

Comparative Efficacy of the Anthelmintic Sumithrin® (Phenothrin) Lotion and Potassium Permanganate Solution in Treatment of Embedded Jiggers (Tungiasis) In Kenya

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Abstract

The study aimed at determining whether the Anthelmintic Sumithrin® (Phenothrin) Lotion, code-named S-1555 lotion throughout the study, was more efficacious than contemporary treatment of embedded jigger lesions with a solution of potassium permanganate. It was an explanatory random clinical trial among highly selected jigger patients recruited from selected sites in western and central regions in Kenya who were each exposed to two Tungiasis treatment regimes on either foot. The design adopted was a double blinded trial that involved a pilot phase followed by a full study. The sample size for pilot was 10 and 90 for the full study. Quantitative methods including significance tests were employed to analyze the data collected. The results of this study showed that there was no significant difference in embedded jiggers' average diameter between the left and right feet before administration of the trial treatment and positive control. After treatment, the average diameters differed significantly between the feet treated with 5% S-1555 lotion and the feet treated with 0.05% KMnO₄ solution (0.1383mm and 0.9088mm differences of means respectively) at 95% confidence interval. Moreover, 34.42% of the jiggers studied showed a positive change in diameter (shrinking) and were therefore unviable or dead. 79.63% of these were on the feet treated with 5% S-1555 lotion, the rest on the feet treated with 0.05% KMnO₄ solution, with an odds ratio of 11.46 (CI=6.28-20.94), thus highly significant. In addition, at follow up on Day 14, the total number of new jigger infestations were significantly less on the trial feet than on the control feet (p-value=0.0009). However, Day 45 follow-up session showed no significant difference in the number of new TP infestations on either foot. As on previous follow-ups no significant adverse effects on the treated skin of either foot were noted. Based on these results, the study concludes that topical treatment of embedded jigger lesions (tungiasis) with the S-1555 Lotion was significantly more efficacious than the contemporary treatment with 0.05% KMnO₄ solution. Moreover, the S-1555 Lotion conferred significant residual protection against new tungiasis infestations, at least for two more weeks after the initial treatment. The treatment by 0.05% KMnO₄ solution did not confer such residual protection. These results can be useful in policy and decision making in regard to registration of the new product and as an alternative option for management of Tungiasis in Kenya.

Key Words: Tungiasis, Anthelmintic Sumithrin® (Phenothrin) Lotion, potassium permanganate, clinical trial

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I. Background

Jigger infestation is an important but neglected public health problem in Kenya. It is a vector-borne parasitic disease caused by the Jigger flea, also known as sand flea, Chigoe or *Tunga penetrans* (TP), an ectoparasite which causes Tungiasis (Ariza et al, 2007). It is a parasitic skin condition of humans and animals (zoonosis). Tetanus is a common secondary infection that has been associated with deaths of non-immunized jigger victims. The flea affects many impoverished communities and families in the country. Approximately 10 million Kenyans are at risk of infestation in more than 20 counties, mostly in the Central, Coast, Western, Rift Valley and Nyanza regions (MOH, 2014). The severity of jigger infestation is its localization in the foot causing serious difficulty in walking and reducing the infected person's ability to work normally or attend school. In endemic areas, prevalence ranges from 15-40% of the population. It is estimated that over 2 million people in Kenya are infested with jiggers (MOH, 2014).

The first recorded mention of this parasitic infection was by Gonzalez Fernandez who, in 1525 described many instances of Spanish conquerors in Haiti who suffered from it. It is thought that jiggers were brought to East Africa by migrants from India who constructed the railway from Mombasa to Kampala in the 19th century. Poor hygiene is blamed for the infestation. However, some affected people think they are bewitched and simply let them run their course instead of trying to remove the insects (Rota Vonjata et al, 2008).

A jigger is an insect that breed in dry, dusty soils. According to its life cycle, the eggs, larvae and pupae live in the soil. It is only the adult female that burrows into the skin of humans and animals. Tungiasis is almost invariably associated with an intense inflammation around embedded fleas, and is associated with considerable morbidity (Feldmeier et al, 2004).

