRIGATION/ TAREHE YA UMWAGILIAJI MAJI YA CHUMVI KWA PUA.		MORNING IRRIGATION/ ASUBUHI	EVENING IRRIGATION/ JIONI
Day 1.			
Day 2.			
Day 3.			
Day 4.			
Day 5.			
Day 6.			
Day 7.			
Day 8.			
Day 9.			
Day 10.			
Day 11.			
Day 12.			
Day 13.			
Day 14.			
Day 15.			

Day 16.			
Day 17.			
Day 18.			
Day 19.			
Day 20.			
Day 21.			
Day 22.			
Day 23.			
Day 24.			
Day 25.			
Day 26.			
Day 27.			
Day 28.			

Date stopped (Tarehe ya kusimamisha)……..

Reason for stopping irrigation (Sababu ya kuwacha matumizi ya mbinu hii ya matibabu)

……

……

……

……

Appendix VI: Questionnaire on Side Effects

Each row represents a day of the intervention and each column represents a side effect. If a symptom is experienced on a particular day, please put a **YES** in the appropriate box. If the symptom is not experienced, indicate with the word **NO**. Please ensure all the boxes are filled.

Kila mstari inawakilisha siku na kila safu inawakilisha athari unayopata. Kama umepata adhari iliyoko katika hiyo siku tafadhali weka **YES** katika sanduku mwafaka. Usipopata athari hiyo jaza neno **NO** katika sanduku inayofaa. Tafadhali hakikisha sanduku zote zimejazwa.

EXAMPLE 1: Participant A had tearing on day 1, headache and tearing on day 2 and all symptoms on day 3.

MFANO 1: Mshiriki A alipata adhari ya kutokwa na machozi siku ya kwanza, siku ya pili alipata maumivu ya kichwa na kutokwa na machozi, siku ya tatu alipata adhari yote iliyotajwa hapa.

DAY/ SIKU	SIDE EFFECTS OF NASAL SALINE IRRIGATION/ MADHARA YA UMWAGILIAJI MAJI YA CHUMVI KWA PUA.						
	BURNING SENSATION/ KUHISI KUCHOMEKA	NASAL BLEEDING/ KUTOKWA NA DAMU KWA PUA	TEARING/ KUTOKWA NA MACHOZI	NASAL IRRITATION/ MWASHO KWA PUA	HEADACHE/ MAUMIVU YA KICHWA	NASAL DRAINAGE/ PUA MAJIMAJI	DIZZINESS/ KUHISI KIZUNGUZUNGU
1	NO	NO	YES	NO	NO	NO	NO
2	NO	NO	YES	NO	YES	NO	NO
3	YES	YES	YES	YES	YES	YES	YES

Have you experienced any of the symptoms mentioned below while using the Saline nasal irrigation?

