



Oral Albendazole Is Superior to Permethrin 5% for Scabies Treatment in Boarding School Indonesia

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Abstract: Scabies is a skin disease caused by *Sarcoptes scabiei* infestation and is classified as a neglected tropical disease (NTD). Permethrin 5% is the first-line treatment for scabies. However, adherence and accuracy in topical creams are common problems. Thus, it is necessary to think of alternative medication that is more accessible, more straightforward, and lower the risk of resistance. Albendazole appears to be an alternative therapy for eradicating scabies in the community base. Sixty subjects diagnosed with scabies were recruited and divided into two groups with randomization. The first group was given 400 mg oral albendazole for three consecutive days on the first and second week. The second group was applied permethrin 5% to the whole body once on the first night of the first and second week. The evaluation was carried out for four weeks, and improvement was stated absence of new lesions and healing of old lesions and pruritus. Data were analyzed using SPSS software (version 25, SPSS Inc., Chicago., IL). The X^2 test was used to examine the difference between groups, and $p < 0.05$ was considered significant. The cure rate of albendazole was significantly superior to permethrin topical (90.0% vs. 63.3%) with a p-value of 0.015. This study revealed the effectiveness of oral albendazole 400 mg/day for three consecutive days in the first and second weeks for treating scabies to topical permethrin 5%. No side effect seen in the use of albendazole and topical permethrin during the study. Albendazole could be an alternative drug option to eradicate scabies in low-middle-income countries.

Keywords: Scabies, Permethrin 5%, Oral Albendazole

1. Introduction

Scabies is an ectoparasite infestation of the skin caused by *Sarcoptes scabiei* var *hominis*. This disease has existed for at least 2500 years and infests 240 million people annually worldwide [1-3]. In 2009, the disease was commonly found as a public health problem and listed as a neglected tropical disease by the World Health Organization in 2013 due to lack of attention at local, national, and international levels [4]. Moreover, it has a higher incidence among the poor [5]. According to the global burden of scabies survey, Indonesia has the most significant scabies burden, followed by China, Timor-Leste, Vanuatu, and Fiji [6]. Based on primary health center data throughout Indonesia in 2008, the prevalence of

scabies is 5.6% - 12.95% [4]. Most of them found in a Muslim boarding school which called "Pondok pesantren" about 74% due to overcrowded, poor personal hygiene, repeated contact between student, and lack of promotive and preventive programs [7].

Transmission of scabies occurs through direct skin contact with infected persons. A minimum of ten minutes after contact could transmit mites to other people. Therefore scabies is highly contagious and hardly eradicated in the community [2, 8].

Scabies' treatment options include permethrin 5% topical as first-line therapy, benzyl benzoate, crotamiton, and sulfur. Although permethrin is potentially safer to use, it has variable effects on the scabietic mite, and the resistance to the

topical drug is emerging rapidly around the globe [9-11]. The topical treatment for the community management of endemic scabies seems impractical, resulting in the low motivation to repeat the treatment process. Recently, oral ivermectin has been used for mass treatment. This drug has been shown to reduce the prevalence of scabies and impetigo, and levels of hematuria in post-streptococcal glomerulonephritis [12]. Unfortunately, the availability of ivermectin in Indonesia was limited. Thus, the need for other drugs for community treatment is urgently required. Albendazole as anti-parasitic drugs will overcome the problems as its low cost and safe to use in children and hopefully have a good response in managing scabies in the community base.

Albendazole is a group of benzimidazole, a class of anti-parasitic drugs used to fight cestode and nematode. The mechanism of action is by inhibiting polymerization of microtubules through binding irreversibly to β -tubulin, an important component of the cytoskeleton of eukaryotes. Albendazole also causes impaired glucose utilization and causes a decrease in the parasite's glycogen stores. At high concentrations, albendazole inhibits parasitic metabolic pathways such as the Krebs cycle by inhibiting key enzymes such as malate dehydrogenase A subsequent decrease in ATP production occurs, which causes energy depletion, leading to the immobilization of the parasite and subsequent death. 13 Albendazole has regularly used as intestinal worm eradication national program in Indonesia since 1975 and has been dramatically reduced the helminthics infestation in Indonesia from 78.6% in 1987 to 8.9% in 2003 [14]. Albendazole is safe to use in children, and side effects are usually mild, ranging from nausea, vomiting, diarrhea, stomach cramps, dizziness, drowsiness, headache, insomnia, fever, and fatigue [15]. There are only limited studies that reported the efficacy of albendazole to treat scabies. For that reason, we conduct a clinical trial to investigate the effectiveness of oral albendazole to topical permethrin 5% for managing scabies.