The penetrating the skin of animals and humans, female sand flea grows rapidly in size in a process called neosomy. It feeds on the host's blood, expels several hundred eggs into the environment, and eventually dies *in situ* and is sloughed off the epidermis by tissue repair mechanisms. Super-infection of the lesions is virtually constant, and a variety of aerobic and anaerobic bacteria have been isolated from embedded sand fleas. Fissures, ulcers, gangrene, localized edema, lymphedema, deformation and loss of nails and auto-amputation of digits are known sequels. In non-immune individuals, tungiasis is a risk factor for tetanus which may cause death. In Kenya, the active ingredient of the 5% S-1555 Lotion is registered by the Pest Control Products Board (PCPB) for formulation of public health products (PCPB, 2016)

Objective

1. To compare the efficacy of topical application of the 5% S-1555 Lotion against embedded jiggers with the contemporary treatment using potassium permanganate solution

II. Methodology

Target population

Persons infested with jiggers on any predilection site in their feet or hands residing in the study sites

Operational Framework

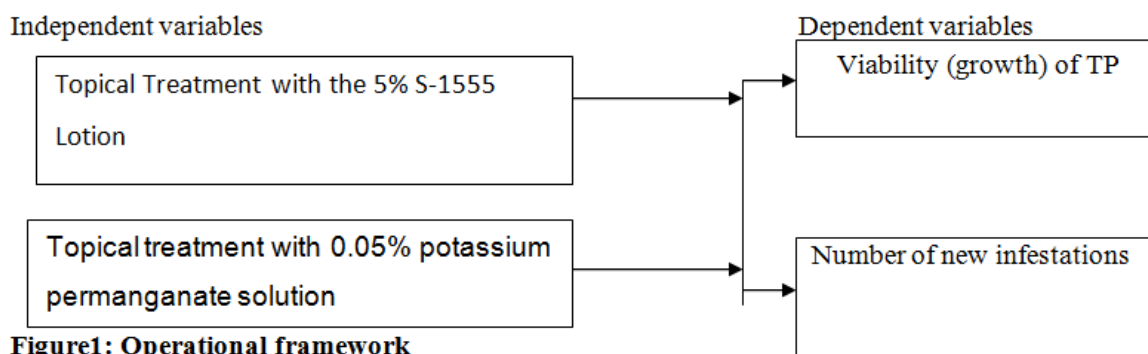


Figure1: Operational framework

Sample

Using fishers et al, 1990 formula for a population of > 10,000 people ($n = z^2 pq/d^2$) where the prevalence of jiggers in Kenya is 4%, then the minimum sample size arrived through this formula using 95% (0.05) desired degree of accuracy is 59 persons. Since we had four sites, this implied that each site required a minimum sample size of 15 people. However, the research team decided to increase the sample size for every site to 30 persons thus giving a total sample size of 100 people infested by jiggers on their feet. These were randomly selected for the two-fold study from four jigger- endemic areas in Kenya namely Busia, Siaya and Nyeri counties (see separate report for the Kiambu county study (pilot phase). Diagnosis was in accordance with Eisele et.al. i.e. flea in *statupenetrandi*: a reddish brownish itchy spot with a diameter of 1-2mm(early lesion); lesions presenting as a white patch with a diameter of 3-10mm with a central black dot (mature lesion); or a brownish –black circular crust with or without surrounding necrosis of the epidermis (dead parasite).

Sampling procedure

Purposive and systematic random sampling was used to select study subjects from a list of jigger-endemic regions and jigger infested persons compiled by the Ministry of Health personnel.

Data collection techniques

One foot was treated with a positive control product (0.05% potassium permanganate solution) and the other by the trial treatment (S-1555 Lotion). The right foot with the KMnO₄ and left foot with S-1555 lotion.

Two parasitic lesions on each foot were treated and recorded photographically for assessment purposes.

The active ingredient of S-1555Lotion was in concentrations of 5%. The positive control (KMnO₄ solution) was in its recommended formulation of 0.05%.

The S-1555Lotion was applied by smearing a light layer of lotion ~60 µl on each lesion containing the embedded *Tungapenetrans* (PT). The treatment was left on lesion for 12 hours after application, without being washed away.

The control treatment was by dipping the parasitic lesions in a solution of 0.05% KMnO₄ for 15 minutes.

PRE-APPLICATION PROCEEDURE: 2 lesions with a Fortaleza classification of level 2 were identified on each foot. They were marked and photographed with an ID number superimposed.

To achieve this, both feet were washed with clean water prepared by project team. The feet were thoroughly cleaned with clean adequate water and soap and then wiped with a clean towel prepared by the project team.