1. Je, umepata adhara yoyote ya umwagiliaji maji ya chumvi kwa pua iliyotajwa hapa?

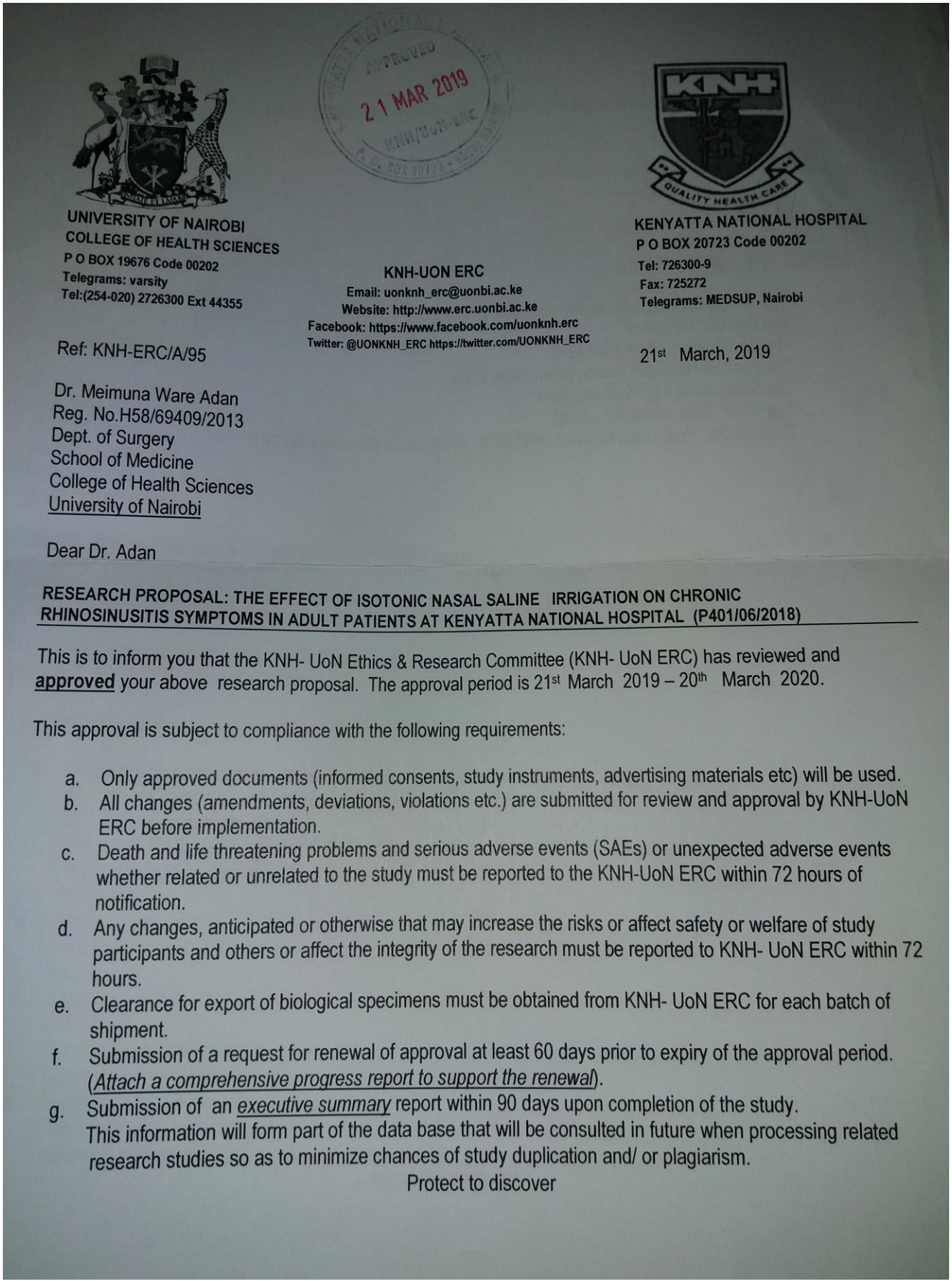
DAY/ SIKU	SIDE EFFECTS OF NASAL SALINE IRRIGATION/ MADHARA YA UMWAGILIAJI MAJI YA CHUMVI KWA PUA.						
	BURNING SENSATION/ KUHISI KUCHOMEKA	NASAL BLEEDING/ KUTOKWA NA DAMU KWA PUA	TEARING/ KUTOA MACHOZI	NASAL IRRITATION/ MWASHO KWA PUA	HEADACHE/ MAUMIVU YA KICHEA	NASAL DRAINAGE/ PUA MAJIMAJI	DIZZINESS/ KUHISI KIZUNGUZUNGU
1.							
2.							
3.							
4.							
5.							
6.							
7.							
8.							
9.							
10.							
11.							
12.							
13.							
14.							
15.							
16.							
17.							
18.							
19.							
20.							
21.							
22.							
23.							
24.							
25.							
26.							
27.							
28.							

Appendix VII: Modified AAO-HNS CRS Diagnostic Criteria:

To be filled by the primary investigator for each participant.

DIAGNOSIS OF CHRONIC RHINOSINUSITIS		
PARTICIPANT STUDY NUMBER: ……		
Twelve weeks or longer of two or more of the following signs and symptoms	**PRESENT**	**ABSENT**
mucopurulent drainage (anterior, posterior, or both),		
nasal obstruction (congestion),		
facial pain-pressure-fullness, or		
Decreased sense of smell.		
And inflammation is documented by one or more of the following findings:		
Purulent (not clear) mucus or edema in the middle meatus or anterior ethmoid region		
Polyps in the nasal cavity or in middle meatus, and or		
Radiographic imaging showing inflammation of the paranasal sinuses		

Appendix VIII: KNH/UON ERC Approval



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

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

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

APPROVED 21 MAR 2019 KNH/UON ERC P. O. BOX 20774 - 00202 NAIROBI

Ref: KNH-ERC/A/95

21st March, 2019

Dr. Meimuna Ware Adan
Reg. No.H58/69409/2013
Dept. of Surgery
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Adan

RESEARCH PROPOSAL: THE EFFECT OF ISOTONIC NASAL SALINE IRRIGATION ON CHRONIC RHINOSINUSITIS SYMPTOMS IN ADULT PATIENTS AT KENYATTA NATIONAL HOSPITAL (P401/06/2018)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 21st March 2019 – 20th March 2020.

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 serious 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. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. 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*).
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.

