

Clinical Trial on the Effectiveness of *Gliricidia sepium* (Kakawati) in Treating Patients with Scabies in the Antipolo CBHP

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ABSTRACT

This is a double blind, randomized, controlled, clinical trial comparing the effectiveness and safety of *Gliricidia sepium* (Kakawati) poultice against sulfur lotion as an anti-scabies agent. Forty four subjects were recruited from a community in Antipolo and included in the study. Subjects were assessed, and then randomized into control and treatment groups. Subjects were re-assessed after 5 days for clinical resolution of the disease manifestations.

This study showed comparable clinical resolution between the treatment and control groups.

"Kakawati" is a promising herbal preparation and has great potential as an effective and safe anti-scabies agent. Further studies involving a larger number of subjects and a longer study period are recommended. (*Phil J Microbiol Infect Dis* 1999; 28(4):147-153)

Key words: scabies, *Gliricidia sepium*, sulfur

INTRODUCTION

Scabies is one of the most important prevalent contagious diseases caused by the human itch mite *Sarcoptes scabiei*.¹ It is the most common cause of itching dermatoses in the world infecting 300 million persons per year.² Exact figures for the incidence of scabies infection in the Philippines are not known. However, data on annual incidence of scabies seen in one health institution in Manila showed a rate of 45 per 1000 patients.³

Currently, there are numerous medical treatments available for scabies. Most of these are quite effective. However, the cost of these medications is quite prohibitive particularly for the segment of the population most commonly affected by this disease. Most of the patients infected with this disease belong to the lower socio-economic bracket.⁴ The highly contagious nature of the disease requires that all other household members be treated simultaneously. This adds to the actual cost to be shouldered by the family. The high cost of the medications results in inadequate treatment hence chronic infestations or re-infections.

Our culture has acknowledged the effectiveness of traditional medicine for a variety of illnesses. The continued rise in the cost of medicines paved the way for physicians and the government to look into herbal preparations as a practical alternative for some of the common ailments in our country. In fact, there are several herbal products that are being advocated by the DOH as effective measures for some common diseases seen in the community. Unfortunately, there is no current recommendation for scabies. In this light, *Gliricidia sepium* offers a promising treatment option.

Gliricidia sepium, locally known as "kakawati," is a tropical plant that has been used for the past years to effectively treat several diseases like dermatophytic infections⁵ and gonorrhea.⁶ It has been used empirically in the community and has been shown to result in clinical resolution of the disease. Although there are no formal studies documenting the effectiveness of "kakawati" in eradicating the human mite, *Sarcoptes scabiei*, it has been shown to have an acaricidal effect against a similar organism, the gallmite *Eriophyes geurreronis*, achieving an efficacy comparable with commercially available medications.⁷

The general objective of this study is to determine the effectiveness and safety of "kakawati" in treating patients with scabies in Antipolo, Rizal. Specific objectives are: to determine if the incidence rate of scabies in patients treated with kakawati is lower than the incidence rate of scabies among patients given sulfur lotion; to determine the number of patients with scabies who are effectively cured following treatment with "kakawati" after 5 days; to compare the cure rate of "kakawati" and sulfur among scabies

patients; and to compare the frequency of adverse reactions among patients treated with “kakawati” and those treated with sulfur.

MATERIALS AND METHODS

A. Plan of Investigation

The study is a double blind, randomized, and controlled clinical field trial comparing the effectiveness of “kakawati” against sulfur in treating patients with scabies. Subjects were recruited on a single dermatology community day. Flyers, posters and house to house visits informing the residents of Bagong Nayon II of the planned study was done a few days before. The assigned Dermatology resident and a community health worker facilitated the clinic. A consent form as well as an initial baseline questionnaire form was provided. Patients were evaluated by the resident for the presence or absence of scabies using the operational definition for clinical disease status (See definitions). A follow-up evaluation was done 5 days later. Another form was administered to the subjects this time checking for resolution of symptoms and appearance of adverse reactions, if any. The medications were provided for free for the patients as incentives to join the study.

A Physical Therapy student, unknown to the investigator, was asked to take a look at the contents of the canisters and note down which canisters have the "kakawati" and which one has sulfur. He was asked to place the paper with the identification inside a long brown envelope. This was only opened after the analysis has been done.

Subjects were assigned to either treatment group randomly by the fishbowl technique. One hundred sixty 2 x 2 inch pieces of paper, eighty bearing the letter A and the remaining eighty bearing the letter B, were folded and placed inside a paper bag. A health worker drew a folded stub, gave the indicated medicine to the subject depending on the drawn letter, then replaced the folded stub back into the bag. Subjects were assigned and identified by case numbers.