ACTUAL TOPICAL APPLICATION: Topical application was repeated on Day 4 after evaluation of treatment outcomes.

CLINICAL ASSESSMENT AFTER TREATMENT: The assessment was carried out by a team comprising a dermatologist, a vector control specialist and 2 research assistants. There were two such teams. These assessments were done on Day 1 and Day 4. Extra follow-ups were done on Day 14 and Day 45.

DETAILS OF ASSESMENT: Clinical assessment by the dermatologist included observation of the state of the TP lesions on both feet, identifying any healing processes underway, from which the cure rates will be derived, based on MOH guidelines. Any adverse reactions to the application were also being noted. Verbal interview with patient elicited overall comments regarding the treatment. These comments were recorded.

1. Effects of the S-1555Lotion on the TP lesions, whether negative or positive, were noted and compared with those of 0.05% KMnO₄ solution treatment (positive control).

2. Effects of the S-1555Lotion on embedded TP, both negative and positive, were noted and compared with those of 0.05% KMnO₄ solution treatment (positive control).

3. All study TP lesions were numbered prior to treatment and their sizes in diameter, and state of inflammation measured using professional tools e.g. calipers and microscopic photographic record. The devices were provided by Sumitomo Chemical Co. Ltd.

4. The viability state of the treated embedded TP was studied on Day 4 and recorded.

Day 14 and Day 45 follow- ups mainly focused on number of new infestations on the respective feet. Any adverse effects or other clinical manifestations were also recorded for analysis of any prophylactic effect.

Quality Control

1. Trial lotion was prepared by Sumitomo Chemical Co. Ltd and verified for Active Ingredient by two representatives from Ministry of Health (NB: clinical dermatologist and research assistants administering the treatment and evaluating treatment outcomes were blinded). Positive Control (KMnO₄) was prepared and provided by MOH.

2. The study was therefore double blind, only the lead investigator and product owner were aware of the actual trial lotion's active ingredient.

Data Analysis Techniques

Quantitative methods including significance tests were employed to analyze the data collected.

Ethical Considerations

Participants had to sign an informed consent sheet upon being provided with the all the necessary information regarding the study including the benefits and dangers that could arise from any of the two chemicals used to treat jiggers as well as voluntarily dropping out of the study at any point.

Internal Ethical approval was by MOH's research coordination unit while external ethical approval was by given the Great Lakes University Ethics and Scientific Review Committee, an organization approved for the purpose by the National Council for Science and Technology (NCST)

FINDINGS

A total of 91 individuals who had jiggers on both legs from three counties: Busia, Nyeri and Siyawere enrolled in this study. In all the three counties, 91 study subjects were treated on the left leg with S-1555 lotion and potassium permanganate (0.05% KMnO₄) on the right leg. The cohort had 62(69%) male and 28(31%) female participants with the mean age of 13yrs (SD=13yrs) ranging from one year old to 67 years old. Out of the 91 study subjects 79(87%) are aged 16yrs and below (children) with mean age of 8.8yrs (SD=3.5yrs) and the rest 11(13%) are aged above 20yrs old (adults) with mean age of 43.9yrs (SD=14.4yrs). In regard to matters of

education, 30/91 (33%) individuals had none and the rest 61/91 (67%) were either in primary school or had completed primary school. Consequently, 69/91 (75.8%) were student, 16/91 (17.6%) had no occupation and 6/91 (6.6%) were self-employed. Only 8/91 (8.8%) participants were married, 6/91(6.6%) of the participants were mentally unstable while 2/91(2.2%) were disabled, one with deformed legs and the other had suffered a stroke. In Nyeri County, all (30/30) of the participants living in temporary houses, 89/89 reported not to have had any reaction experiences to any drug, chemical or lotion.

