University of Nairobi, College of Health Sciences
School of Medicine

ASSESSMENT OF DOSE RELATED RESPONSE OF INTRA-LESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF KELOID SCARS AT KENYATTA NATIONAL HOSPITAL: A CLINIC BASED RANDOMIZED CONTROL STUDY

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DECLARATION

I, **Dr. Were Andrew Onyino,** declare that this thesis is my original work. No part of it has been presented for the award of a degree at any other University.

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DEDICATION

I dedicate this thesis to my late mother Susan Ayoma Were, for instilling in me the value of education and the constant encouragement to complete my masters' education despite the competing needs.

ABBREVIATIONS

DSMB	Data and Safety Monitoring Board
ERC	Ethics and Research Committee
FDA	US Food and Drug Administration
5 FU	5 Fluorouracil
HR	Heart Rate
KNH	Kenyatta National Hospital
PI	Principal Investigator
RA	Research Assistant
RR	Respiratory Rate
SAE	Severe Adverse Event
TAC	Triamcinolone Acetonide
TGF-β	Transforming Growth Factor Beta
TNF	Tumour Necrosis Factor
VEGF	Vascular Endothelial Growth Factor
WHO	World health Organization

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ABSTRACT

Background: Keloids are benign dermal fibro-proliferative disorders that arise as a result of trauma or infection that surpasses the margins of the original lesion. The lesions continue to enlarge over time, pain and itching are the predominant symptoms in these patients. The scars have a high relapse rate after surgical removal and thus alternative non-operative measures are recommended for the primary keloid treatment. Triamcinolone acetonide injection is a first line treatment in the management of this condition and is usually administered through the intra-lesional route. This will ameliorate the symptoms and, in some instances, can lead to remission of the keloid scars. However, there is no agreed dosage per cm^2, duration and frequency of treatment amongst different surgeons. This leaves the patient at the mercy of the surgeon's discretion despite the triamcinolone acetate (TAC) having adverse effects especially if administered in very high dosages. These effects range from abnormally hypo-pigmentation, subcutaneous fat atrophy, telangiectasia, tissue necrosis, ulcerations and cushingoid habitus. Keloids are common in African and Asian communities with very low incidences reported amongst the Caucasians.

Objective: To determine safe, effective dosage of triamcinolone acetate in the management of keloids in African population.

Methodology: This was a randomized control study where patients presenting with keloids at The Kenyatta National Hospital were randomly assigned into three groups each having a minimum of 25 patients. The study arms had either $5mg/cm^2$ or $10mg/cm^2$ intra-lesional TAC injection while the control group had 7.5 mg/cm^2 of TAC administered. The frequency of treatment was a single dose every four weeks for a total of 12 weeks making a total of 3 injections per keloid scar. Treatment outcomes and adverse effects were noted and documented 30 days after each injection. The data were cleaned and uploaded to the SPSS version 21 software for analysis. A $p \leq 0.05$ indicates the rejection of the null hypothesis.

Results: A total of 34 patients who presented with 109 keloids were recruited into the study. Fifty three point eight percent (53.8%) were female and 43.6% were males. Seventy eight point one percent (78.1%) of the study participants were between 18 -40 years, 7.3% between 41-60 years while 9.1% were above 61 years. A decrease in height and surface area of the keloid was noted in all 3 arms of the study. The greatest decrease of height was 2.055 cm (46.58%) seen in the 7.5mg/ml arm followed by 5mg/ml and 10mg/ml arms which recorded a decrease of 1.87 cm

(56.55%) and 1.649cm (49.92%) respectively. The greatest margin reduction in scar size was seen in the 5 mg/ml arm at 2.54 cm^2 followed by 10mg/ml and 7.5mg/ml which had a decrease of 2.16 $cm^2$and 1.81 cm^2 respectively.

The 10mg/ml dosage had the highest decrease of pain at 100% followed by 7.5 mg/ml at 96.98 % and 5mg/ml at 96.80%. There was also a decrease in itchiness of the keloids with the highest decrease seen in the 7.5mg/ml arm at 95.95% followed by 5mg/ml and 10mg/ml arms that had symptomatic decreases of 94.56% and 92.31% respectively.

There was a 20.46% (Poor) reduction in the mean VSS score on Day 30, 35.62% (Good) reduction by Day 60 and 52.95% (Very Good) reduction by Day 90 of the study after 3 injections sessions of TAC.

Adverse effects of TAC occurred across the 3 arms of the study. Under the 5mg/ml arm, 7.69% of the patients had scar ulceration and 2.56% had scar hypo pigmentation occurring. Eight point thirty three percent (8.33%) of the patients under the 7.5mg/ml arm reported scar ulceration with that reporting scar hypo pigmentation being at 2.78%.

The study participants were, generally satisfied with the outcome, with the average rating of their satisfaction at 1.79 on a scale of 1 – 10. Majority of the patients who were most satisfied reported the disappearance of pain, pruritus and softness of the scars as their most improved aspects of their scars.

Conclusion: All the 3-dosage concentration in the study showed improvement in the symptoms, had similar morphological changes and comparable patient satisfaction scores.

1.0: INTRODUCTION

1.1: Background

Keloids are benign dermal fibro proliferative disorders that arise as a result of trauma or infection that extends beyond the margins of the original wound (1). The underlying abnormal wound healing process arises from dys-regulation of the cell proliferation and repair with resultant prolonged inflammatory phase and with a disordered proliferative phase with haphazard lying down of collagen by fibro-blasts grammar (1). They continue to grow overtime with pain and pruritus as the predominant symptoms. These lesions commonly affect the ear lobes, upper back, shoulders and chest. Several theories in formation of keloids have been proposed and include (2):

- Mechanical Stress/Tension theory
- Genetic immune dysfunction
- Sebum reaction/Endocrinological theory
- Tissue hypoxia theory and abnormal epithelial mesenchymal interaction
- Increased hyaluronic acid production

Nang'ole *et al*, in 2019, suggested that the pathogenesis of keloids is as a result of diverse genetic and environmental agents with the inflammatory cells playing a critical role than previously thought (1). They further suggested that inflammatory cells found in high concentration in most histopathology specimens were macrophages, neutrophils, mast cells, Langerhans cells and lymphocytes (4). High levels of cytokines namely Tumour Necrosis Factor (TNF), Interleukin (IL) IL-6 and IL-13 have been implicated in keloid scar formation and proliferation (5). Other growth factors implicated in their formation include Transforming Growth Factor (TGF) beta group and Vascular Endothelial Growth Factor (VEGF).

Transforming Growth Factor beta family is linked to increasing structural protein production in keloid fibro-blasts. In a study by Thian-Sze Wong *et al* in 2016, TGF-β1 treatment stimulates the making of structural proteins in keloid fibro-blasts but not in normal skin fibro-blasts (6).

Histological, increased pile up of ground substance and cell propagation are unique for these lesions with structural protein organized in a random way as opposed to the precise arrangement

of collagen bundles in normal skin or wound (7). Significant type 1 collagen and slightly less type 3 collagen fibres are noted, resulting in a high type 1 to 3 structural protein ratio. An inconsistently arranged degenerated translucent glass-like structural protein bundle with tongue-like infiltration of the uppermost layer of the dermis is seen histological. There is excessive fibro-blasts proliferation with decreased apoptotic rates. Notable too is that individuals with HLA B14, BW16, DR5 and Rh factor A seem to be susceptible to keloids (1, 3, 8).

As a result of increased keloid scar recurrence after surgical removal, non-operative measures are considered as primary therapy. Several therapeutic treatment approaches exist in the market, they include: intra-lesional Triamcinolone Acetonide (TAC) injection, surgical excision, Bleomycin injection, 5Floro-Uracil (5FU), Interferon therapy (IFN), Verapamil, Laser therapy, silicone sheet dressings, radiotherapy, vitamin A derivatives, fujimycin, quinolin-4-amine or polytherapy (9).

Triamcinolone acetonide is the most common non-surgical treatment of Keloids at Kenyatta National Hospital (KNH) Plastic Surgery department. The administered dose varies from 20mg to 60 mg injection per Keloid (9). These dosages are determined arbitrary by the surgeon administering the medication using the size of the keloid as a guide.

1.2: Standard Keloid Scar Management at the Kenyatta National Hospital

When a patient present with a Keloid at the KNH they first go to the Accident and Emergency department where they are reviewed and referred to the Plastic Surgery Clinic for definitive management. Following review and depending on the size, number or location of the keloid, surgical excision or Triamcinolone Acetonide injection instituted every 4 weeks is done until there is resolution of the symptoms of the keloid. Patients who undergo surgical excision normally receive an intra-lesional TAC injection followed by superficial radiotherapy as an adjunct to treatment to prevent recurrence.

Triamcinolone Acetonide is administered at various dosages depending on the size of the keloid per cm^2 diluted with Lidocaine solution at a ratio of 1;1 before injection. The dosage to be administered is determined arbitrarily by the surgeon using the size of the keloid at presentation

as a guide. A study done by Nghi Dinh Huu *et al* demonstrated a higher rate of occurrence of adverse effects when Triamcinolone Acetate was used at a higher dosage of 15mg/cm^2 of keloid surface area compared to when administered at a lower dosage of 7.5mg/cm^2 (3).This demonstrated a direct correlation between the dosage of TAC and occurrence of side effects.

1.3: Study Justification

Triamcinolone acetonide intra-lesional injection is the first line treatment for management of keloids but no standardized treatment protocol exists in terms of the dosage, duration and frequency of injection of the drug(8). TAC dosage for treatment of keloids has been administered at concentration range from 10-40mg/ml (14). Used as mono-therapy, responses range from 50 - 100% and a recurrence rate of 9-50% (5,13). As a result of the variable treatment responses, no standard dosage protocol has been developed and the concentration chosen is left at the discretion of the clinician. Rahban and Garner in their study administered 2 or 3 injections at a dosage of 10mg/ml, approximately 1-2 months apart while Darzi *et al* administered the dosage based on the scar surface area; 1-2 cm^2 received 20-40mg, 2-6cm^2 received 60-80mg and 6-12 cm^2 received 80-120mg with varied outcomes (5,13). The wide range of TAC dosage concentration administered has the risk of causing potential catastrophic adverse effects from injection of the drug especially if it infiltrates the normal surrounding tissues. The adverse effects of the keloid are seen across various dosages with more adverse effects encountered at dosages higher than 7.5 mg/cm^2 according to a study conducted in the Asian population (3). Therefore, there is need to establish the dosage of TAC that can be safely administered with minimal side effect and a favourable outcome to the patient. The study aims to assess the acute outcomes from intra-lesional injection of TAC using three different dosage concentrations of 5 mg/cm^2 and 10mg/cm^2 with 7.5 mg/cm^2 as the control. This will help us determine the effective dosage of TAC in terms of the decrease of the symptoms and regression of the keloid scars surface area in African population and help us develop a standardized treatment protocol that is evidenced based.

1.4: Research Question

Is there a difference in effectiveness when different standard doses of intra-lesional triamcinolone acetonide injection are administered in the treatment of keloids?

1.5: Objectives of the Study

1.5.1: Broad Objective

To determine the dose related response of intra-lesional triamcinolone acetonide injection per cm^2 in treatment of patients with keloids at the Kenyatta National Hospital.

1.5.2 Specific Objectives

1. To determine the effects of TAC on keloids morphology.
2. To determine TAC effect on keloids symptoms.
3. To determine TAC dose related side effects. To determine patient's satisfaction

1.6: Null Hypothesis

There is no statistically observed difference in the treatment outcomes of keloids with administration of 5 mg/cm^2, 7.5mg/cm^2 and 10mg/cm^2 of Triamcinolone Acetonide.

2.0: LITERATURE REVIEW

Intra-lesional triamcinolone acetonide injection is one of the first line treatments in the management of keloids (8). This decrease the symptoms of the keloids and in some instances can lead to remission of the keloid (6). However, there is no agreed upon dosage, duration and frequency of treatment. This leaves the patient at the discretion of the surgeon despite the known adverse effects that range from hypo-pigmentation, skin and sub-coetaneous fat atrophy, telangiectasias, necrosis, ulcerations, and cushingoid habitus (10).

2.1: Pharmacology of Triamcinolone Acetate

Triamcinolone Acetonide is an acetonide salt form of triamcinolone, a synthetic glucocorticosteroid with immune-suppressive and anti-inflammatory activity (10). Triamcinolone acetonide binds to specific cytosolic glucocorticoid receptors and subsequently interacts with glucocorticoid receptor response elements on Deoxyribonucleic Acid to alter gene expression (10). As a result, there is an induction of the synthesis of certain anti-inflammatory proteins while inhibiting the synthesis of certain inflammatory mediators. Consequently, an overall reduction in chronic inflammation and autoimmune reactions are accomplished.

Triamcinolone acetonide is a synthetic glucocorticoid that is the 16,17-acetonide of triamcinolone. It is an 11 beta-hydroxy steroid, a 20-oxo steroid, a 21-hydroxy steroid, a 3-oxo-Delta (11) steroid, a glucocorticoid, a cyclic ketal, a fluorinated steroid and a primary alpha-hydroxy ketone. It is derived from the hydride of a pregnane.

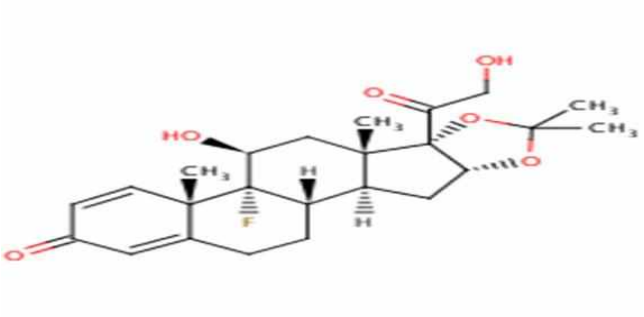


Figure 1: Chemical Structure of Triamcinolone, Adapted from https://www.ebi.ac.uk/chebi/

2.2: Triamcinolone Acetonide effect on Keloid treatment

Triamcinolone acetonide injection is the most commonly used treatment in our set up as mono-therapy or part of combined therapy (8,15-16,20,24,27). Triamcinolone acetonide is a synthetic corticosteroid that exhibits inflammation inhibition and immune-suppression attributes. It acts by inhibiting the phospholipase A2 enzyme on the plasmalemma phospholipid layer, and thus prevents the breakdown of leukocyte lysosomal membranes and the formation of arachidonic acid (12).