This is a double blind study. Patients were not told what treatment modalities they received. Likewise, the evaluator, health worker, and the principal investigator had no knowledge of which medication (A or B) was given to the patients. The actual contents of the medications were only revealed after the analysis of the study. Patients were followed up after 5 days of daily treatment and re-assessed.

B. Study Area

The CBHP in Bagong Nayon II, Antipolo Rizal, started in 1987. This was initially a resettlement area for squatters. A single health center aptly called Phase I was opened to provide a means of providing primary health care for the residents of this community and to promote and maintain efficient health care delivery systems. Since then, several other health centers were opened within the community. At present, there are 6 existing health care system. Among these centers, Ephphetha functions as the main center for all the areas in this site. It also has the highest outpatient census among the 5 other health centers. The study is conducted in this area to maximize patient recruitment.

The study area was chosen because of the high incidence of scabies infestation. In fact, there is a high annual incidence rate of about 17.386 per 1000 population.⁸ Moreover, the presence of a CBHP in an economically depressed areas can benefit from a less expensive alternative treatment to a disease which affects many.

C. Preparation of Materials

Sulfur:⁹ Commercially prepared sulfur lotion 5% was obtained from a drug company (MCB Pharmaceuticals, Manila). It was transferred to black film canisters with gray top.

“Kakawati.” Fresh dried “Kakawati” prepared according to the instructions. The kakawati poultice is then transferred to black film canisters identical to those used for the preceding preparation.

D. Subjects

1. Recruitment of Subjects

Subjects chosen for the study included only residents of Bagong Nayon II. Persons of all ages are eligible to participate in the study. Subjects were recruited during the dermatological special clinic day. They were assessed as having scabies clinically based on the questionnaire that the author prepared. The clinic was conducted by a dermatology resident on the said day with the help of community health workers acting as pharmacists. A consent form and an initial baseline questionnaire were provided. This questionnaire has been initially pre-tested among other patients not having scabies prior to its actual usage. Responses to the items in the questionnaire were coded. Free medications were given to the patients as an incentive for join the study.

Subjects were evaluated by one dermatology resident and included in the study if they met the operational definition of a case. After securing the consent to join the study, each subject was given the test medication depending on whether he gets A or B treatment based on the fishbowl technique. Subjects were assigned case numbers. Each patient received two units of same-lettered medication.

Since the disease is very contagious, other family members were given or prescribed Crotamiton (Eurax) lotion to be applied all over the body for 3 days. Only one type of baby soap (Johnson’s Baby Soap) was recommended. Likewise, only one type of anti-histamine was prescribed: (Chlorphenamine maleate)

At the end of each recruitment day, baseline questionnaires were tallied. Confounders were identified.

2. Sample Size: n= 81

3. Operational Definition:

a) Clinical Disease Status

This was determined through the following: first, history and physical examination by the dermatology resident assigned to the community for that day; second, checking for the following information on the most common lesions found in scabies² using the baseline questionnaire:

1. Burrows (slightly elevated, gray linear or S-shaped lines in the skin)
2. Nodules on the penis/scrotum
3. Erythematous papules on the hands/fingers
4. Vesicles and papules on the finger webs
5. Diffuse eruption sparing the face
6. Pinpoint erosions/crusts/papules on buttocks
7. Erythematous papules on inguinal area
8. Pustules on palms and soles of infants
9. Papules on upper extremities
10. Papules on lower extremities
11. Papules on the feet
12. Papules/ erosions on the umbilicus

The presence of severe nocturnal itching at night, other household members who experienced similar symptoms and at least two of the above mentioned lesions qualified the patient as a case.

b) Risk Factors:

These were collected in the initial baseline questionnaire

1) Exposure factors

- number of household members
- family member with scabies

2.) Confounding factors

- socio-economic conditions (occupation of head of household, monthly income, educational attainment)
- hygienic practices
- overcrowding

c) Inclusion criteria (definition of subjects)

- resident of Bagong Nasyon II, Antipolo, Rizal for 6 months
- diagnosed to have scabies according to the study's operational definition
- not receiving any treatment for scabies at time of study

d) Variables collected

1.) Independent variables

- Treatment with "kakawati": application of "kakawati" lotion from neck down, leave on the skin for 24 hours then rinse. Reapply sulfur daily for 5 consecutive days.
- Treatment with sulfur: application of sulfur lotion from neck down, leave on skin for 24 hours then rinse. Reapply for 5 consecutive days.