Table 1: Demographic characteristics of the study persons

County n (%)	Gender distribution	Age Statistics	Proportion of Children to adults
Busia 30(32.97%)	Male 21(70%)	Mean=10.2yrs	Children 30(100%)
	Female 9(30%)	Sd=2.75yrs	Adults 0(0%)
		Range=(2-4yrs)	
Nyeri 30(32.97%)	Male 16(55%)	Mean = 19.1yrs	Children 20(66.7%)
	Female 13(45%)	Sd=19.7yrs	Adults 10(33.3%)
		Range =(2-67yrs)	
Siaya 31(34.06%)	Male 25(80.6%)	Mean =9.9yrs	Children 29(94%)
	Female 6(19.4%)	Sd =7.5yrs	Adults 2(6%)
		Range =(1-45yrs)	

Table 2: Distribution of jiggers by Foot Site in Day One of the Study

1 st Toe	2 nd Toe	3 rd Toe	4 th Toe	5 th Toe	Heel	Margin	Sole
66(21.4%)	46(14.9%)	34(11.0%)	60(19.5%)	79(25.7%)	16(5.2%)	5(1.6%)	2(0.6%)

A total of 308 jiggers were surveyed on both legs with mean diameter of 2.7mm (SD=1.3mm) with the range (0.4-7.1mm). 155(53.6%) were on the left legs while those on the right legs were 143(46.4%). The jiggers were distributed on the first, second, third, fourth, fifth, heel, sole and margin as shown in table 2

Size of Jiggers in mm during Day One of the Study

A total of 155 jiggers were surveyed on the left legs with mean diameter of 2.66mm (SD=1.32mm) with the range (0.6-7.1mm) while 153 jiggers were surveyed on the right legs with mean diameter of 2.7mm (SD=1.32mm) with the range (0.4-6.9mm). The results show that there was no significant difference of jiggers' average diameter between the left and the right legs on day one, paired t-test: p = 0, 2885

Table 3: Comparison of Size of Jiggers across the Study Counties in day one

County	Average diameter of jiggers	Average diameter of jiggers by gender
Busia	4.4474mm	On Male participants =4.7461 On Female participants=3.8
Nyeri	1.7965mm	On Male participants =1.7688 On Female participants =1.8134
Siaya	2.4034mm	On Male participants =2.4569 On Female participants =2.1869

An ANOVA was run to check if the average jigger sizes differ across the counties and the results were as in table 3. Thus averages of jiggers diameter surveyed on different counties differ significantly. Busia County had significantly larger jiggers than the rest of the counties, chi square test, p= 0.0000

Size of the jiggers in Day Four of the Study

A total of 260 jiggers were surveyed on both legs with mean diameter of 3.18mm (SD=1.31mm) with the range (0.-6.8mm). 128(49.2%) were on the left legs while 132(50.8%) were on the right legs. The jiggers were distributed on the first, second, third, fourth, fifth, heel, sole and margin as follows

Table 4: Number of Jiggers Surveyed In Day 4 of the Study

1	2	3	4	5	Heel	Margin	Sole
51(19.6%)	40(15.4%)	31(11.9%)	46(17.7%)	71(27.3%)	14(5.4%)	5(1.9%)	2(0.8%)

Table 5: Comparison of Jiggers by Left and Right Foot

	Sample size	Mean	Standard deviation	Range
Left	128	2.8	1.22	0.8-6.3
Right	132	3.5	1.28	0-6.8

The jiggers on the left and right legs statistics are summarized in table 5. The results in table 4 further shows that on day four the average jigger diameter differed significantly between the left and the right legs, t-test: $p = 0.0000$

The table6: Average Diameter of jiggers Surveyed in Different counties

County	Average diameter of jiggers	Average diameter of jiggers by sample
Busia	4.1487mm	On left legs=3.9026mm
		On right legs=4.3947mm
Nyeri	2.5277mm	On left legs=2.1023mm
		On right legs=2.9170mm
Siaya	3.0202mm	On left legs=2.5595mm
		On right legs=3.4808mm

General observations

The general observation from table 6 was that in day four Busia County had the biggest jiggers on average of diameter followed by Siaya county and Nyeri county with the smallest Jiggers by average diameter. Additionally, in all the three counties the average diameter of jiggers on the right legs was greater than the average diameter of jiggers on the left legs. However the largest difference was observed in SiayaCounty (0.9213mm) and the least in BusiaCounty (0.4921).

Table7: Average Diameter of Jiggers Surveyed On Different Gender

Gender of participant	Average diameter of jiggers	Average diameter of jiggers by sample
Male participants	3.2676mm	Left legs= 3.0232mm
		Right Legs=3.5035mm
Female participants	3.0215mm	Left legs= 2.4152mm
		Right Legs=3.6149mm

From table 7 it can be noted that the jiggers on male participants were bigger compared to the jiggers on the female participants. Moreover, the difference (Right legs- left legs) of means of female participants (1.2mm) is higher than the difference (Right legs- left legs) of means male participants (0.4mm).