It ultimately decreases the expression of cyclooxygenase (COX) and lipoxygenase (LOX) and thus prevents biosynthesis of prostaglandins and leukotrienes, respectively (12). Triamcinolone acetonide manifests anti-inflammatory effects via inhibiting macrophage and leukocyte migration to the affected site by reversing vascular dilation and permeability. These actions lead to reduced oedema, erythema, and pruritus. Another important anti-inflammatory mechanism gets conveyed by the prevention of nuclear factor kappa-B (NF-k-B), which leads to decrease protein expression of interleukin-6 (IL-6), interleukin-8 (IL-8), mono-cytechemo-attractant protein-1 (MCP-1), COX-2 (12).

Triamcinolone acetonide injection works mainly by: limiting the pain, reddening, increased temperature and swelling, reducing fibro-blast growth and proliferation, depriving adequate supply of oxygen and reducing inhibitors of the enzyme that catalyses proteolysis thus allowing the breakdown of peptide bonds in collagen by enzymes (7).

Variable response is seen in treatment of keloids with intra-lesional TAC. Used as mono-therapy, responses range from 50 - 100% and a recurrence rate of 9-50% (5,13). As a result of the variable treatment responses, no standard dosage protocol exists in the market. Rahban and Garner in their study administered 2 or 3 injections at a dosage of 10mg/ml, approximately 1-2 months apart (5). Darzi *et al* administered the dosage based on the scar surface area; 1-2 cm^2 received 20-40mg, 2-6cm^2 received 60-80mg and 6-12cm^2 received 80-120mg with variable outcomes (13).

A study by Nghi Dinh Huu *et al* on intra-lesional TAC in patients with keloids established an optimal dosage of 7.5 mg/cm^2 of scar tissue (3). ·This was a clinical trial with two arms of patients with one being injected 7.5mg/cm^2 and the control being given 15mg/cm2. Injections were given 4 times until there was symptomatic resolution of the symptoms and significant decrease in the scar thickness. The resolution of pain and itching after treatment were 86.6% and 95.5% in the studied group and 78.1% and 80% in the control group ($p< 0.05$) respectively. Cushing syndrome was rare and was mostly encountered in the paediatric group. Patients who received a higher dosage of 15mg/cm^2 had a higher rate of occurrence of side effects for example, acne, ulceration, hypo-pigmentation and disturbances in menstrual cycle (8). Robles *et al* recommended TAC injection to be administered at concentration range from 10-40mg/ml (14). Table 2 shows different dosage regimens as administered by different surgeons the frequency of administration and the duration of the treatment.

Table 1 Dose of TAC used by different authors when using TAC in monotherapy and in combination therapy

Study	TAC dose and/or concentration	Associated treatment	Number of injections	Interval between sessions (weeks)
Rahban and Garner[26]	10 mg/mL	–	2–3	4–8
Darzi et al[27]	10–20 mg/cm^2	–	4	–
Robles et al[9]	10–40 mg/mL	–	Multiple	4
Acosta et al[28]	4–40 mg/mL	–	1–5	4
Ahuja and Chatterjee[37]	40 mg/mL	–	Maximum 8	3
Danielsen et al[38]	1 mg/cm (maximum 5 mg)	Surgical excision (before TAC injection)	4	4
Kant et al[39]	2–4 mg of TAC 40 mg/mL	0.05–0.1 mL of verapamil 2.5 mg/mL	3	Second injection after 1 week, third injection 3 weeks later
Saha and Mukhopadhyay[43]	40 mg/mL	–	Maximum 6	1
Fitzpatrick[45]	1 mg	5-FU 45 mg	5–10	–
Khan et al[46]	4 mg	5-FU 45 mg	8	1
Tan et al[71]	40 mg/mL	–	–	4
Kassab and El Kharbotly[63]	40 mg/mL	980 nm diode laser	2–5	–
Payapvipapong et al[77]	10 mg/mL	–	3	4

Abbreviations: 5-FU, 5-fluorouracil; TAC, triamcinolone acetonide.

Table 1: Dose of TAC used as mono-therapy and combined therapy

2.3: Adverse effects of Triamcinolone Acetonide

The injection of steroid in the lesion may result in both local and systemic adverse side effects. Local side effects include; dark red blotches on the skin as a result of dilated capillaries. Skin and sub-coetaneous fat atrophy, pigment changes (hypo-pigmentation and hyper-pigmentation), skin necrosis and ulceration. Systemic effects include; Cushing's syndrome (15). The danger of local complications is greater with accidental injection of surrounding normal tissue. Cushing's syndrome with adrenal insufficiency associated with intra-dermal corticosteroid injection is rare. Possible complications are usually reported in children, although a few cases were described in adults as well.

3.0: CONCEPTUAL FRAMEWORK

3.1: Narrative

Triamcinolone acetonide direct injection in the lesion is the standard treatment administered in KNH for management of Keloids that are not amenable to surgical excision. Those that are excised also do receive Triamcinolone acetonide injection and superficial radiotherapy as an adjunct treatment to prevent the recurrence of the keloid. There is no standardized treatment dosage regimen for treatment of keloids and most surgeons use their discretion in determining the dosage. This carries the risk of adverse effects or administration of suboptimal dosages. The study will help determine the effective dosage to be administered in the management of keloids in the African population, duration of treatment, and hence develop a uniform treatment regimen for keloids in KNH.

3.2: Diagrammatic Representation

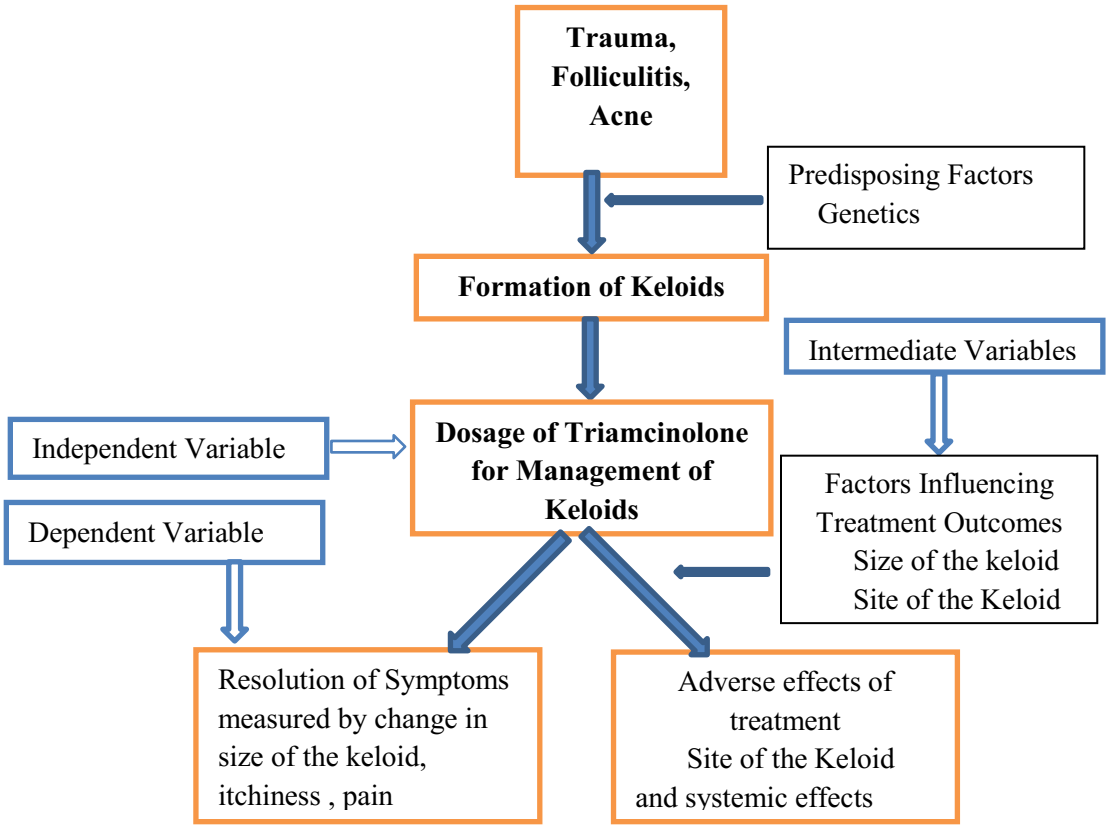


Figure 2: Conceptual Framework

4.0: METHODOLOGY

4.1: Study Design

This was a randomised control study, where the treatment outcomes and side effects of using TAC at a dose of 5 mg/cm^2 and 10mg/cm^2 used in the management of keloids in KNH was investigated. A dosage of 7.5 mg/cm^2 had been established as an effective dosage in a comparative study done by Nghi Dinh Huu *et al* in the Asian population (3) and this served as the control group for the study. This was an interventional study where the TAC was administered by the principal investigator alone to ensure standardization of the intra-lesional injections. The TAC was diluted at a ratio of 1: 1 with Lignocaine to provide an analgesic effect. The TAC administered was procured from a single manufacturer Bristol-Myers Squibb, KENALOG^{TM} injection to ensure uniformity of TAC aqueous suspension chemical and was injected admixed with Lignocaine anaesthetic solution using gauge 21 (green) needle.

The patients who received the TAC intra-lesional injections were observed at Days 30, 60 and 90 after TAC injection outcomes noted and documented for analysis using the Vancouver Scar Scale (15,17-19,21,24,29). The keloid scar size was measured in cm^2 on Day 1 of the treatment with TAC and again at day 30, day 60 and 90 days before each subsequent injection. In total, each keloid was injected 3 times. The principal investigator was blinded from knowing what dosage concentration was administered per cm^2 of each keloid that was recruited and injected with TAC.

4.2: Study Area

The study was carried out at KNH Plastic surgery outpatient clinic where the patients were recruited and KNH Clinic 24 minor theatre where the measurement and injection of the keloids was done for the duration of the Study.

4.3: Study Population

The study population were patients above the age of 18 years who presented to KNH with Keloid. A total of 109 patients were recruited into this study with no dropouts reported.

4.4: Inclusion Criteria

1. Patients presenting with keloid at the Plastic Surgery Outpatient Clinic (PSOC)
2. Patients that needed non-surgical methods of management of the keloids.

3. Patient with recurrent keloids after surgical excision or superficial radiotherapy
4. Patients who have consented

4.5: Exclusion Criteria

1. Patients with known allergy to Triamcinolone Acetonide
2. Patients with known immune-suppressive condition such as Human Immune-deficiency Virus (HIV) or Diabetes Mellitus (DM)
3. Patients with infected Keloids.
4. Pregnant or Lactating mothers
5. Patients who have received intra-lesional TAC injection in the last 6 months.
6. Patients who have not consented to the study

4.6: Sample Size Determination

The sample size was calculated using the formula for calculating sample size for a finite population (500) as shown below. The assumptions of the calculated sample size was generated from a similar study conducted by Nghi Dinh *et al* in Vietnam where using the Henderson's criteria to score the response rate to use of TAC, 86.6% of the patients reported a good outcome (3).

$$n \geq \frac{NZ^2_{1-\alpha/2}p(1-p)}{d^2(N-1)+Z^2_{1-\alpha/2}p(1-p)}$$

Applying the following assumptions in the formula where:

n = sample size per arm

N= Population Size = 150

d= Estimated error, 0.05%

Ṕ =Proportion with complete response based on scar size = 79%

Zα = Value corresponding to the normal standard deviate at 95% C.I in this case = 1.96, with 0.05 level of significance

Applying the assumptions into the formula, the calculated sample size = 25

Number of clusters = 3

The calculated sample size = 75 (25 per arm)

4.7: Sampling & Randomization Procedure

Participants and those assessing the outcomes were blinded to group assignment. Based on simple randomization, participants were assigned to receive either either 5mg/cm^2, 10mg/cm^2 or 7.5 mg/cm^2 intra-lesional TAC administered intra-lesional.

All patients who attended the clinic for the treatment of keloids were informed about the study by the triage nurse. Those who met the inclusion criteria were provided with individualized information about the study. The decision to include the patients in the study was made after ascertaining the clinical suitability and performing a clinical examination. This was done by the research assistants/principal investigator from the outpatient clinics.

The informed consent was then administered to the eligible patients, in either Swahili or English language and those who consented to the study, signed the consent form. This was countersigned by the principal investigator. Any pertinent questions regarding the study from the patient was answered at this point. The process of consenting was free from coercion and was purely voluntary.

Withdrawal from the study was allowed at any stage without any negative consequences, and reasons for the withdrawal were to be documented. However, we had no drop out from the study.

4.7.1: Randomization

The study participants were selected through random sampling from the eligible patients attending the outpatient treatment for management of keloids. Following the signing of the informed consent form by the recruited patients, they were randomly assigned into control and intervention groups in a ratio of 1:1:1 using simple random sampling technique. A randomization list for allocations to the each of the study arms was created prior to the commencement of the study. This list was in the custody of the principal investigator, and was used to generate unique numbers that were used to randomly identify subjects during the study.

4.7.2: Blinding and Un-blinding

Blinding procedure

The study was a randomized controlled double blinded study. In order to conceal the dosage of the TAC given to each participant, the following steps were taken:

1) The preparation and labeling of the vials containing the different strengths of the triamcinolone was prepared by the hospital pharmacist, the vials were then sealed off using a similar piece of making tape. All vials had been stored in the KNH Pharmacy.
2) The vials were then assigned a code (by the pharmacist) corresponding to the participant's number e.g. vials labeled from 001A, 001B and 001C up to 025A, 025B were assigned to participants with code number 001 to 025 respectively.
3) These coded vials were then arranged systematically in carton boxes to ensure ease of dispensation to the principal investigator during the study; the vials were kept in the pharmacy under lock and key and the ones needed for any particular day were mixed and presented on the day of the study. The pharmacist did not divulge any information regarding the blinding procedure to anyone involved in the study (primary investigator, research assistant and doctors in the out-patient clinic).
4) Dispensation was carried out by the primary investigator who kept a log of the vials (number of bottles) dispensed to any participant.