2.) Dependent variables

- Clinically cured with "kakawati" or sulfur: resolution of itching and disappearance lesions initially noted and no new lesions on the patient following "kakawati" or sulfur application for 5 consecutive days.
- Not clinically cured with "kakawati" or sulfur: persistence of itching and/or scabies lesions initially noted on the patient following "kakawati" application for 5 consecutive days
- Adverse reaction to "kakawati" or sulfur appearance of intense itching, rashes, and redness within 24 hours following application

3.) Confounding variables:

- Socio-economic factors (income, educational attainment)
- Hygienic practices
- Overcrowding

4. Quality Control and Potential Biases:

a.) Quality control measures were implemented throughout the course of the study.

- 1.) spot checks by the principal investigator
- 2.) regular spot checks done by the health workers
- 3.) random household spot check by the health workers to see if medications are being applied; health workers were instructed only to ask if the medications are being applied and not to observe actual application of the medication as this might defeat the purpose of blinding.

b.) Potential sources of bias were identified. Measures to minimize these were achieved through the following:

1.) Selection Bias

All patients diagnosed to have scabies according to the operational definition were recruited. Subjects were randomly assigned to the 2 treatment groups by the fishbowl technique. "Kakawati" and sulfur were provided for free. A baseline questionnaire was administered before enrolling subjects in the study that identified confounding factors. Matching will control confounders such as socio-economic status, overcrowding, and hygienic practices. To ensure that both treatment groups are compatible, midway through the study, at around noontime,

characteristics of all subjects recruited were matched. If the two groups are not comparable, subjects will be matched.

2.) Inter-observer Bias

Only one dermatology resident experienced in the clinical diagnosis of scabies conducted the initial evaluation of the subjects. The same resident saw the subjects after 5 days of daily application and assess for the presence or absence of symptoms.

3.) Lost to Follow-up

An additional 25 % of subjects were intended to be added to the sample size calculations to compensate for potential cases lost to follow up.

The health workers obtained addresses of all subjects and the same health workers followed up these patients. Subjects who have lived for less than 6 months in Bagong Nasyon II were not be included in the study to exclude transient residents who might not be around for the subsequent follow-up.

4.) Risk Factors

Risk factors were identified through the initial questionnaire. Response choices were provided to ensure that risk factors can be easily and properly classified. Risk factors identified as confounding variables were handled by matching subjects to ensure comparability for the two treatment groups.

5. Data Processing and Analysis

a.) Data processing was done using SPSS version 7.5 and statistica version 5.0

b.) Data analysis to test for significance for the 2 independent treatment groups made use of Fisher's Exact Probability Test

RESULTS

A total of 44 patients were included as subjects in this study based on the operational definition of cases outlined. Twenty subjects were randomly assigned to treatment group A, while twenty four were randomly assigned to treatment group B. Sex distribution was comparable with females comprising majority of the population in both groups. Age of subjects between the two treatment groups was likewise comparable as most of the subjects were in the 21 and below age range with majority in the 1 to 10 year age group. Most of the heads of households of the patients finished high school. Most of the patients had four to five family members in the household. Monthly income for the families of the patients ranged from Php 3,000 to Php 5,000 pesos. Most of them bathed at least once daily. Majority of the patients had other family members with pruritus. Most of them experienced increased severity of pruritus at night. Most commonly affected sites were the hands and buttocks. There were also 2 pregnant mothers who were included in each of the two treatment modalities. The risk factors were noted in each group and were assessed to be comparable between the two groups and matching of the subjects was not done anymore.

Five days after the patients were initially seen, the patients were re-examined. Subjects were evaluated for the presence or absence of pruritus and scabies lesions noted on initial examination based on the questionnaire administered. Results of the intervention showed 75% clinical resolution of symptoms among those given treatment A. An 87.5% clinical improvement was noted in the other group. However, there were 3 patients (or 15%) from treatment group A who did not show up for follow-up as against 2 patients (8.4%) from treatment group B. Two patients in group A still manifested with pruritic papules on follow-up. Treatment group B also had one patient still with pruritic and erythematous papules on the affected areas. Fisher's exact test showed a two-tailed measurement of 1.000.

On follow-up, the subjects were also evaluated for the presence of adverse reactions during the course of treatment. However, not a single subject complained of the development of redness, increased itchiness or development of rashes different from the initial scabies lesion after application of the medications in either group. The subjects noted ease of application, acceptable odor and a tolerable

amount of stickiness with treatment group A. Likewise there was ease of application but slightly unacceptable odor and relative stickiness for those who applied the medication in treatment group B.