Table 8: Comparison of Jigger in Day One and DayFour by Average Diameter

	Average diameter on Day 1	Average diameter on Day 4	Difference of means
Left	2.6369	2.7762	-0.1393
Right	2.6835	3.5923	-0.9088

Table 8 shows at a glance the comparison of average (mean) diameter of jiggers on day one and day four for the two samples. Although the jiggers on both legs continued to grow the growth on average diameter of jiggers on the right legs was significantly higher than the growth on average diameter of jiggers on the left legs.

Table 9: Comparative Difference of Jiggers by Day One Day Four

	Sample size	Average difference	Standard error of the differences
Left legs	117	-0.0197mm	1.05mm
Right legs	119	-0.6440mm	1.2mm

Out of the 155 jiggers surveyed on day one 117(75.5%) were traced on day four on the same position. The difference of the diameter of the jiggers on the two days was summarized in the table 9.

Table10: Comparison of Jiggers Size by Gender and Foot

Gender	Average change (sample size)	Average change by sample (sample size)		P-value
Male	-0.5078(152)	Left (75)	-0.189	0.0001
		Right (77)	-0.818	
Female	-0.0780(82)	Left (41)	0.219	0.5711
		Right(41)	-0.375	

On both samples (left and right legs) the difference is significant (significantly different from zero) with $p\text{-value} < 0.001$. However, jiggers on the left legs has a significantly ($p\text{-value} =$) lower average change compare to the jiggers on the right legs. Comparison of the differences between genders showed that the average change of jiggers' diameter among the male participants was significantly larger than the average change of jiggers' diameter on female participants. Moreover, among the female participants the average change of the left legs was positive, meaning that the jiggers actually shrunk.

Table 11: Comparison of Jiggers Size By age group and Foot

Age groups	Average change (sample size)	Average change by sample (sample size)		P-value
0-5yrs	0.11 (40)	Left (19)	0.3368	0.7216
		Right (21)	-0.0952	
6-11yrs	-0.580 (107)	Left (54)	-0.1037	0.0001
		Right (53)	-1.066	
12-17yrs	-0.569(58)	Left (28)	-0.2464	0.0079
		Right (30)	-0.87	
>18yrs	0.3678 (28)	Left (14)	0.2214	0.5015
		Right (14)	0.5142	

As indicated in table 11, comparison among the age groups shows that two age groups had a positive average change: 0-5yrs and >18yrs. With >18yrs having the highest positive average change.

Table 12: Comparison of Jiggers by Size and Counties

County	Average change (sample size)	Average change by sample (sample size)		P-value
Busia	-0.6047(84)	Left()	-0.1725mm	0.0001
		Right()	-0.9977mm	
Nyeri	0.4057(70)	Left()	0.4805mm	0.2167
		Right()	0.3264mm	
Siaya	-0.6902(82)	Left()	-0.3097mm	0.00001
		Right()	-1.0707mm	

As shown in table 12, comparison among the counties revealed that the average change in the jiggers' diameter was positive in Nyeri county while in Siaya and Busia the average change in the jiggers' diameter was negative (the jiggers grew in diameter).

Table 13: Mortality Situation of the Jiggers in Day Four

	Dead	Alive	Total
Left	86	42	128
Right	20	112	132
	106	154	260

Out of 308 jiggers surveyed on day 1 106/308(34.42%) were dead on the fourth day. 86/106(79.63%) were on the left legs and the rest on the right legs.

From the above table the odds ratio was calculated to be 11.46 (CI=6.28-20.94). Thus the odds (chance) of a jigger on the left leg being dead on day four is 11 times compared to the jigger on the right legs. This is highly significant.