2. Patients and Methods

This study was approved by the ethics committee of the Faculty of Medicine Universitas Sebelas Maret No. 183/UN27.6/KEPK/2018. All the subject or their caregivers was obtaining informed consent.

2.1. Literature Search

The literature search was conducted using PubMed and Google Scholar with the term "scabies", "albendazole" to identify other studies that reported albendazole treatment for scabies. The full texts of retrieved literature were read carefully.

2.2. Patients Recruitment

This study was conducted at Islamic Boarding School Surakarta junior and senior high school, ranging from 12 to 18 years old. All students were examined to determine the

diagnosis of scabies. Students diagnosed with scabies were asked to participate, and 60 students agreed to participate in the study. The participants with other dermatologic diseases like dermatitis, psoriasis, and urticaria are excluded from the study. The patient who has an allergy to albendazole or has secondary infections is also excluded. Simple randomization was done using odd-even numbering.

2.3. Clinical Assessment

Diagnosis of scabies was performed from clinical assessment. Clinical diagnosis was carried out at least two of the four cardinal signs: nocturnal pruritus, tunnel or burrows by clinical presentation, papules or pustules in specific classical sites, and close contact group with similar symptoms. Light microscopy and dermoscopy were also performed to enhance the diagnosis in the initial treatment.

2.4. Treatment Measurement and Evaluation

After the diagnosis of scabies was established, subjects were divided into two groups by simple random sampling. Group A received 400 mg/day oral albendazole for three consecutive days at first and second week, as recommended for soil-transmitted helminth infection [16]. Group B was applied permethrin 5% cream throughout the body at night on the first and second week as previously recommended [17]. Clinical evaluation was done every week for four weeks by experienced investigators blinded to the treatments received. At each visit, the investigators recorded the pruritus intensity as decreased or increased pruritus, the presence or absence of the parasite, and changes in lesion counts. "Cure" was determined if the absence of new lesions and healing of all old lesions regardless of the presence of post scabietic nodules. If new lesions were confirmed microscopically at the four-week follow-up, it was defined as "treatment failure." This definition was modified from Goldust et al. study [18]. Participants who have any signs of scabies after four weeks of treatment would then be treated with permethrin. Local or systemic adverse events which occurred from both treatments were documented.

2.5. Statistical Analysis

Data were analyzed using SPSS software (version 25, SPSS Inc., Chicago, IL). The X^2 test was used to examine the difference between groups, and $p < 0.05$ was considered significant. The Kolmogorov-Smirnov test was performed to test the normality of the data distribution.

3. Results

Participants' age and gender in both groups were no significant differences (Table 1). The dermoscopy examination revealed positive results on three patients but no positive result on microscopic findings in the initial examination.

Table 1. The characteristic of Subjects based on age and gender.

| Characteristic | | Group of Intervention | | | | p-value |
|----------------|-------------|-----------------------|------|------------|------|---------|
| | | Albendazole | | Permethrin | | |
| | | n | % | n | % | |
| Age | 12-14 years | 22 | 73.3 | 20 | 66,7 | 0,720 |
| | 15-18 years | 8 | 26,7 | 10 | 33,3 | |
| Gender | Male | 24 | 80,0 | 27 | 90,0 | 0,472 |
| | Female | 6 | 20,0 | 3 | 10,0 | |

The participant defined it as a "cure" after two weeks of observation and increased on week four ($p=0.015$). At the first week follow up on week two, the cure rates in the albendazole group was 14 (46.7%) higher than the permethrin 5% group with only 9 participants (30%) effectiveness. There was no significant difference between groups ($p=0,184$). However, in the third week, the cure rates in albendazole rose to 27 subjects (76.7%) higher than that of the permethrin group (53.3%), though no significant statistical differences were found. In the last week of follow-up, the albendazole groups reached a 90% cure rate

significantly higher than permethrin 5% (19%). The adverse effect from each group was not reported (Table 2).