Un-blinding procedure

For patients who had abnormal response to the treatment or had any other indication for stopping the administration of the TAC identified, the injection was stopped, the type concentration of the TAC noted and the patient managed based on the treatment protocols of the KNH. If no complication arose, all participants (unless one opts out of the study) were to be followed to the point of completion of all the doses. Upon completion, the TAC concentration was revealed for analysis purposes.

4.7.3 Study Interventions

Before commencing the study, a meeting was held in the KNH plastic surgical unit to educate the healthcare attendants on the protocol, assess their understanding of its procedures, and assess whether they are able to practice the required procedures. The aim was to sensitize the nurses, senior house officers and consultant surgeons about the study and placement of appropriate labels about the study in the surgical outpatient department.

All the study participants went through the triage area, where the triage nurses (or clinician) checked vital signs (blood pressure, heart rate, respiratory rate and weight). This was followed by a physical and keloid site examination. In addition, the triage nurse informed the participants about the study and the inclusion criteria. Upon receiving verbal consent for a repeat examination relevant to the study, the triaging nurse informed the research assistant and/or principal investigator to confirm the findings and administer a consent form for signing before proceeding with the study enrollment process. Patients who signed the consent form were randomized as per the study arm in a ratio of 1:1:1.

For ease of follow up and identification, the patients' files were then marked with a red sticker for ease of identification during the subsequent follow up visits as per the treatment protocol. On average, seven participants were enrolled per day until the targeted sample size was arrived at.

4.8: Ethical Considerations

Ethical approval was given by the Kenyatta National Hospital and University of Nairobi Ethics Research Committee (ERC) to carry out this study as part of the UON thesis dissertation procedure. Permission was sought from the Research Committee and the Surgery department at KNH. Posters explaining the study procedure were placed at strategic places in the surgical outpatient clinic. A continuous medical education (CME) session was held at the clinic to enlighten the healthcare workers about the study.

All the study participants were subjected to opt out consenting procedure, and were only to be enrolled upon voluntarily signing the consent form. The procedure for administration of the TAC was further explained to the participants by the principal investigator (PI) and research assistant (RA), and individually during the individual consenting process. The routine anti septic and administration procedures was followed and any adverse events recorded in the Severe Adverse Event (SAE) form. Patients who got any adverse event were managed by the surgical team in the department and a clinical trial insurance cover was taken for all the study participants. The cost of all the treatment was to be borne by the PI and insurance company in case a SAE occurred.

To ensure confidentiality of the participants' data, personal details were de-identified by use of an assigned unique identifier, only applicable to the study. This coded information will be

uploaded to the excel sheet and password protected. Back up data was kept in a password encrypted external hard drive, only known to the PI.

4.9 Study Flow

The following study flow was used in this study.

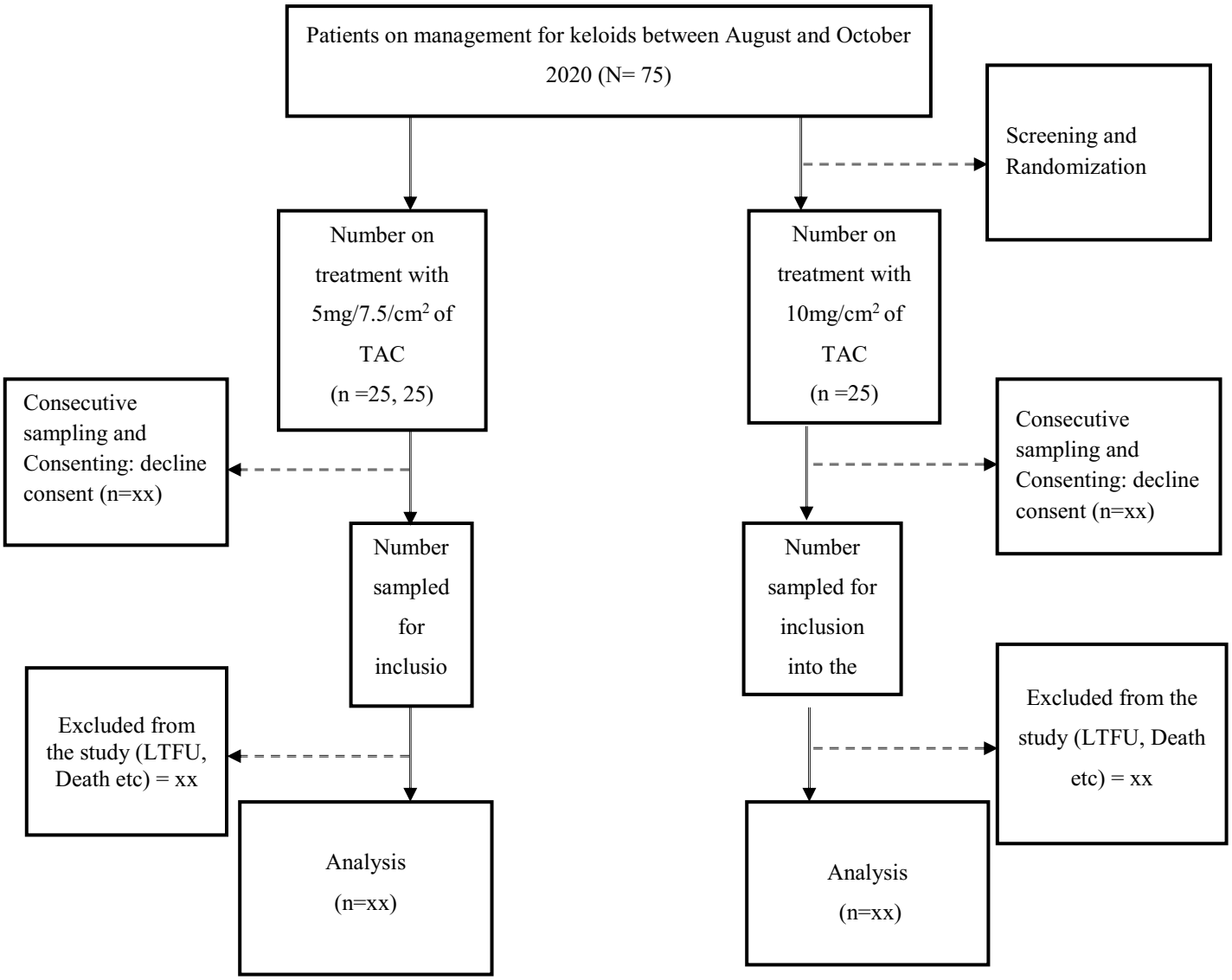


Figure 3: Study Flow Diagram

4.10: Study Procedures

4.10.1: Training of the Study Team

A one-day training of the study team that included the research assistants, the data manager and the consultants was conducted from the department's seminar room. The training entailed a review of the study protocol, the study procedures and the follow up of the study participants. A practical session at the PSOC was done to orient the participants on the administration of TAC and the patient flow at the clinic.

4.10.2: Administration of Triamcinolone Acetonide

Administration of TAC followed the general treatment and follow up guidelines at the KNH plastic surgical treatment unit (Figure 2). Though not customized into a standard operating procedure (SOP), the guiding principles entailed review of patients with keloids at the Accident and Emergency (A&E) department before booking at the PSOC for definitive management. The vials come in dosages 40mg/ml and will be diluted by the pharmacists to achieve concentrations of 5mg, 7.5mg and 10mg that will be administered per cm^2 surface area of the keloid scar.

Upon review in the PSOC department, the patients were referred to the Minor theatre for injection with TAC if they met the inclusion criteria. Surface area calculation was done for every keloid using a calliper ruler to measure length and breadth. The height of keloid was also measured using calibrated calipers before the dosages 5 mg/cm^2, 7.5mg/cm^2 and 10mg/cm^2 of TAC that has been mixed with 2 % Lidocaine solution is injected intra-lesional. This was done on Day 1 and every other visit before injection of the TAC. Patients were randomly selected until each arm had a minimum of 25 patients each. TAC intra-lesional injection was instituted on Day 1 and repeated every 4 weeks for a maximum of 3 TAC injections.

Assessment of the acute outcomes of TAC treatment was done from Day 30, Day 60 and Day 90. The TAC was administered at dosages 5 mg/cm^2, 7.5mg/cm^2 and 10mg/cm^2 after dilution with 2% lignocaine. The Lignocaine solution provided intra-operative and post-operative pain control.

TAC 1st Injection TAC 2nd Injection TAC 3rd Injection

Figure 4: Study Procedure

Patients who received 5 mg/cm^2, 7.5mg/cm^2 or 10mg/cm^2 of TAC during the first visit were enrolled into the study and followed up for documentation of the treatment outcomes during the subsequent treatment visits. We assessed for the decrease in the height using calibrated calipers, size of the Keloids in cm^2, reduction in pain and pruritus, and patient's satisfaction with the results using a Vancouver scar scale.

We also recorded the side effects of the treatment that occurred with treatment at 5 mg/cm^2, 7.5mg/cm^2 and 10mg/cm^2 and the date of occurrence.

The modified Vancouver scar scale will be used to collect the data by the research assistants and the PI who will be blinded on the dosage of TAC administered. The resolution of pain, pruritus and reduction of scar thickness were noted as indicators of improvement. The dosage administered frequency of administration and duration of the treatment was noted and analysed 30 days after injection of the last dosage of TAC.

4.10.3: Quality Assurance and Safety Monitoring

Triamcinolone Acetonide was approved for use by Pharmacy and Poisons board of Kenya and the FDA and from the studies conducted using the drug no severe adverse event was reported. We did not encounter any severe adverse events.

These will include:

i. Any adverse event that is life threatening, or places the participant at immediate risk of death.
ii. Any adverse event that requires or prolongs hospitalization.
iii. Any adverse event that causes persistent or significant disability or incapacity.
iv. Any adverse event that is another condition which investigators judge to represent significant hazards.

All hospitalizations from expected causes were to be reported in the quarterly report to the DSMB.

The Data and Safety Monitoring Board

The Data and Safety Monitoring Board (DSMB), responsible for monitoring the progress of a clinical trial and review safety and effectiveness during the trial,

4.10.4: Reporting of Adverse Events

All SAEs were to be promptly reported to ERC. An expedited report of an SAE was to be submitted via telephone or email to the Investigator within 24 hours. The report was to be followed by a detailed, written SAE report immediately. Follow up information required and asked by the ERC was to be provided in full.

4.10.5 Data Collection Procedures

The PI, together with the RAs collected data using a specially designed questionnaire that captured the socio-demographic and clinical characteristics of the study participants and the treatment outcomes following the administration of TAC. Data were collected using a modified score chart that scored changes in pain, pruritus, scar pliability and patient satisfaction. The adverse effects were recorded at the different dosages of TAC. The collected data were checked on the day when it was collected and uploaded into a password protected excel sheet by the data manager for review and analysis.

4.10.6 Data Variables

Table 2Data Variables

Objective	Variables	Variable Definition
To assess the optimal dosage of TAC	Dosage of TAC	Independent Variable
To assess the response to the different doses of TAC	Scar Pliability, Size, Pruritis Pain and adverse effects	Dependent Variables
To describe the socio-demographic characteristics	Age, Location of Keloid	Intermediate Variables

4.11 Data Analysis and Presentation

The data collected during the study were sorted, coded and processed using SPSS version 23. Demographic data was summarized by mean, median and standard deviation and presented as proportions for the different groups. The mean size change of the keloid was analysed using student t-test, while pruritis, pliability was presented using a Likert scale aggregate points. The association between the different dosages of the TAC was done using Chi Square test and presented as Odds Ratios. Further analysis was done using the one-way ANOVA, controlling for possible confounding. The results were visualized as tables, pie charts and line graphs. A *p*-value of 0.05 was taken to be significant statistically.

5.0: RESULTS

A total of 34 patients who presented with 109 keloids were recruited into the study. Fifty three point eight percent (53.8%) were female and 43.6%male. Seventy eight point one percent (78.1%) of the study subject were between 18 -40 years, 7.3% between 41-60 years while 9.1% were above 61 years. The mean age of the patients was 33.56 years (18-84 years). All participants were of African descent. Most patients had a family history of keloid scar formation (57.1%), of which 39.8% had a maternal history, 1% had a paternal history, and 16.3% had both

paternal and maternal family histories. Forty two point nine percent (42.9%) of the patients did not have any known family history of Keloids.

5.1: Scar characteristics

Table 3: Tabulated summary of the locations of the keloids

Location of the keloid		
	Frequency	**Percentage (%)**
Back	10	9.17
Breast	12	11.00
Chest	32	29.36
Ear	23	21.10
Face	18	16.51
Thigh	6	5.51
Arms	8	7.34
Total	109	100

Most keloids were located on the chest, with the ear being the next most common site. The face, breast, back, arms and thighs followed in order frequency of the keloid presentation.

Most keloids developed spontaneously (56.7%) as compared to those that formed following trauma (43.3%). The majority of keloids were more than 1 year old (90.4%). Additionally, the majority were noted to be index cases (55.8%).

Table 4: The ways in which the participants' keloids arose

Keloid Aetiology	**Frequency**	**Percentage (%)**
Trauma	13	11.93
Spontaneous	51	46.78
Burns	8	7.34
Ear piercing	16	14.68
Acne	9	8.26
Post Varicella Zoster Virus (VZV)	2	1.83
Post Human bite	4	3.67
Folliculitis	1	0.92
Total	109	100

In the management of the keloids six months or more prior to this intervention, triamcinolone acetonide (TAC) was administered to 27.9% of the participants. The remaining patients who joined this study with recurrent keloids, surgical excision was done in 1%; both surgical excision and TAC in 4.8%; surgical excision, TAC and radiotherapy were done in 11.5%; and silicone dressing was applied in 3.8% of the cases.

5.2: Average Scores on the Vancouver scale on Days 1, 30, 60 and 90

The Vancouver Scar Scale was used to track the progress of each keloid scar over the study period.

Day 1

On day 1, the baseline scores and measurements were taken. These were mean scores for the total VSS for each arm of the study before the injection of TAC.