New infestations and adverse effects

Table 14: subjective adverse or side-effects of the treatments on the skin and new infestations on Day 4

Factor	sample	Yes	No	OR (95%CI) p-value
Irritation during application	Right	19	16	OR=1.1875 95% CI=(1.1875,0.0000) p-value=0.0025
	Left	0	35	
Ease of application	Right	21	0	No significant difference
	Left	21	0	
Appearance of the skin texture	Right(smooth)	18	1	No significant difference
	Left	18	1	
Texture of jigger lesion	Right(hardened)	19	0	No significant difference
	Left	19	0	
Number of new infestation	Right	25	2	OR= 0.0030 95% CI=(0.0003,0.0347) p-value<0.0001
	Left	1	27	

From the above table the odds ratio that either treatment would cause irritation during application was calculated to be 1.1875 (95%CI= [1.1875, 0.0000] p-value=0.0025). Thus there was a probability that the treatment by 0.05% KMnO4 solution would cause irritation on the subject's feet during application. Treatment with the S-1555 lotion did not cause any irritation on the subjects' feet.

Table 15: Number of Jiggers Reported In Day 14 and Prevalence of Dermatitis

Sample (sample size)	Total no. of jiggers	Maximum no. of infestation	Prevalence of dermatitis
Left	55	12	2/91 (2.91%)
Right	144	13	3/91(3.3%)

The total numbers of jiggers reported on day 15 were 199 with 144 being on the right side while 55 were on the left side as summarized on the Table 15, with five study subjects reported to have dermatitis.

Table 16: Comparison of Jiggers by Left and Right Foot in Day 45

Sample (sample size)	Total no. of jiggers	Maximum no. of infestation	Prevalence of dermatitis	of	Prevalence of edema
Left	156	14	2/91 (2.91%)		1/91(1.1%)
Right	211	19	2/91 (2.91%)		1/91(1.1%)

Considering the total number of jiggers the left side had less jiggers significantly (p-value= 0.0009), while considering the prevalence of dermatitis there is no significant difference. However, considering the total number of jiggers the left side had less jiggers there was no significant difference (p-value= 0.1534). Additionally, the adverse infections of dermatitis and edema were typically the same.

III. DISCUSSIONS

Demographics

The following demographical characteristics were notable: of the subjects, 69% were Males; the mean age of the entire sample was 13 years. On Education background, 75.8 % were still in primary school. 6.6 % of the subjects were mentally unstable While 2.2 % were physically disabled.

Because the subjects were selected at random from the study population, these characteristics of the subjects confirm findings by past studies that primary school –age boys; the mentally and physically challenged to be most at risk of jigger infestations. This can be attributed to poor personal hygiene, especially lack of frequent feet washing habit among boys in the country and the neglect of the mentally - challenged individuals by family members. The long hours spent by physically challenged individuals on dusty floors expose them to the environmental risk factors for jigger infestations (MOH Kenya, *National Policy Guidelines on Prevention and Control of Jigger infestations*, 2014).

Comparative efficacy

On Day 1, there was no significant difference between the mean sizes (diameter) of jiggers on either left or right feet. This was purposive as per the study design. Out the total number of jiggers on either foot, only 2 jiggers per foot and of the same development stage in lifecycle (Fortaleza stage 2) were selected for the study.

The main predilection sites were toes (92%) as is known from other studies (e.g.JörgHeukelbach, Thomas Wilcke, Margit Eisele and Hermann Feldmeier, *Ectopic Localization of Tungiasis*,Am.J.Trop.Med.Hyg.,67(2),2002,pp.214-216) , the rest of the infested sites being heels, soles and foot margins.

On examination at Day 4, the average size (diameter) of treated jiggers differed significantly between left and right feet, with the left feet having a mean jigger size (diameter) of 2.8mm while that of jiggers on the right feet was 3.5mm. This means the treatment by the S-1555Lotion either slowed the growth of a significant number of embedded jiggers or killed them altogether. This is shown by the difference between the means of jigger sizes on Day 1 and Day 4(-0.1393 for left feet and – 0.9088 right feet respectively). This result means the treatment by the S-1555Lotion slowed the growth of a significant number of embedded jiggers. In some cases, e.g. comparison by gender, the difference in means was actually positive on the left (0.219), meaning that a significant number of jiggers shrunk by size and had therefore been killed by the S-1555 Lotion treatment on Day 4.

By comparison, the treatment by the 0.05%KMnO4 solution did not slow down the growth of a significant number of embedded jiggers nor did it kill a significant number of them.

On odds ratio calculation, the chance of an embedded jigger being killed by the S-1555 Lotion by Day 4 of treatment was 11 times that of being killed by the 0.05% KMnO4 solution.