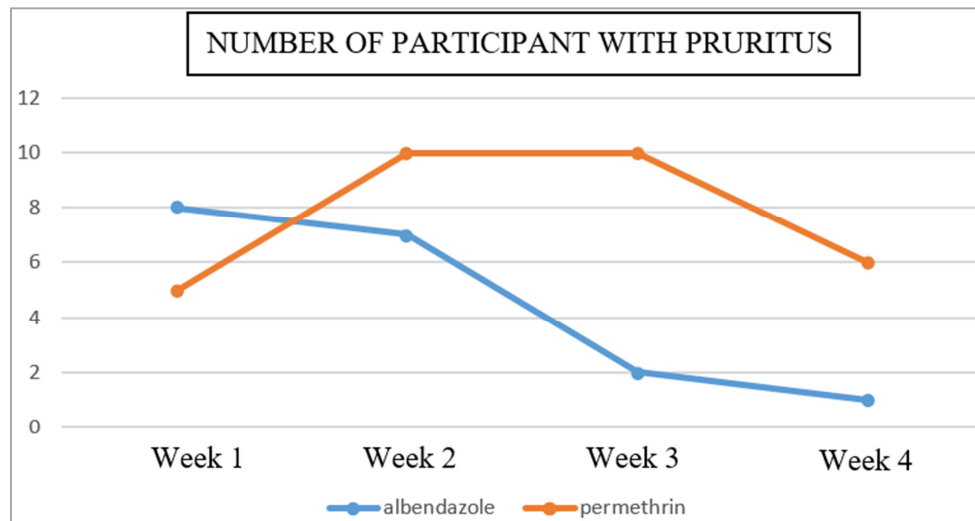
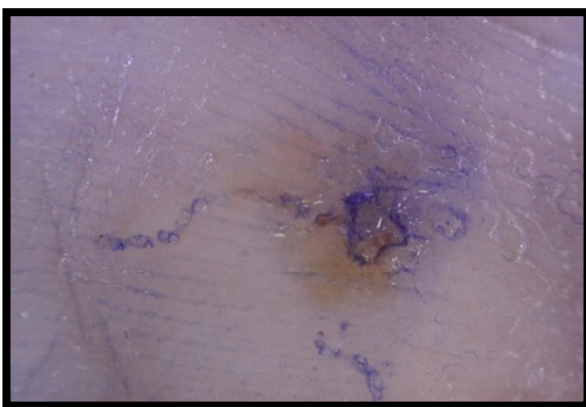
Table 2. Comparison of the effectiveness of oral albendazole with permethrin 5% in curing scabies.

| No lesion scabies in | Groups | | | | p* |
|-------------------------|------------|------|------------|------|-------|
| | Albendazol | | Permethrin | | |
| | n | % | n | % | |
| 1 week | 0 | 0,0 | 0 | 0,0 | — |
| 2 week | 14 | 46,7 | 9 | 30,0 | 0,184 |
| 3 week | 23 | 76,7 | 16 | 53,3 | 0,058 |
| 4 week | 27 | 90,0 | 19 | 63,3 | 0,015 |

* Chi-square test

The pruritus intensity was lower in the albendazole group after three and four weeks of follow-up significantly (Figure 1).

The microscopy and dermoscopy examination in the initial examination only showed positive results in three (5%) patients, and none of the microscopic examinations had positive results (Figure 2).

**Figure 1.** The number of participants with pruritus on follow-up weeks. The number of subjects with pruritus in the albendazole group was reduced significantly than the permethrin group.**Figure 2.** A positive result of a dermoscopy examination with a jet with condensation trail on the skin layer (reference: author's data).

4. Discussion

This study demonstrated that the efficacy of albendazole oral 400mg/day, which was given for three consecutive days in the first and second weeks, was significantly superior to topical permethrin 5%. This finding concordance with the result other case reports used albendazole 800-1000mg for treating crusted scabies, with excellent results [19, 20]. We found four articles that reported the use of albendazole on scabies. Three of them were case reports, and only one clinical study was found. Three case reports used albendazole for crusted scabies; one of them fail to cure scabies. One clinical trial was established and show no superiority of albendazole over permethrin 5% (Table 3).

Table 3. Articles that reported the use of albendazole on scabies.

| No. | Population | Intervention | Comparison | Outcome | Authors |
|-----|--|--|---|---|------------------------|
| 1. | Cases report of 2 patients with crusted scabies | Albendazole 1000 mg oral with fatty meals for three consecutive days and an application of a 5% salicylic acid ointment once daily for one week. | None | The pruritus disappeared within five days. Skin scrapings performed at the 1-week control visit on residual skin lesions did not reveal any <i>Sarcoptes</i> mites. Lesions disappeared entirely within ten days. No side effects or recurrence was observed during three months of follow-up. | Ayoub et al. [19] |
| 2. | Case report of a 22 y.o female with crusted scabies | 800 mg of albendazole with fatty meals for three consecutive days and an application of a 5 percent salicylic acid in crotamiton twice daily for one week | None | Successfully treated | Douri et al. [20] |
| 3. | Case report of 81 y.o man with crusted scabies | multiple misdiagnoses and incorrect and potentially detrimental treatment with steroids (methylprednisolone 20 mg three times a day for three days) and albendazole 400 mg per day for eight days. | specific treatment with both systemic therapy with ivermectin 200 mcg/kg on days 1, 7, 9, and 15 and topical therapy with permethrin 5% cream on the whole body followed by permethrin baths on days 1, 2, 14, and 15 | The patient was followed up with seriate microscopic examinations of skin samples, which showed live <i>Sarcoptes scabiei</i> mites on days 2, 4, and 10 from the beginning of treatment. The first sample which tested negative was obtained on the 15th day of treatment. | Bonazzetti et al. [21] |
| 4. | 102 scabies patient from Al Muayyad Islamic boarding school. | Subjects were separated into two groups. 50 with permethrin, 52 with albendazole tab 800mg/day, three consecutive days | Permethrin 5% | on the 14 th day of evaluation, the cure rate for albendazole was 86,4% meanwhile, permethrin cream 94% ($p>0.05$). Furthermore, observation of the quality of life, severity of the lesion, and itchiness reduction, both permethrin and albendazole indicated excellent effectiveness ($p<0.05$). both groups did not demonstrate any serious side effects | Risadini et al. [22] |