Protect to discover

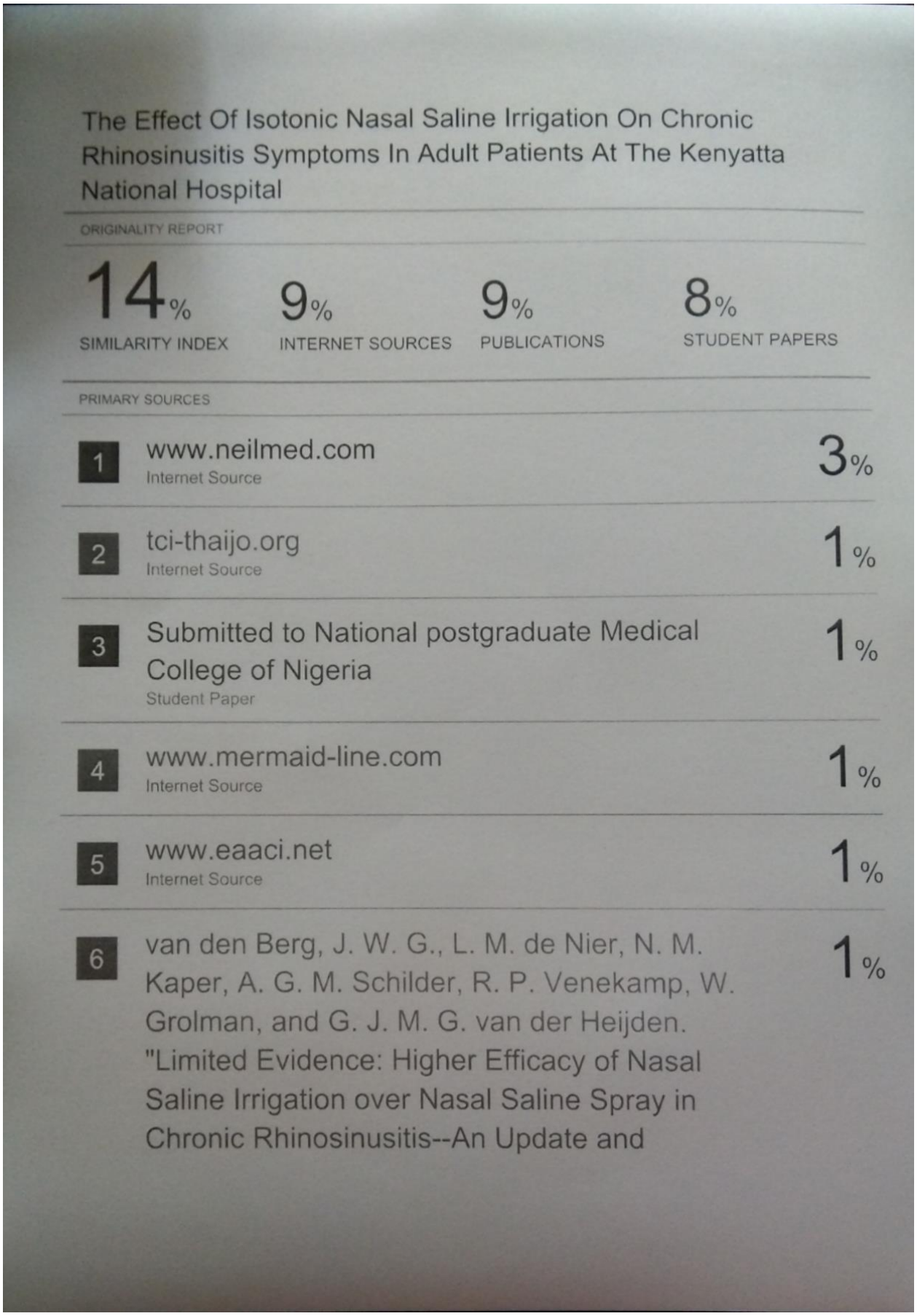
For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Surgery, UON
Supervisors: Prof. Isaac M. Macharia(UON), Dr.Mwanisa Omutsani M(KNH)

Appendix IX: Anti-Plagiarism Certificate



The Effect Of Isotonic Nasal Saline Irrigation On Chronic Rhinosinusitis Symptoms In Adult Patients At The Kenyatta National Hospital

ORIGINALITY REPORT

14%	9%	9%	8%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.neilmed.com Internet Source	3%
2	tci-thaijo.org Internet Source	1%
3	Submitted to National postgraduate Medical College of Nigeria Student Paper	1%
4	www.mermaid-line.com Internet Source	1%
5	www.eaaci.net Internet Source	1%
6	van den Berg, J. W. G., L. M. de Nier, N. M. Kaper, A. G. M. Schilder, R. P. Venekamp, W. Grolman, and G. J. M. G. van der Heijden. "Limited Evidence: Higher Efficacy of Nasal Saline Irrigation over Nasal Saline Spray in Chronic Rhinosinusitis--An Update and	1%