On adverse reactions e.g. skin or lesion irritation during application, ease of application, difference of appearance of skin texture or jigger lesion texture or appearance before and after treatment, there was no significant difference between the respective treatments

However, by the same day, treatment using theS-1555Lotion seemed to have conferred significant protection against new infestations. This was judging by the total number of subjects presenting with new infestations on either feet. 25 subjects presented with new (one or more) infestations on the right foot, with only 1 subject presenting with new infestations on the left foot (P=<0.0001).

Follow up in respect to number of new infestations and adverse effects

In addition to checking for any adverse effects of either treatment, the variable of protection against new infestations was also assessed during follow-up sessions on Day 14 and Day 45. On Day 14, theS-

S-1555 Lotion showed significant protection against new infestations. But this prophylactic effect had declined to insignificant levels by Day 45. Secondary infections by dermatitis and edema were not significantly different by foot or by treatment.

The treatment by 0.05% KMnO₄ solution continued to show no prophylactic effect on either of the follow-up sessions.

At the same time, no significant adverse effects of either treatment were observed during these follow-ups. This was consistent with pharmacological literature contained in the S-1555 Lotion label and accompanying pamphlet. 0.05% KMnO₄ solution had also been used for long in the country to treat embedded jiggers without adverse reactions.

Notwithstanding these findings, irritation on the skin by 0.05% KMnO₄ solution during application was mentioned by more than half of the subjects. None of the subjects reported any irritation during application of the S-1555 lotion. This was consistent with safety studies by the developer as well as contained in the user's pamphlet accompanying the drug. 0.05% KMnO₄, like other disinfectants and anti-septic, is known to irritate skin especially open wounds.

IV. Conclusions

Based on the results of the study, the topical treatment of embedded jigger lesions (tungiasis) with the S-1555 Lotion was significantly more efficacious than the contemporary treatment of dipping the lesions in a 0.05% KMnO₄ solution.

Therefore, comparatively, the topical application of the S-1555 Lotion against embedded jiggers is clinically more preferable compared to the contemporary treatment using potassium permanganate solution.

Moreover, the S-1555 Lotion conferred significant residual protection against new tungiasis infestations, at least for two more weeks after the initial treatment. The treatment by 0.05% KMnO₄ solution did not seem to confer such residual protection. The non-significant difference on residual protection at Day 45 may be attributable to washing off or falling off of the topical drugs due to repeated washing and exposure.

The two treatments also did not cause any significant adverse effects and are therefore safe for use in the country.

V. Recommendations

The Kenya Pharmacy and Poisons Board should consider registering the S-1555 Lotion for use in the country as a curative and preventative treatment of tungiasis. The Clinical Guidelines for Kenya (2002) on treatment of embedded jiggers (tungiasis) as well as the National Policy Guidelines on Prevention and Control of Jigger Infestations (2014) should also be revised to include topical treatment with residual pyrethroids such as the S-1555 Lotion.

The developer, Sumitomo Chemical Co. Ltd should consider other formulations and dosages of the S-1555 Lotion's Active Ingredient that can penetrate deeper into the epidermis where the jigger flea embeds. This would hopefully provide better knockdown effect on embedded jiggers and therefore provide faster relief for patients, as well as more residual protection.

Further studies should be done with the S-1555 Lotion and other formulations of the AI to determine their precise efficacy, susceptibility and resistance profiles, including the knockdown and residual effects.

References

- [1]. Ariza L, Seidenschwang M, Buckendahl J, Gomide M, Feldmeier H, Heukelbach J. (2007) *Tungiasis: a neglected disease causing severe morbidity in a shantytown in Fortaleza, State of Brazil, Ceará*. Rev Soc Bras Med Trop. 40(1):63-67.
- [2]. Feldmeier H, Eisel M, Marck EV, Mehlhorn H, Ribeiro R. (2004). *Investigations on the biology, epidemiology, pathology and control of Tungapenetrans in Brazil*. IV. Clinical and histopathology. Parasitol Res 94:275-282.
- [3]. Ratovonjato J, Randriambeloso J, Robert V. (2008). *Tunga penetrans (Insecta, Siphonaptera, Tungidae) à Madagascar: une nuisance négligée*. Revue Médecine Vétérinaire 11:551-556.
- [4]. MOH (Kenya) 2014, *National Policy Guidelines on Prevention and Control of Jigger infestations*.
- [5]. PCPB (Kenya) 2016, *Fully Registered Pest Control Products*.

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