Table 5: The mean values of the total VSS per arm of the study, as assessed on day 1, 30, 60 and 90

	Mean ± SD		
	5 mg/cm2	**7.5 mg/cm2**	**10 mg/cm2**
Day 1	8.44 ± 2.43	8.43 ± 1.88	8.06 ± 1.84
Day 30	6.19 ± 2.28	6.82 ± 2.33	6.83 ± 1.86
Day 60	5.21 ± 2.04	5.60 ± 2.59	5.23 ± 2.10
Day 90	3.56 ± 2.54	4.24 ± 3.01	3.92 ± 2.45

An objective assessment of these 3 last parameters was also done using mean presentation of the heights and analysis of the pain and pruritus scales

Table 6: The average VSS score, keloid height, Surface area, and average keloid pain and itchiness scored in the three arms of the study on Day 1

	Overall Mean (Range)	**Mean (5mg/ml)**	**Mean (7.5mgmg/ml)**	**Mean (10mg/ml)**	**Statistically significant differences between concentrations of TAC (p-values)**
VSS score	8.31±2.05	8.44 ± 2.43	8.43 ± 1.88	8.06 ± 1.84	0.627
Height of keloid scar (mm)	3.673 (0-15)	3.308 (0 – 10)	4.412 (1 – 15)	3.303 (0 - 12)	0.172
Pain score	2.56 (0-9)	2.82 (0-9)	2.32 (0-9))	2.58 (0-9)	0.688
Itchiness	4.18 (0-9)	4.05 (0-9)	4.44 (0-9)	4.03 (0-9)	0.172
Surface Area (cm^2)	3.26 (0.020-50.30)	3.67 (0.07-50.3)	2.75 (0.1 – 15.4)	3.28 (0.02 – 19.43)	0.934

On day 1, there was no statistically significant difference between the parameters evaluated using the VSS for keloids that were to be allocated to the three arms of the study. There was also no statistically significant difference between keloids in the three arms of the study as regards their height, pain, pruritus and surface area.

The four parameters that were scored included: height of keloid in millimetres, surface area of the keloid in centimetres squared (cm^2), pain score on a scale of 0 to 10 where 0 corresponded to 'no pain' and 10 corresponded to 'unimaginable, unspeakable pain', and itchiness score on a scale of 0 to 10 where 0 corresponded to 'no itchiness' and 10 corresponded to 'worst itchiness possible', those who received 7.5 mg/ml were noted to have a higher average height of keloid scar (4.41mm) prior to injection with TAC, while the lowest average height of 3.31mm was recorded in those who received 10mg/ml of TAC. The keloids in the 7.5mg/ml arm of the study showed the highest average itchiness score, the lowest average pain score and the lowest average surface area of the three arms. The keloids in the 5mg/ml arm of the study showed the highest average pain score and the highest average surface area. The lowest average itchiness score was recorded in the keloids in the 10mg/ml arm.

There was, however, no statistically significant difference between these parameters in the three arms of the study when the ANOVA test was performed.

Day 30

On day 30, there was an average decrease by 1.70 points from the baseline scores of the mean VSS scores on day 30 across the 3 arms of the study.

Those in the 7.5 mg/ml arm of the study were noted to have the highest of the three average keloid heights (3.409 mm) after the first injection with TAC, while the lowest average height of 2.28 mm was recorded in those who were to receive 10mg/ml of TAC

There was no statistically significant difference between the mean scores of all the parameters in the three arms of the study when a one-way ANOVA test was done.

Table 7: Table showing the average VSS score, keloid height, Surface area, and average keloid pain and itchiness scored in the three arms of the study on Day 30

	Overall Mean	**Mean (5mg/ml)**	**Mean (7.5mg mg/ml)**	**Mean (10mg/ml)**	**Statistically significant differences between concentrations of TAC (p-values)**
VSS Score	6.61± 2.29	6.19 ± 2.28	6.82 ± 2.33	6.83 ± 1.86	0.467
Height of keloid scar	2.683 (0-10)	2.297 (0-7)	3.409 (0-10)	2.28 (0-7)	0.078
Pain score	0.80 (0-7)	0.92 (0-7)	0.94 (0-7)	0.53 (0-2)	0.724
Itchiness	1.23 (0-8)	0.62 (0-8)	1.52 (0-8)	1.70 (0-7)	0.223
Surface Area	2.17 (0 - 18.7)	1.65 (0.07-14.3)	3.05 (0-18.7)	1.78 (0.19 – 8.8)	0.223

On Day 60, there was an average decrease by 2.96 points from the baseline scores of the mean VSS scores across the 3 arms of the study.

While there was no statistically significant difference between the other parameters in the three arms of the study, there was a significant difference in the average itchiness score

Those in the 7.5 mg/ml arm of the study were noted to have the highest of the three average keloid heights (2.441 mm) after the first injection with TAC, while the lowest average height of 1.882 mm was recorded in those who were to receive 5mg/ml of TAC.

There was no statistically significant difference between the mean scores in the three arms of the study when a one-way ANOVA test was done (

Table 8: The average VSS score, keloid height, Surface area, and average keloid pain and itchiness scored in the three arms of the study on Day 60

	Overall Mean	**Mean (5mg/ml)**	**Mean (7.5mg mg/ml)**	**Mean (10mg/ml)**	**Statistically significant differences between concentrations of TAC (p-values)**
VSS Score	5.35±2.24	5.21 ± 2.04	5.60 ± 2.59	5.23 ± 2.10	
Height of keloid scar	2.116 (0-10)	1.882 (0-7)	2.441 (0-10)	1.983 (0-7)	0.345
Pain score	0.13 (0-3)	0.35 (0-3)	0.03 (0-1)	0 (0-0)	0.066
Itchiness	0.20 (0-2)	0.15 (0-2)	0.12 (0-1)	0.37 (0-2)	0.147
Surface Area	1.96 (0 – 16.25)	1.34 (0 – 11.6)	2.59 (0-16.25)	1.80 (0.19-8.8)	0.223

Day 90

On Day 90, there was an average decrease by 4.4 points from the baseline scores of the mean VSS scores on day 90 across the 3 arms of the study.

There was no statistically significant difference between the mean scores in the three arms of the study when a one-way ANOVA test was done.

There was no statistically significant difference between the other parameters measured in the three arms of the study.

Table 9: The average VSS score, keloid height, Surface area, and average keloid pain and itchiness scored in the three arms of the study on Day 90

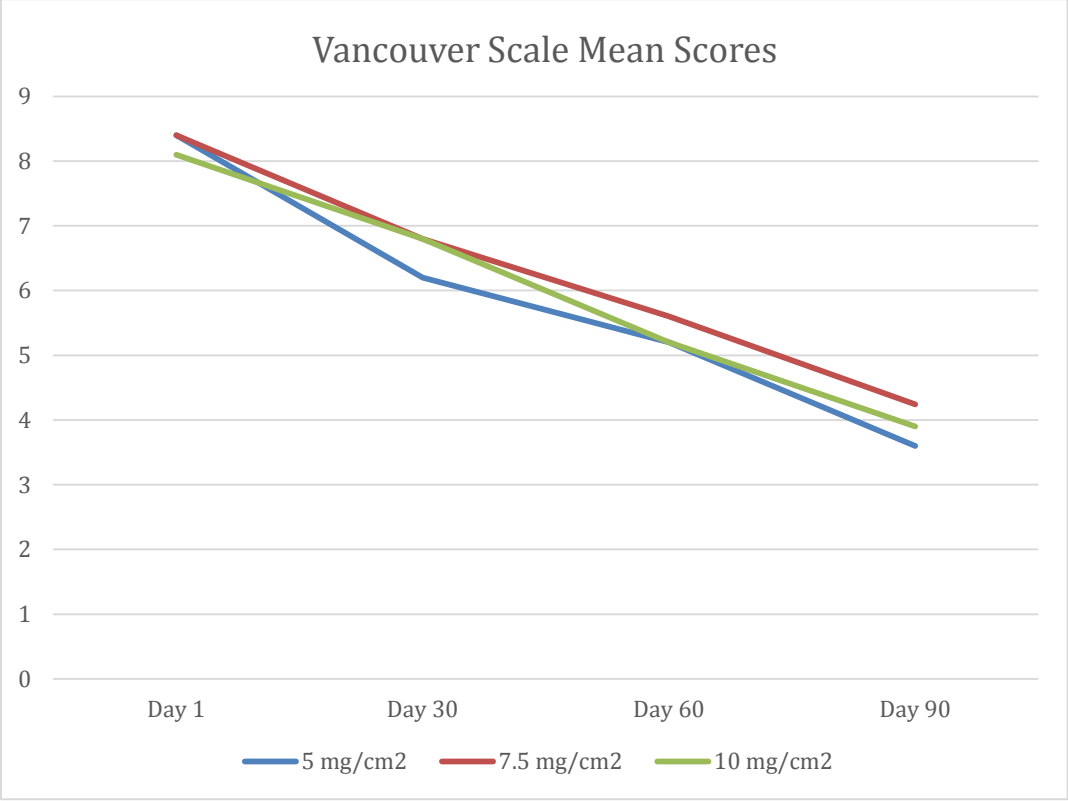
	Overall Mean	**Mean (5mg/ml)**	**Mean (7.5mg mg/ml)**	**Mean (10mg/ml)**	**Statistically significant differences between concentrations of TAC (p-values)**
VSS Score	3.91±2.67	3.56 ± 2.54	4.24 ± 3.01	3.92 ± 2.45	0.764
Height of keloid scar	1.79 (0- 9)	1.438 (0-7)	2.357 (0-9)	1.654 (0-6)	0.336
Pain	0.06 (0-2)	0.09 (0-2)	0.07 (0-2)	0 (0-0)	0.724

score					
Itchiness	0.23 (0-3)	0.22 (0-3)	0.18 (0-3)	0.31 (0-2)	0.868
Surface Area	1.06 (0 - 11)	1.13 (0 – 11.6)	0.921 (0-5.32)	1.12 (0 – 2.64)	0.927

By day 90, the lowest average scar height was recorded in the 5mg/ml arm, while the lowest surface area was recorded in the 7.5mg/ml arm.

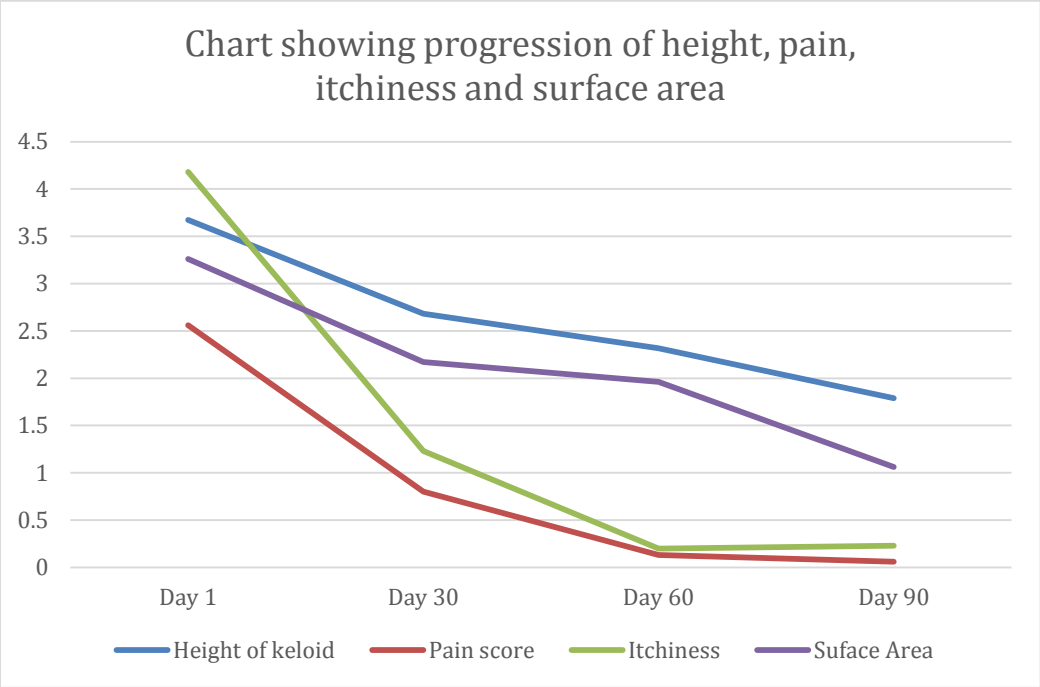
5.3: Trends

Figure 3: Chart showing the progression of VSS mean scores over the course of 90 days



There was a mean decrease in the VSS mean scores over the duration of 90 days

Figure 4: Progression of height, pain, itchiness and surface area of the keloid scars over the course of 90 days.



There was a decrease in the height of keloid, pain score, itchiness score, and surface area of keloids in all arms of the study from day 1 to day 90 (figure 4)

5.4: Comparison tests to assess significant differences between the keloid scores on days 1, 30, 60 and 90 of the study

For most of the scores, there were statistically significant differences observed in the keloid height, pain, itchiness as well as surface area as observed from day 1 to day 90 of the study period.

Table 10: The statistically significant differences between the mean VSS Scores for 5mg/ml group from Days 1, 30, 60, and 90, as assessed using the paired t-test

5 mg/ml group	**Mean difference**	***P*-values (p > 0.05*)***
Day 1 to day 30	2.19	0.000
Day 30 to day 60	1.09	0.005
Day 60 to day 90	1.61	0.000

There was statistically significant decrease in the mean VSS scores for the 5mg/ml arm form Day 1 to day 90.

Table11: The statistically significant differences between the mean VSS Scores for 7.5mg/ml group from Days 1, 30, 60, and 90, as assessed using the paired t-test

7.5 mg/ml group	**Mean difference**	**P values (p > 0.05)**
Day 1 to day 30	1.59	0.000
Day 30 to day 60	1.29	0.000
Day 60 to day 90	1.14	0.012

There was statistically significant decrease in the mean VSS scores for the 7.5mg/ml arm from Day 1 to day 90.

Table12: The statistically significant differences between the mean VSS Scores for 10 mg/ml group from Days 1, 30, 60, and 90, as assessed using the paired t-test

10 mg/ml group	**Mean difference**	**P values (p > 0.05)**
Day 1 to day 30	1.28	0.001
Day 30 to day 60	1.60	0.000
Day 60 to day 90	1.50	0.008

There was statistically significant decrease in the mean VSS scores for the 10 mg/ml arm from Day 1 to day 90.