Study conducted by Risadini et al. compared the efficacy of oral albendazole 800mg/day for three consecutive days on the first weeks, another group with topical permethrin 5% in the first and second week. Both drugs had the same effectiveness. Nevertheless, the short two weeks follow-up in Risadini's limited the result of their study [22].

Albendazole 400 mg single-dose administration or mebendazole 500 mg single dose is recommended by WHO to control soil-transmitted helminth (STH) in at-risk populations, including pre-school and school-age children. However, the anthelmintic regimen possesses a low cure rate for *T. trichiura* (34%). Thus Sungkar et al. using 400 mg albendazole for three consecutive days increased the effectiveness in treating STH [16]. Learn from those studies, and we used 400 mg albendazole in children for three straight days to treat scabies. The albendazole as anti-parasitic drugs, kill the mites possibly by energy depletion, leading to the immobilization of the parasite and subsequent death [13].

Mohammed et al. reported the rapid decline of scabies and STH infection in Zanzibar Tanzania for five years after the filariasis mass drug administration treated with albendazole and ivermectin [23]. However, this finding needs to be further addressed whether albendazole or ivermectin contributed to the scabies cases reduction. Nevertheless, the use of albendazole for scabies mass drug administration could be challenging and used as an alternative in future studies.

Permethrin 5% topical is widely used as the standard of care for scabies and was the most effective topical therapy to lindane and crotamiton but is associated with resistance, poor

patient compliance, and allergic reactions [11]. The Austria study in 2020 reported the cure rate of two applications of permethrin 5% cream around 29% to 31%, which supports the conclusion of existing resistance on permethrin [10]. Patients' compliance on topical treatment was lower than oral treatment [24]. Topical scabicides' most frequent complications are persisting post-scabies eczema resulting from irritant effects of the various formulation that may accelerate xerosis and worsen delayed-type eczema [24]. The low cure rate of permethrin 5% in our study was possibly caused by resistance and poor patient compliance. All participants well tolerated both topical permethrin 5% and oral albendazole. None of the side effects were reported by the patients or their caregivers.

Diagnostic test for scabies is complicated. Besides clinical assessment using a combination of history and visual examination techniques, identifying mites by microscopic examination of skin scraping is time-consuming, operator-dependent, poorly tolerated in children, and has low sensitivity [25]. Our study fails to identify mites by microscopic examination. However, the clinical findings confirmed the diagnosis of scabies.

Dermoscopy is helpful to diagnose scabies. On x10 magnification, the mite head and trailing burrow can be visualized in the "delta-wing jet" sign. The baseline study revealed areas of spotty itching and at the predilection sites its presence as burrows or comma-like papules called kite signs. Despite the ease and accuracy of dermoscopy, its use is limited by operator experience and low sensitivity in mild disease [3]. Our study revealed that only 5% (3/60) patients had positive

dermoscopic results, which is the limitation of our study. Kaur et al. modified dermoscopy examination to be easier to perform using the transillumination technique [26].

The high cost of scabies treatment in boarding school is one of the drawbacks in the low-middle country. The cost per person of two weeks of permethrin 5% cream application is about 143.000 rupiah, higher than using albendazole 400mg oral for two weeks, around 9.000 rupiahs. Thus, albendazole will provide cost-effective treatment is to eradicate scabies in Indonesia.

The limitation of our study is the small number of participants involved and the single-blind randomized trial rather than double-blind. Further investigation with the more extensive subject and actual diagnostic test will enhance the quality of the study.

5. Conclusions

This study revealed the effectiveness of oral albendazole 400 mg/day for three consecutive days in the first and second weeks for treating scabies to topical permethrin 5%. No side effect seen in the use of albendazole and topical permethrin during the study. Albendazole could be an alternative drug option to eradicate scabies in low-middle-income countries.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

Author Contributions Statement

FAA wrote the first draft of the manuscript. SW leads the study and corresponding author. YF edited and analyzed the results. AF, SM, and MM contributed to the concept and design of the study. All authors have taken part in the manuscript equally.

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