Treatment group A received “kakawati” while treatment group B received sulfur lotion. This was determined after all the results have been collected and analyzed.

DISCUSSION

The subjects recruited for the study and segregated into the two treatment groups are comparable and reflective of the actual demographic characteristics of the patients afflicted with scabies. Sex distribution showed a slight predominance of females with 60% comprising treatment group A and 67 % comprising treatment group B. Reports assessing overall sex differences among patients afflicted with scabies show inconsistent results,¹⁰ but a local review¹¹ showed a slight female predominance. Several studies have shown a greater prevalence of infection among children and young adults.^{10,12} The age distribution of patients in this study parallels existing evidence in literature. Majority of the patients in either group A or B are within the 21 years and below range, 70% and 75 %, respectively.

Most of the heads of the household for the subjects in both groups were able to finish high school. Ten percent of the household heads of the families in Group A finished grade school, compared to almost thirty percent of those in Group B. Family size was also comparable as well as daily bathing of the subjects in both groups. Exposure and socio-economic factors identified initially, namely increased number of household members, presence of other family members with scabies, overcrowding, poverty, low educational attainment and poor personal hygiene, contribute greatly to the spread of the mites.¹⁰

In this study, majority of subjects had a family size of about 5 to 7 members with an average monthly income of about Php 4,000 to Php 5,000 per family. Most of the subjects shared their bed with at least one other person. Almost all subjects in the study had other family members presenting with pruritus and papules in the commonly affected areas of the body.

The evaluator made use of history and physical examination to document the presence or absence of scabies making use of the coded questionnaire. The examination of epidermal scrapings in the microscope is the only available objective modality for the confirmation study.² This method, although highly specific, is not very sensitive. An individual afflicted with scabies usually harbors, on the average, 11 mites.¹³ Nocturnal itching was noted in 70% of the subjects in the “kakawati” treatment group and 88% of those in the sulfur treatment group. The most common sites affected are outlined consistent with the findings of a previous study.³

Sulfur was chosen as the control medication because of its relatively high clinical cure rate at 88 %¹⁴ and it is the treatment of choice when cost of medication is the over-riding concern.⁹ In addition, sulfur is the treatment option most commonly utilized for children below 2 years of age and pregnant women. Other medications available like Lindane or Crotamiton for scabies are not recommended for these two groups. One preparation, Permethrin, can be used for these two groups and is actually the present drug of choice. However, this medication is very expensive and not yet commercially available in the country.

In terms of adverse reactions, it was interesting to note that none of the subjects in either group complained of any irritation despite both medications being applied and left on the skin for 24 hours.

The computations for the Fisher’s Exact Test only included those who completed the treatment program. It is another limitation of this study that a correction factor should have been applied to subjects lost to follow-up. The difference observed between the cure rates of the “kakawati” and sulfur groups was determined to be not statistically significant ($p > .05$). Based on this, “kakawati” is just as effective as sulfur lotion as an anti-scabies agent. However, the paper cannot say whether the “kakawati” preparation truly has a comparable cure rate or an inferior efficacy. The results are actually limited by the inability of

the study to reach the required sample size. These findings may not be truly reflective of the potential of the “kakawati” preparation.

CONCLUSIONS AND RECOMMENDATIONS

This study concludes that the “kakawati” preparation is just as effective as sulfur lotion in the treatment of scabies. However, this finding is limited by the inability of the study to reach the ideal sample size computed. Despite this limitation, we cannot discard the observation that “kakawati” indeed is a promising drug and future studies are in order so as to show its potential in this disease.

The potential of “kakawati” as an effective treatment option against scabies can be realized with further studies involving a larger number of subjects, ideally approximating or even exceeding the sample size computed. Correction for subjects lost to follow-up may be achieved by having additional subjects for recruitment on top of the sample size or have an efficient method of following-up patients at home with the help of the health workers. A longer study period is recommended. A six month or year long duration would be ideal to be truly reflective of the actual incidence of scabies in the study area. A better diagnostic method of confirming disease presence or absence is in order to provide an objective means of diagnosis.

LIMITATIONS OF THE STUDY

1. This study failed to reach the computed sample size therefore the results are not truly reflective of the curative potential of the test drug.
2. There were subjects lost to follow-up, which might have improved the results of either drugs used in the study.
3. The study covered only a single day of screening and evaluation of patients.

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