The one-way ANOVA test was done to assess whether there was any statisticalllysignificantt difference between the mean VSS total values for the three arms of the study on each day of assessment.

Table 13: The statistical significances differences in the mean VSS scores of the keloids in each arm of the study (One-way Anova)

	***P* - values**
Day 1	0.627
Day 30	0.467
Day 60	0.630
Day 90	0.764

There was no statistically significant difference in the mean VSS scores of the three arms of the study on all 4 days of assessment of the keloids.

Table 14: The statistically significant differences between the average keloid heights observed on Days 1, 30, 60, and 90, as assessed using the paired t-test

Test Statistics[a]			
	Height Day 30 – Height Day 1	Height Day 60 – Height Day 30	Height Day 90 – Height Day 60
Asymp. Sig. (2-tailed)	.000	.095	.001

There was a statistically significant decrease in the average keloid height from day 1 to day 30, and from day 60 to day 90, but there is no difference between day 30 and day 60.

Table 15: The statistically significant differences between the average pain score reported on Days 1, 30, 60, and 90, as assessed using the Wilcox on test

Test Statistics[a]			
	Pain Day 30 – Pain Day 1	Pain Day 60 – Pain Day 30	Pain Day 90 – Pain Day 60
Asymp. Sig. (2-tailed)	.000	.000	.705

There was a statistically significant decrease in pain scores from day 1 to day 60, from where there is no difference between day 60 and day 90.

Table 16: The statistically significant differences between the average itchiness score reported on Days 1, 30, 60, and 90, as assessed using the Wilcox on test

Test Statistics[a]			
	Itchiness Day 30 - Itchiness Day 1	Itchiness Day 60 – Itchiness Day 30	Itchiness Day 90 – Itchiness Day 60
Asymp. Sig. (2-tailed)	.662	.000	.088

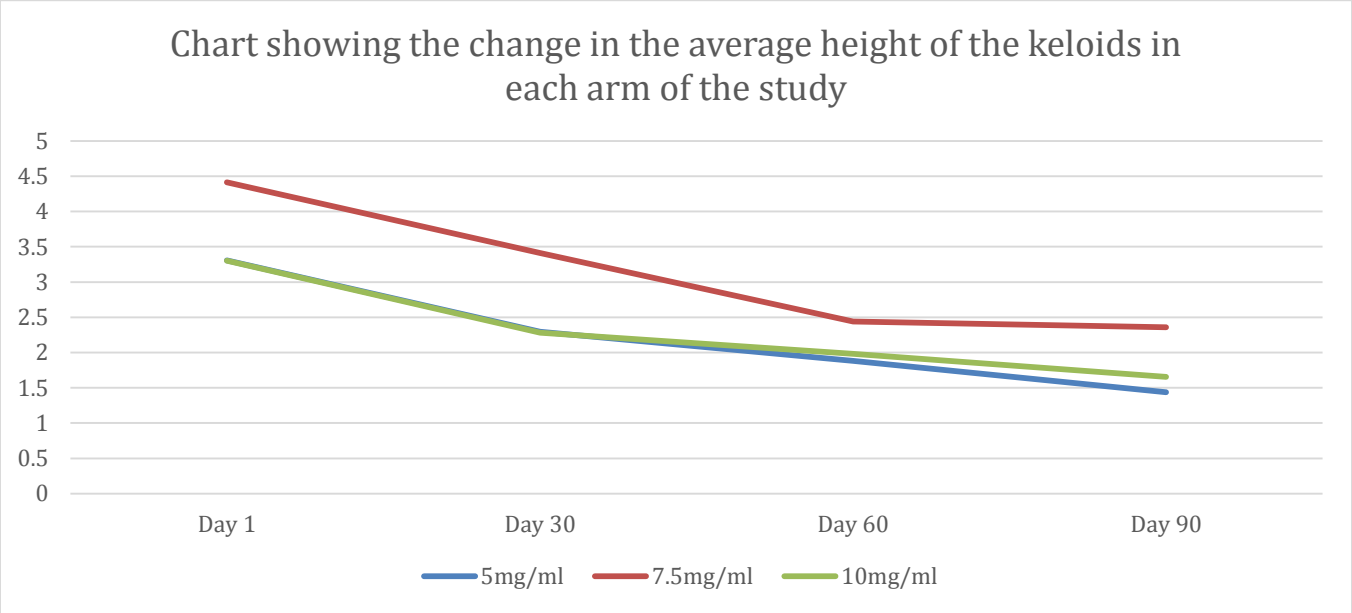
There is a statistically significant decrease in itchiness scores only between day 30 and day 60.

Table 17: The significant differences between the average surface area measured on Days 1, 30, 60, and 90, as assessed using the paired t-test

Test Statistics[a]			
	Surface Area Day 30 – Surface Area Day 1	Surface Area Day 60 – Surface Area 30	Surface Area Day 90 – Surface Area 60
Asymp. Sig. (2-tailed)	.000	.000	.000

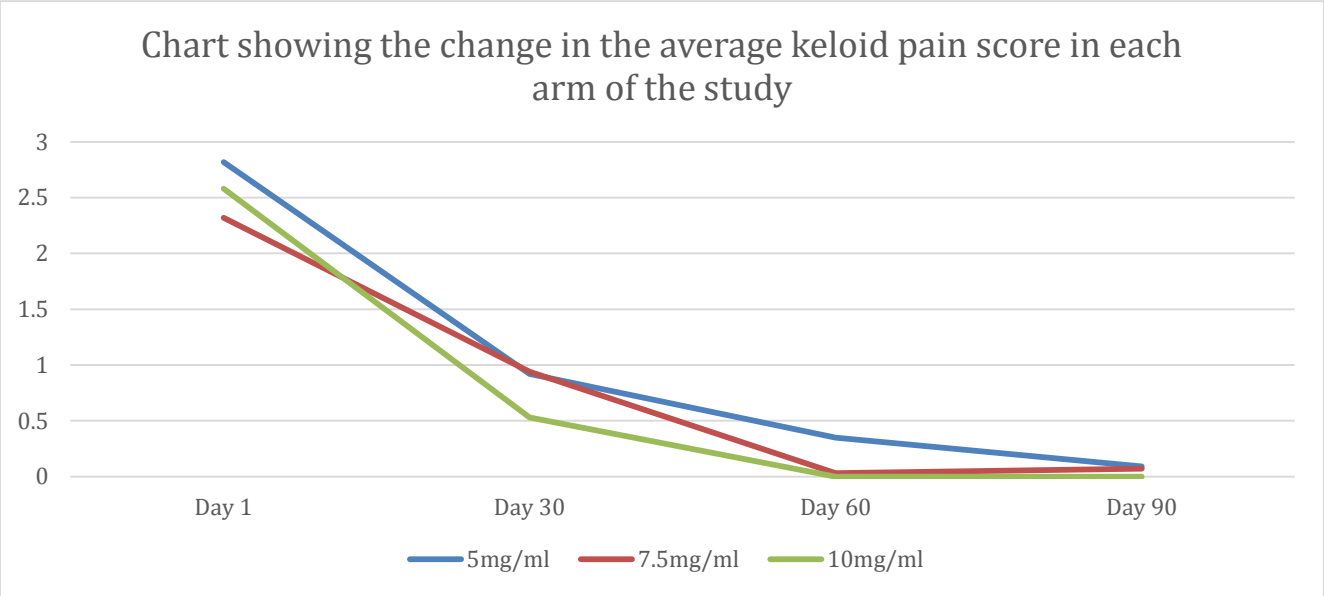
The decrease in surface area was statistically significant on all days.

Figure 5: Line graph showing the change in the average height of the keloid scars in each arm of the study from Day 1 to Day 90



There was reduction in the keloid height from day 1 to day 90 among the three arms, with the greatest average decrease being in the 7.5mg/ml arm (2.1mm). Those in the 5mg/ml had a decrease of 1.9mm, while those in the 10mg/ml group had a decrease of 1.6mm (figure 5).

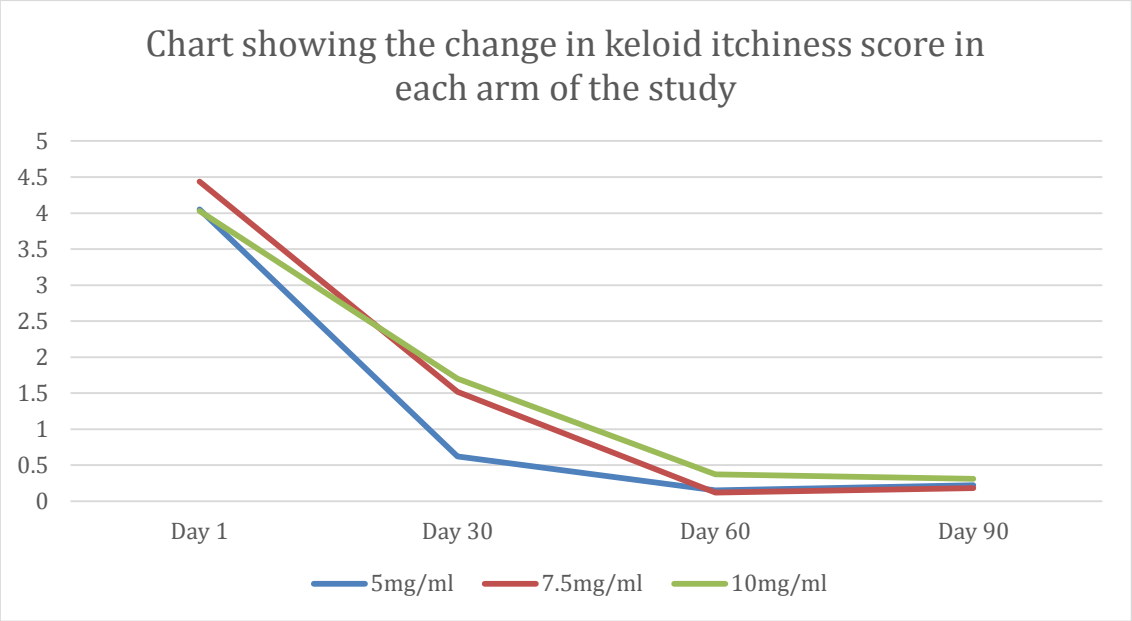
Figure 6: Line graph showing the change the average keloid pain score in each arm of the study



from Day 1 to Day 90

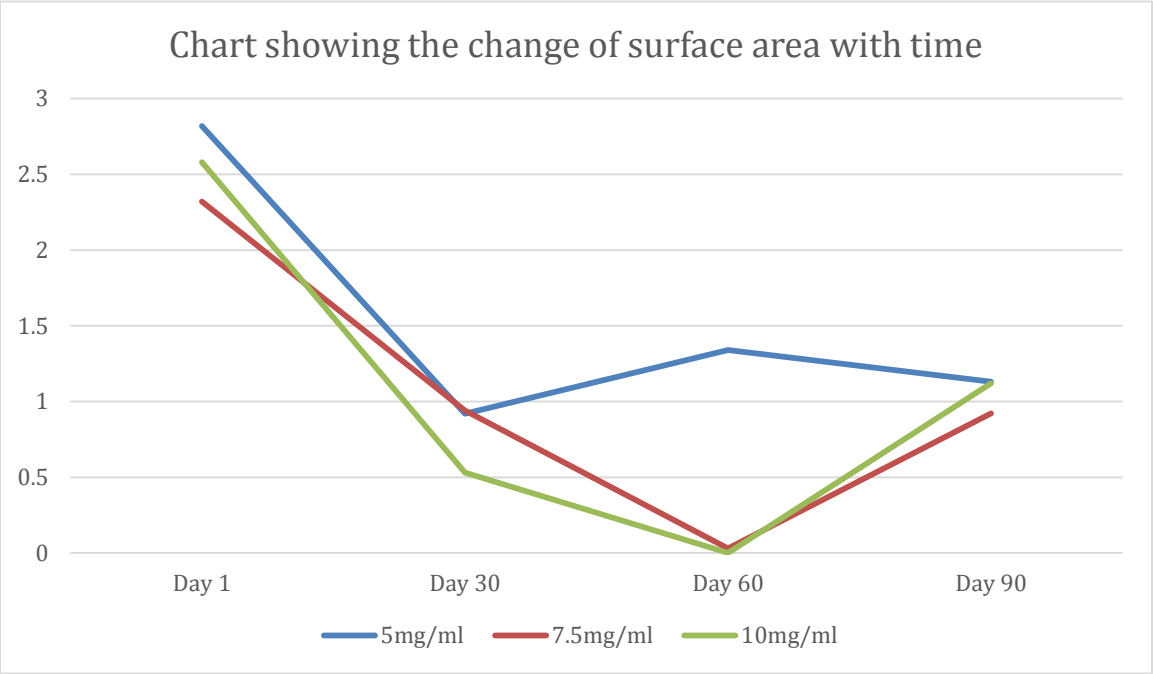
There was reduction in the average keloid pain score from day 1 to day 90 among the three arms, with the greatest average decrease being in the 5mg/ml arm (2.7). Those in the 7.5mg/ml had a decrease of 2.3, while those in the 10mg/ml group had a decrease of 2.6 (figure 6).

Figure 7: Line graph showing the change the average keloid itchiness score in each arm of the study from Day 1 to Day 90



There was reduction in the average keloid itchiness score from day 1 to day 90 among the three arms, with the greatest average decrease being in the 7.5mg/ml arm (4.3). Those in the 5mg/ml had a decrease of 3.9, while those in the 10mg/ml group had a decrease of 3.7 (figure 5).

Figure 8: Line graph showing the change the average surface area in each arm of the study from Day 1 to Day 90



There was a decrease in surface area of the keloids for the groups receiving 7.5mg/ml and 10mg/ml until day 60, where an increase was noted. In the group which received 5mg/ml, a decrease was noted until day 30, from where there was increase until day 60, and another decline until day 90 (figure 8).

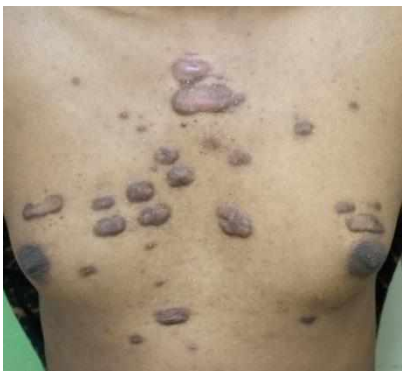
5.5: Participants' Satisfaction with the Outcome of the Intervention

Table 18: The average patient satisfaction score reported in each arm of the study

	Overall Mean	**Mean (5mg/ml)**	**Mean (7.5mg/ml)**	**Mean (10mg/ml)**
Patient satisfaction scale	1.790 (1 - 10)	1.438 (1 - 10)	2.357 (1 - 10)	1.654 (1 - 10)

The study participants were, generally satisfied with the outcome, with the average rating of their satisfaction at 1.79 on a scale of 1 – 10 where 1 stood for 'improved' and 10 stood for 'worsened' (table 18). The difference in patient satisfaction scores between the three arms of the study was not statistically significant ($p>0.05$).

Below are pictorial examples of keloid improvement



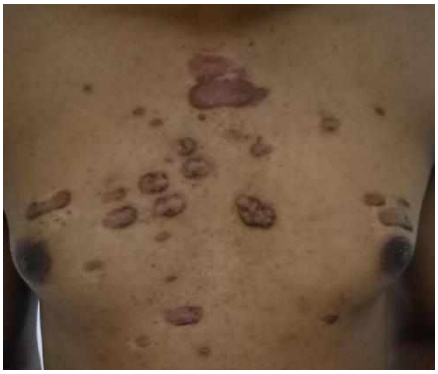


Image1:Participant A's keloids on day 1 **Image 2**: Participant A's keloids on day 60

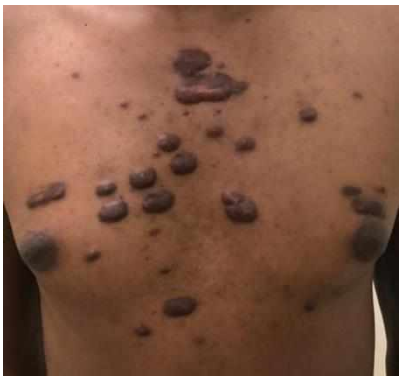


Image 3: Participant A's keloids on day 90

Image 4: Participant B's keloid on day 30

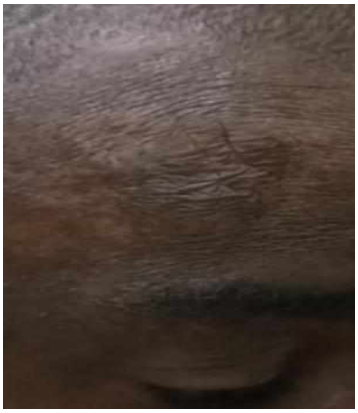


Image 5: Participant B's keloid on day 90, flattened

5.6: Complications

Table 19: The complications that occurred in each arm of the study

Complication	**Number of keloids in 5 mg arm**	**Number of keloids in 7.5mg arm**	**Number of keloids in 10mg arm**	**Total**
Ulceration	**3**	**3**	**0**	**6**
Hypo-pigmentation	**1**	**1**	**0**	**2**
Cushing oid Features	**0**	**0**	**1**	**1**
Total	**4**	**4**	**1**	**9**

Complications were noted across the 3 arms of the study irrespective of the drug concentration that was administered.

6.0: DISCUSSION

The precise patho-physiology of keloids is still unknown with it being considered a benign dermal fibro-proliferative disorder that arises as a result of dys-regulation of the cell proliferation and repair with resultant prolonged inflammatory phase and with a disordered proliferative phase with haphazard laying down of collagen by fibro-blasts (1,14,26,28).

Triamcinolone Acetonide is the most widely used treatment for keloids either as mono-therapy or with combination with other chemotherapeutic agents like 5-Flourouracil (5-FU) and Verapamil, or as part of combined therapy with silicone sheets or with cryo-therapy (6,8,15,20,24,27). TAC is postulated to induce remission of the keloid scars by interfering with collagen synthesis through reduction of fibro-blast density or accelerating the disintegration of the same. It also has a powerful anti-inflammatory effect too (6,16). This leads to the decrease of keloid symptoms that includes decrease in pain, pruritus and scar thickness. However, this is not without adverse effects that range from scar ulceration, hypo-pigmentation, telangiectasias, sub-cutaneous fat atrophy to cushingoid habitus features (3, 7).

From our study it seems to have a more female preponderance with 53.8 % being female and 43.6% of the patients presenting with keloids at our clinic being male. Fifty seven point one percent (57.1%) of the patients had familial history of keloids compared to 42.9 % who had no familial history. This is keeping with findings by Chenyu Huang *et al* who in their research discussed the potential keloid associated Loci in the African-American families that have been identified on chromosomes 7p11,40(2). The responsible genes are yet to be identified.

Most keloids were located on the chest, back and breast combined with the ear being the next most common site. This is in keeping with the mechanical theory of Keloid formation where it

has been postulated that most keloids occur in areas of the body high in mechanical stress/physical tension and movement (2).

We had three arms of study with 39 patients getting 5mg/ml/cm^2, 36 patients received 7.5mg/ml/cm^2, control group and the remaining 34 patients got 10mg/ml/cm^2. On day 1 of the study, we used the Vancouver Scaleto take the baseline scores and measurements (17-19, 21,24,29). These included the vascularity, Pigmentation, Pliability, Height of scar, Pain and Itchiness. Further, four parameters were scored: height of keloid in millimetres, surface area of the keloid in centimetres squared (cm^2), pain score and itchiness score. Pain and Itchiness were noted as the most commonly reported symptoms by the patients as they sought treatment.

There was, however, no statistically significant difference between these parameters in the three arms of the study (p-value > 0.05) hence no bias at the baseline of the study.

The patients were followed in the 3 arms of the study and on Day 90 after having received the 3rd injection 30 days prior, the baseline scores and parameters were assessed.

6.1: Effect of TAC on Keloids Morphology

A decrease in height in all 3 arms of the study was also noted with the greatest decrease of 2.055 cm (46.58%) seen in the 7.5mg/ml arm followed by 5mg/ml and 10mg/ml arms which recorded a decrease of 1.87 cm (56.55%) and 1.649cm (49.92%) from the baseline heights respectively. This clearly shows the anti-inflammatory properties of TAC and its ability to inhibit collagen formation hence the decrease in the size and height of the keloids (3,7,9,15-16,24). This is keeping with findings by Garg A.M *et al* who demonstrated the efficacy of TAC (20mg.ml) as an anti-inflammatory agent in the treatment of keloids (7).

There was a statistically significant decrease in the average keloid height from day 1 to day 30, and from day 60 to day 90, but there is no difference between day 30 and day 60 probably because collagen degradation had already occurred with no further synthesis occurring.

There was an average decrease of scar size in all the three arms of the study with the greatest margin seen in the 5 mg/ml arm at 2.54 cm^2 followed by 10mg/ml and 7.5mg/ml which had a decrease of 2.16 $cm^2$and 1.81 cm^2 respectively. This indicated that all the dosage concentration injected had an effect in the morphology of the keloid scars. There was a decrease in surface area of the keloids for the groups receiving 7.5mg/ml and 10mg/ml until day 60, where an increase was noted. This might have been as a result of flattening out of the keloids as a result of subcutaneous atrophy hence giving a false impression of increasing surface area when measured. In the group which received 5mg/ml, a decrease was noted until day 30, from where there was increase until day 60, and another decline until day 90. However, the decrease in surface area was statistically significant on all days.

6.2: Effect of TAC on Keloid Symptoms

The 10mg/ml dosage had the highest decrease at 100 % of pain followed by 7.5 mg/ml at 96.98 % and 5mg/ml at 96.80% when evaluated at Day 90 of the study. There was a statistically significant decrease in pain scores from day 1 to day 60, from where there was no difference between day 60 and day 90.

There was also a decrease in itchiness of the keloids with the highest decrease seen in the 7.5mg/ml arm at 95.95% followed by 5mg/ml and 10mg/ml arms that had symptomatic decreases of 94.56% and 92.31% respectively (3,9). The decrease in keloid scar symptoms after

the injection of TAC was also noted in a study by Nghi Dinh Huu *et al* where 82.3% of the patients had a decrease in itch and 75.9% had a decrease in pain as outcomes (3).

Scar vascularity, pigmentation, pliability, height, pain and itchiness were evaluated by Vancouver Scar Scale (VSS) score.

The percentage reduction in VSS was graded according to the Quartile score with ≤25% reduction in VSS graded as Poor, 26-50% reduction as Good, 51-75% reduction Very good and >75% reduction as Excellent response (7).There was 20.46% (Poor) reduction in the mean VSS score on Day 30, 35.62% (Good) reduction by Day 60 and 52.95% (Very Good) reduction by Day 90 of the study (9).

The reduction in the VSS mean scores was in keeping with findings in the studies conducted by Ahuja RB *et al* and Uzair M *et al* in their respective studies (31-32).

6.3: TAC Dose-related Side Effects

Adverse effects of TAC occurred across the 3 arms of the study irrespective of the dosages administered). Under the 5mg/ml arm, 7.69% of the patients had scar ulceration and 2.56% had scar hypo-pigmentation occurring. Eight point three three percent (8.33%) of the patients under the 7.5mg/ml arm reported scar ulceration with that reporting scar hypo-pigmentation being at 2.78%. The patients also had different body weights that may have had an impact as far as the adverse effects were concerned.

The occurrence of adverse effects across the different dosage ranges is in conformity with findings in a study by Nghi Dinh Huu *et al* on intra-lesional TAC in which patients with keloids

developed adverse effects in both the 7.5 mg/ml and 15mg/ml of TAC administered per cm^2 of scar tissue in the Asian population (3).

One patient who had multiple keloids and received a combination of the doses developed cushing oid habitus symptoms (Image 13-15) but had normal cortisol and blood sugar levels on follow up.

6.4: Patient Satisfaction with treatment Outcomes

The study participants were, generally satisfied with the outcome, with the average rating of their satisfaction at 1.79 on a scale of 1 – 10 where 1 stood for 'improved' and 10 stood for 'worsened'. The difference in patient satisfaction scores between the three arms of the study was not statistically significant ($p>0.05$). Majority of the patients who were most satisfied reported the disappearance of pain, pruritus and softness of the scars as their most improved aspects of their scars.

6.5: Complications -Ulceration and Cushingoid Features

Cushingoid features was reported in one of the patients who had multiple keloids injected with different doses and this was more apparent on Day 90 of assessment indicating a cumulative effect of the TAC injection on the patient. The most commonly reported side effect of the injection was ulceration of the injected keloids which was noted in six of the injected keloids that had gotten $5mg/ml/cm^2$ and $7.5mg/ml/cm^2$ injections. Two of patients in the same arms reported hypo-pigmentation of the scars as side effects. Notably, the dosages used in this study showed fewer complications 9/109 compared to those reported clinically (3,7). It is also worth noting that all 3 arms of the study reported adverse effects as reported.

6.5.1: Hypo-pigmentation

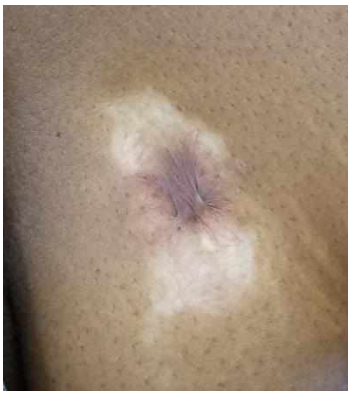


Image 6: Hypo-pigmentation of skin surrounding keloid number 822 observed on day 90 (5mg/ml)

The keloid was injected with TAC at a concentration of 5mg/ml, with the dosage administered totalling 2.0 mg (Day1: 1mg, Day 30: 0.5mg, Day 60: 0.5mg).

6.5.2 Ulceration

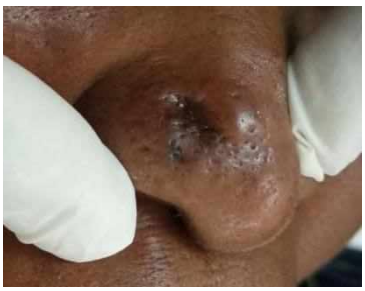


Image 7: Ulceration of keloid number 873 observed on day 30 (injected with 5mg/ml TAC)

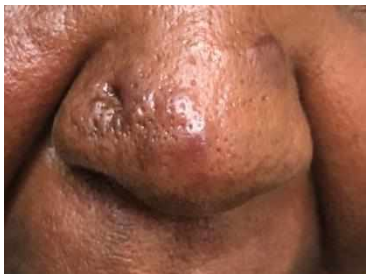


Image 8: Resolving ulceration of keloid number 873 observed on day 60 (injected with 5mg/ml TAC)

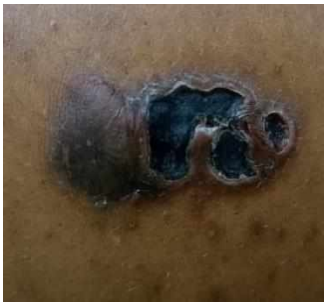


Image 9: Ulceration of keloid number 12 observed on day 60 (injected with 5mg/ml TAC)

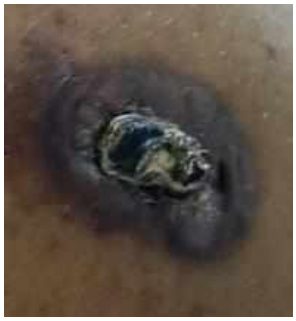


Image 10: Ulceration of keloid number 12 observed on day 90 (injected with 5mg/ml TAC)

7.5.3: Purulent ulceration

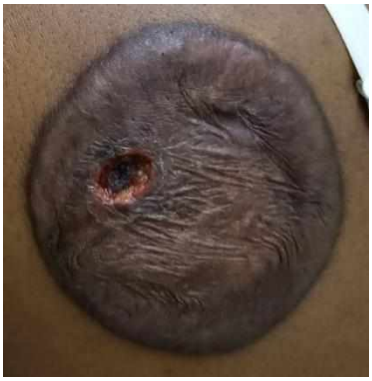


Image 11: Purulent ulceration of keloid number 422 observed on day 30 (TAC concentration 5 mg/ml)

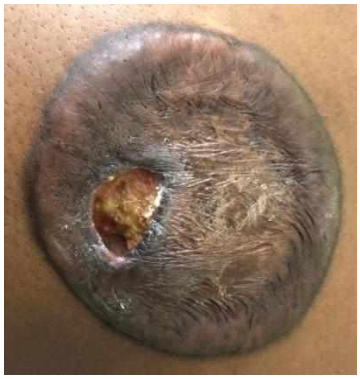


Image 12: Purulent ulceration of keloid number 422 observed on day 60(TAC concentration 5 mg/ml)

6.5.4 Cushingoid feature

Image 13: Patient A prior to TAC injections

Image 14: Patient A with moon faces observed on day 60

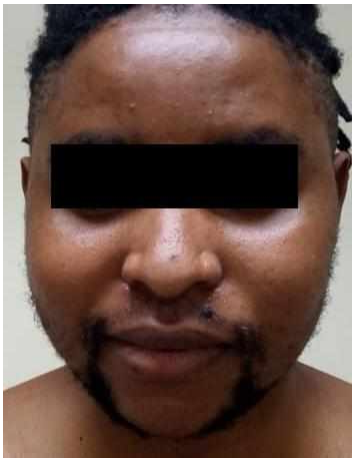


Image 15: Patient A with moon faces observed on day 90

7.0: CONCLUSION AND RECOMMENDATION

7.1 Conclusion

The results of this study show that Triamcinolone Acetonide is effective in the treatment of keloids where it has an anti-inflammatory, antimitotic effect in suppressing collagen formation and enhances collagen degradation through activation of collagenase activity (9,15-16,24-25,27). From our findings, all the 3 arms of the study had significant improvement of the outcomes over the study period. The TAC concentration of 7.5mg/ml/cm^2had comparatively better outcomes cumulatively. It had the lowest keloid height, lowest itchiness score and lower pain score with minimal complications reported.

Therefore, all the 3-dosage concentration in the study showed improvement in the symptoms, almost similar morphological changes and all the patients in the 3 arms were satisfied with the outcomes of the treatment.

7.2 Recommendations

1. Triamcinolone Acetonide dosagesof 5mg/ml, 7.5 mg/ml and 10mg/ml concentration are effective in management of keloids with minimal adverse effects in the African population.
2. Long term follows up of the patients in the study to be carried out to determine long term outcomes, adverse effects and recurrence rates of the keloid scars in our population.
3. Histo-pathological studies to establish the molecular changes in the scars at the different dosages to correlate the findings from the study.

8.0 Study Limitation and Delimitations

8.1 Study Limitations

There were some confounding factors that were difficult to avoid in this study. The patients recruited in the study had different body weights and this was not factored in the calculation of the dosages to be administered and might have affected the response of the Keloid to the TAC. The keloid sizes recruited for the study were also not standardized. Assessment of the vascularity and pigmentation on the VSS was subjective as most of the participants were dark skinned. Pigmentation subscale was also less applicable to large, heterogeneous scars that presented with mixed pigmentation picture.

Lignocaine was used as the diluents and might have affected the stability of the TAC and further studies need to be done to establish its effect on the final dosage delivered. The Lignocaine and TAC mixture did not form a homogenous solution and hence might have affected the final dosage delivered to the keloid despite efforts to mix the solution before injection. There was lack of patient perception in the scoring of the VSS. The measurements of the keloids were done manually using calliper rulers and we could not completely rule out human error in the accurate determination of Keloid heights and surface areas.

The follow up duration of 30 days after the last TAC injection might not have given me an accurate assessment of the outcome and was a major limitation of this study.

8.2: Study Delimitations

1. Triamcinolone Acetonide drug was procured from a single manufacturer to ensure uniformity of the chemical used.

2. Pre study training was done to improve skills of measurement, mixing of the dosages and collection of results by the RAs.

3. All the injections were performed by the PI/Surgeon using a standardized technique with 21-gauge needle.

8.3: Study Strengths

1. This is a clinic based randomized control study which makes it a Level 1B evidence study therefore results will offer a compelling argument.

2. Some of the key outcomes were measured clinically.

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APPENDICES

10.1 Appendix I: Consent Form

ASSESSMENT OF DOSE RELATED RESPONSE OF INTRA-LESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF KELOID SCARS AT KENYATTA NATIONAL HOSPITAL: A CLINIC BASED RANDOMIZED CONTROL STUDY

This is the Consent form is to be administered to patients with keloids at the Kenyatta National Hospital. It will be administered to the patients from the age of 18 years and above and the guardians of those below 18 years. We are requesting these patients to participate in this research project whose title is:

'ASSESSMENT OF DOSE RELATED RESPONSE OF INTRALESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF KELOID SCARS AT KENYATTA NATIONAL HOSPITAL: A CLINIC BASED RANDOMIZED CONTROL STUDY

Principal Investigator: Dr. Were Andrew Onyino
Institution: Department of Surgery, School of Medicine - University of Nairobi
Supervisors:

1. Dr. Benjamin Wabwire
2. Dr. Ferdinand Wanjala Nangole
3. Prof. Stanley Ominde Khainga

This informed consent has three parts:

I. Information sheet (to share information about the research with you)
II. Certificate of Consent (for signatures if you agree to take part)
III. Statement by the researcher

You will be given a copy of the full Informed Consent Form.

Part I: Information Sheet

Introduction

My name is Dr. Were Andrew Onyino; I am a post-graduate student at the School of Medicine, University of Nairobi. I am carrying out a study to assess the optimum dosage of intra-lesional triamcinolone acetonide in treatment of keloid scars in Kenyatta National Hospital.

Triamcinolone Acetonide is a drug that has been FDA approved for use in Keloids treatment and other medical conditions.

Purpose of the Research

Triamcinolone acetonide intra-lesional injection is the first line treatment for management of keloids but no standardized treatment protocol exists in terms of the dosage, duration and frequency of injection of the drug. This is despite the risk of potential adverse effects from injection of the drug especially if it infiltrates the normal surrounding tissues. The study aims to assess the acute outcomes from intra-lesional injection of TAC and recommend a standardized treatment regime for use in KNH hospital. This study is also a requirement for any doctor who aspires to graduate from our college as a surgeon.

Voluntary Participation/Right to Decline or Withdraw

An invitation to participate in this study is hereby extended to you. You will have the opportunity to ask questions before you decide on your participation (or your kin). You may seek clarification regarding any bit of the study from me or my assistant(s) should any part be unclear. The decision to participate in this study will be entirely voluntary after you have comprehensively understood the details herein. By refusing to participate in the study, you (or your kin) will not be denied medical care. Furthermore, you may stop participating at any time with no consequences whatsoever.

Confidentiality

All the information which you provide regarding yourself (or your kin) will be kept confidential; only the key personnel involved in this research work will access this information. The questionnaire will be identified by a code and only the researcher can relate the number to the patient. Your name will not be exhibited on the questionnaire. All the information obtained from you will be used for research only.

Sharing of Results

Following authorization by the Kenyatta National Hospital/University of Nairobi – Ethics and Research Committee (KNH/UoN-ERC), which is a committee whose work is to make sure research participants are protected from harm, relevant medical information yielded from this study may be shared with fellow doctors through scientific seminars, workshops and publications. Personal information will not be disclosed whatsoever.

Risks

As with any research, therapy or procedure there is a potential for risk but efforts are made to minimize the risks. As with any drug there are potential side effects. Triamcinolone acetonide has been approved by the United States Food and Drug Administration Agency (FDA) and therefore shows it is not harmful to the human body. Nonetheless previous studies similar to this one have been conducted and none of them reported any life-threatening event. The common side effect includes telangiectasias, skin and subcutaneous fat atrophy, pigmentary changes (hypo-pigmentation and hyper-pigmentation), skin necrosis and ulcerations, and systemic effects, such as Cushing's syndrome. Nevertheless, the patient will be monitored weekly for any event and any event will be assessed, recorded and managed appropriately. Any event can also be reported to me, the principal investigator or my assistants using the contacts provided herein.

Benefit of Participating in this Study

Information you provide in this study will help improve the understanding and management of Keloids.

Cost and Compensation

There will be no extra cost incurred by you (or your kin) from participation in this study, and there is also no compensation.

Part II: Certificate of Consent

I have read the above information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate in this research.

Name of Participant _____

Signature of Participant _____

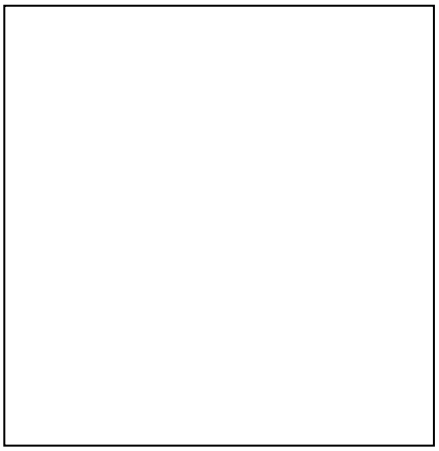
Date _____

If illiterate:

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Print Name of witness_____

Thumbprint of participant



Signature of witness _____

Date _____

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   Tel +254-020-2726300-9 Ext 44355

   Email: uonknh_erc@uonbi.ac.ke or KNHplan@Ken.Healthnet.org

Part III: Statement by the Researcher

I have accurately read out the information sheet to the participant, and to the best of my ability made sure that the participant understands that the following will be done:

- Refusal to participate or withdrawal from the study will not in any way compromise the care of treatment.
- All information given will be treated with confidentiality.
- The results of this study might be published to facilitate optimal care of patients with keloids.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this Informed Consent Form has been provided to the participant.

Name of researcher/person taking consent

_____

Signature of researcher/person taking consent

_____

Date_____

10.2 Swahili version of the consent form

Fomuza idhini kwa kujihusisha kwa utafiti kuhusuku tibu kovu kutumia viwango tofauti vya dawa yaaina ya Triamcinolone Acetonide namadhara yake mwili ni katika hospital ikuu jijini Nairobi Kenya

Jina la mpelelezi mkuu: Dkt. Were Andrew Onyino

Jina la shirika: Chuo kikuu cha Nairobi

Jina la mdhamini: Hospitali kuu ya Kenyatta

Hii fomu ya idhiniina sehemu mbili:

- Karatasi ya habari (kueleza habari kuhusu utafitinawe)
- Cheti cha idhini (sainii wapouna chagua kushiriki)

Sehemu ya kwanza. **Karatasi ya habari**.

Dibaji

Mimi ni……..nafanya kazi na mwenzangu Dkt Were Andrew Onyino aliye mwanafunzi katika chuo kikuu cha Nairobi. Tunafanya utafiti kuhusu kutibu kovu kutumia viwango tofauti vya dawa ya aina ya Triamcinolone Acetonide namadhara yake mwilini. Nitawapa maelezo nakuwaaalika kuhudhuria katika utafiti huu. Kabla ya kuamua, ukona uhuru wakuulizia ufafanuzi Zaidi kutoka kwa yeyote kwa starehe zako. Fomu hii yaidhini/ ridhaa huendaika wana maneno ambaye huyaelewi. Tafadhali niulize usipoele watu naavyo pitia habari name ntachukua muda wangu kukueleza. Vilevile, kama una maswali baadaye waweza kuniuliza mimi, ama wenzangu hapa.

Madhumuni/ niaya utafiti

Ugonjwa wa kovusana sana hutibiwa kutumia dawa ya Triamcinolone Acetonide ambayo inaweza kusababisha madhara kwa miili ya wanadamu. Sehemu ambazo huadhiriwa kwaurahisi nikama sehemu ya ngozi ambapo inaweza kupoteza rangi yake, kufanya kidonda au kuenda katika mwili wote nakufanya madhara zaidi. Kwa sababu hii, naili tuweze kujua kiwango asili ya hii dawa ambayo haiwezi kudhuru miili ya binadamu, tungependa kufanya utafiti ili tuweze kugundua kipimo asili ya dawa ya Triamcinolone Acetonide ambayo inaweza kutumiwa kutibu makovu bila kuleta madhara katika mwili.

Tunaamini unaweza kutusaidia kwa kushiriki katika huu utafiti ili tuweze kuboresha maarifa ya jinsi ya kutibu jangahii la makovu katika waafrika.

Aina ya kuingilia kati

Huu utafitiutahusishaushirikiwakokibinafsi. Utachukuadakikaishirinitu.

Ushirikiwahiari

Ushirikawakokatitautafitihuunikwahiariyakomwenyewe. Ni chaguolakokushiriki au kutoshiriki. Ukichaguakutoshiriki,
hudumazoteunazopokeaklinikiyaplastikizitaendeleakamakawaidanahakunakitakachobadilika.

Utaratibu

A. Tutakualikautusaidiekujuazaidikuhusumakovuulionayomwilini. Tunakualikakujiungana hi mpangohuuwautafiti. Ukikubali, utaulizwakujibumaswalimachachenitakayokuuliza.

B. Utajazafomuyautafitiambayonitapeana ama mwenzangunatutasanya au wawezakujibudodosowewemwenyewe, ama ukisomewanaunawezasemakwasautijibuunalotakaniandikechini. Kama hautakikujibuswalilolotekatikautafiti,wawezaendakwaswalilingine. Habari itakayopeanwaniyasiri,najinalakohalitanakiliwakwafomu, nibaaadhituambaowatakutambuana hakuna mwengineilamkaguziwatakwimu (data) atakayeafikiautafitiwako.

Hatari

Japokwakatikautafitihutahisivizurikuongeleaswalafulani, hautalazimishwakujibuswalilolote au kujihusishanamajadiliano/mahojiano/utafitikamahuhisikufanya vile nani bora pia. Huna lawamayakutupatiasababuyakutojibuswalilolotelile, au kwakukataakujihusishanautafiti.

Faida

Hakutakuanafaida za mojakwamojakwakowewelakinikuhudhuriakwakohuendakukatusaidiakujuamengikuhusiananajin siyakuboreshakupeanahuduma zaafyakatikajamiiyako.

Kulipia

Hutapewamalipoyanamnayoyotekuchangiautafiti.

Siri

Huu utafitiutakavyofanyikakatikajhamiihuendaikavutiawatunaiwapoutahudhuria,wawezakuulizwama swalinabaadhiyawatukatikajamii. Hatutapeanahabarikukuhusunjeyakundiletu. Habari ambayotutachukuakutokananahuuutafitiitaekwakibinafsi. Habari yoyotekukuhusuitakuwananambaribadalayajinalako.

Watafitipekeendiowatakaojuanambariyakonahaitafikiwanayeyotetu.

Kugawanamatokeo

Hakuna kileutakachotwambiakitajadiliwanayeyote yule njeyakundihili la utafiti, na hakuna kitakachoidhinishwajinalako.

Ujumbeambaotutapatakutokananahuuutafititutajadilianawenajamiikablaiwehurukwawatuweng ine. Kila atakayeshirikiatapokeamaelezokiufupiyamajibu. .Tutachapishamajibundiposawenginewalionanahamuwawezekujifunzakutokananautafiti.

Haki yakukataa au kujitoa

Sio lazimaushirikikatikautafitihuukamahunaniayakufanyahivo, nakuchaguakutoshirikihaitadhurukuupokeahudumazinazopeanwakatikakliniki za plastikikwanjiayoyoteile.

Wakuwasilianano

Ikiwa una swalilolote, unawezaukaulizasasahivi ama baadaye. Kama una niayakuulizabaadaeunawezawasilianamikupitiawafwatao: Dkt. Were Andrew kwa 0722251637 ama KNH-UON ERC kwanambari 0799495829 Hilipendekezo la utafitilimepitiwanakukubaliwanabodiyachuokikuu cha Nairobi pamojana Hospital kuuya Kenyatta; chanzo chao nikuhakikishakwambawashirikiwautafitiwanalindwakutokananamadhara.

Sehemuyapili:Cheti cha idhini/ridhaa

Nimealikwakushirikikatikautafitikuhusu mambo yanayochangiaupatikanajiwahuduma za afya. Nimepitiahabariifuatayo, ama nimesomewa. Nimekuananafasikuulizamaswalikuhusukuihusunamaswaliyoyoteambayonmeulizwanimeyajibuk adriyaufahamunautosheleziwangu. Ninaidhinikibinafsikuwamshirikakatikastadihii.

Jina la uchapishaji la mshirika……

Saini yamshirika……..

Tarehe ……

Iwapohunaelimu

Nimehudhuriausomajikamiliwafomuyaidhinikwahuyumshirika, nayeamekuananafasiyakuulizamaswali. Nina uhakikakuwahuyuamepeanaidhinipasipokulazimishwa.

Jina la uchapisho la shahidi…… alamayakidoleyamshirika……..

Saini yashahidi…….

Tarehe ……

Wasilisho la mtafiti/mwenyekuchukuaidhini.

Nimemsomeakitaratibukaratasiyahabarihuyumwenyeuwezowakushiriki, nakwakadriyauwezowangunimehakikishakwambahuyumshirikaanaelewakuwayafuatayoyatafanyika:

1.

2.

3.

Nathibitishakuwamshirikaalipewanafasiyakuulizamaswalikuhusuutafitihuu, namaswali yote aliyoulizamshirikayamejibiwakisawasawanakwakadriyauwezowangu.

Nathibitishakwambahuyuhajalazimishwakupeanaidhininaidhiniimepeanwa bure nakwakujitolea.

Jina la uchapisho la anayechukuaidhini……..

Saini yaanayechukuaidhini……..

Tarehe …….

10.3 Appendix II: Data Collection Sheet

Study Code:

Age:

Sex:

Race:

Weight:

Family history of Keloids: Location of the scar:

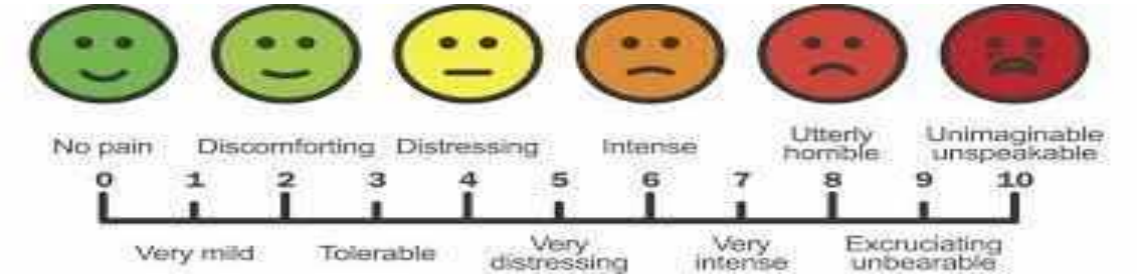
Date of Injection: Time of Injection:

Surface area of Scar in cm^2: Height of Scar in cm:

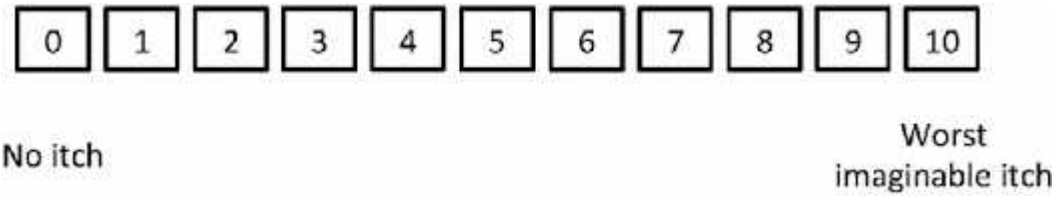
Study Data:

1. How did the keloid scar arise?
    a. Following Trauma
    b. Following Surgical intervention
    c. Spontaneous
    d. Secondary to skin infection
2. How long have you had the keloidal scar?
    a. < 3 months
    b. Between 3 – 6 months
    c. > 6 months
    d. > 1 year
3. Is the Keloid the index case or a recurrence following surgical excision?
    a. Index case
    b. Recurrence following surgical excision
    c. Recurrence following TAC injection > 6 months
4. If Question 3 above is a recurrence, how was the keloid initially managed?
    a. TAC only
    b. Surgically excision
    c. Surgical excision + TAC
    d. Surgical excision + TAC + Radiotherapy
    e. Others e.g. Bleomycin Injection, Verapamil et

5. Do you feel pain in the Keloid? If yes, how painful is it according to the pain scale below?



6. Does the keloid feel itchy or pruritic? If Yes, how do you rate the itchiness according to the numerical rating scale below?



7. Assessment of Keloid pre and post administration of 5 mg/cm^2, 7.5mg/cm^2 and 10mg/cm^2 of Triamcinolone Acetonide using the Vancouver Scar Scale

Feature		Score
Vascularity	Normal	0
	Pink	1
	Red	2
	Purple	3
Pigmentation	Normal	0
	Hypo-pigmentation	1
	Mixed-pigmentation	2
	Hyper-pigmentation	3
Pliability (Elasticity)	Normal	0
	Supple (flexible with minimal resistance)	1
	Yielding (giving way to pressure)	2
	Firm (inflexible, not easily moved, resistant to manual pressure)	3
	Banding (rope-like tissue that blanches with extension of the scar)	4
	Contracture (permanent shortening of scar, producing deformity or distortion)	5
Height	Flat	0
	< 2 mm	1
	2-5 mm	2
	> 5 mm	3
Pain	None	0
	Occasional	1
	Requires medication	2
Itchiness	None	0
	Occasional	1
	Requires medication	2

8. Please note if the following side effects occurred during treatment with 5mg/ml,7.5mg/ml and 10 mg/ml of TAC per cm^2 of Keloid and when they were noted (Time Interval: Day 0, Day 30 and Day 60)?
    a. Hypo-pigmentation
    b. Telangiectasia
    c. Sub-cutaneous fat atrophy
    d. Necrosis
    e. Ulceration
    f. Cushingoid syndrome

9. How satisfied are you with the outcome of the keloid treatment?

YES	1	2	3	4	5	6	7	8	9	10	NO
Improved											Worsened

Kiambatisho II: Karatasiya Mkusanyikowa data

Nambariya Kujifunza:

Umri:

Ngono:

Mbio:

Uzito:

Historia ya Familia yaMakovu: Mahali pa kovu:

Tareheyasindano: WakatiwaChanjo:

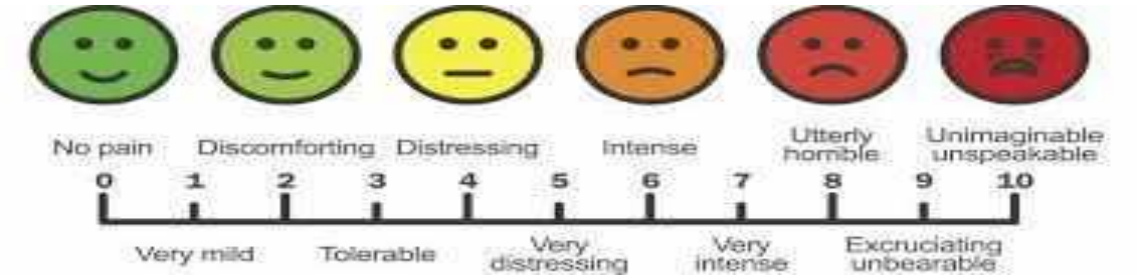
Upanawakovukwa cm $^{2:}$ Kadiri ya Kovu kwa cm:

Takwimu za Kujifunza:

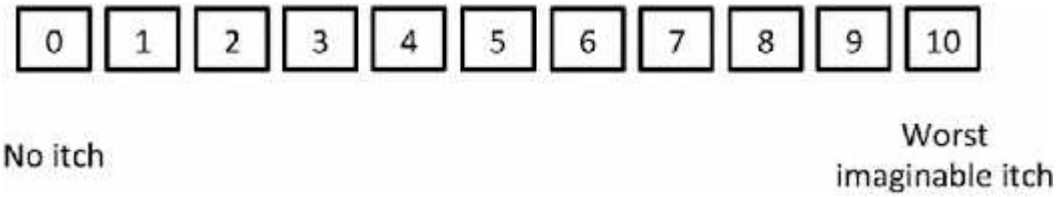
1. Je! Kovu ya keloid ilitokeaje?
    a. Kufuatiakujikwaa au Kukatwa
    b. Kufuatia uingiliajiwaupasuaji
    c. Mara mojabilasababu
    d. Kufuatiamaambukiziyangozi
2. Je! Umekuwanakovukwamudagani?
    a. Chini yamiezisita
    b. Kati yamiezi tatu nasita
    c. Zaidi yamiezisita
    d. Zaidi yamwakamoja
3. Je! Keloid nikesiya kwanza au inarudiakufuatiaupasuaji?
    a. Kesi ya kwanza
    b. Kurudiakufuatiauvumbuziwaupasuaji
    c. Kurudiakufuatiasindanoya TAC Zaidi yamiezi 6
4. Ikiwaumejibuswali la 3 hapojuuyakwambakovuimerjeabaadayamatibabu, kovuhapoawaliilitibiwakivipi?
    a. Sindanoya TAC pekee
    b. Ilifanyiwaupasuajikuiondoa

c. Upasuajinasindanoya TAC
d. Upasuajinasindanoya TAC nabaadayekuchomwa(Radiotherapy)
e. Kutumiamfumomwinginekamasindanoya Bleomycin ama kutumiadawayaainaya Verapamil.

5. Je!Unahisimaumivukwenyekovu? Ikiwaunahisi, niuchunguwakiwangoganikulingananakiwango cha maumivuchini?



6. Je!Unahisikujikunakwenyekovu? Ikiwaunahisikujikuna, nikiwangoganikulingananakiwango cha hesabuchini?



7. Upimajiwadalilinamorphologiawaugonjwawakovubaadayakutumiaviwangotofautivyada waya TAC kwa vipimovya 5mg/cm^2, 7.5mg/cm^{2}na 10mg/cm^{2}vyaukitumiawigowa Vancouver Scar.

Feature		Score
Vascularity	Normal	0
	Pink	1
	Red	2
	Purple	3
Pigmentation	Normal	0
	Hypo-pigmentation	1
	Mixed-pigmentation	2
	Hyper-pigmentation	3
Pliability (Elasticity)	Normal	0
	Supple (flexible with minimal resistance)	1
	Yielding (giving way to pressure)	2
	Firm (inflexible, not easily moved, resistant to manual pressure)	3
	Banding (rope-like tissue that blanches with extension of the scar)	4
	Contracture (permanent shortening of scar, producing deformity or distortion)	5
Height	Flat	0
	< 2 mm	1
	2-5 mm	2
	> 5 mm	3
Pain	None	0
	Occasional	1
	Requires medication	2
Itchiness	None	0
	Occasional	1
	Requires medication	2

8. Tafadhalikumbukaikiwaatharizifuatazozilitokeabaadayakutumiaviwangotofautivyadaway a TAC kwa vipimo vya 5mg/cm^2, 7.5mg/cm^{2}na 10mg/cm^2 (Muda: Siku 0, Siku 30 na Siku 60)?
    a. Ngozi kupotezarangi
    b. Telangiectasia
    c. Mafuta yangozikuwanyembamba
    d. Koozakwenyekovu
    e. Kutokwanakidondakatikangozi
    f. Dalili yaugonjwawa Cushingoid
9. Umeridhikanamatokeoyamatibabuyakovukutumiasindanoya TAC ?

NDIYO	1	2	3	4	5	6	7	8	9		10	HAPANA
Imeboresha												Imedhiririkazaidi

10. Appendix III: Serious Adverse Event Form

Title of Proposal: ASSESSMENT OF THE OPTIMUM DOSAGE OF INTRA-LESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF KELOID SCARS AT KENYATTA NATIONAL HOSPITAL

Principal Investigator Dr Andrew Were

Supervisors: Dr Benjamin Wabwire, Dr Ferdinand Wanjala Nang'ole, Prof Stanley Khainga

1. Study participant identification number:

2. Date of serious adverse event:

3. Study participant age and sex:

4. Study participant identification number:

5. Study participant enrolment date:

6. Provide a description explanation of the serious adverse event: Was the serious adverse event related to the study:

Date:

Prepared by

Sign