

Review articles

The efficacy of topical and oral ivermectin in the treatment of human scabies

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ABSTRACT. Scabies is an itchy skin condition caused by the microscopic mite *Sarcoptes scabei.* The itching is caused by an allergic reaction to the mites. The treatment of choice is still controversial. It is commonly treated with topical insecticides. The aim of this study was to assess the efficacy of topical and oral ivermectin in the treatment of human scabies. We searched electronic databases (Cochrane Occupational Safety and Health Review Group Specialised Register, CENTRAL (The Cochrane Library), MEDLINE (Ovid), Pubmed, EMBASE, LILACS, CINAHL, Open Grey and WHO ICTRP) up to September 2014. Randomized controlled trials (RCTs) or cluster RCTs which compared the efficacy of ivermectin with other medications in the treatment of scabies. Interventions could be compared to each other, or to placebo or to no treatment. The author intended to extract dichotomous data (developed infection or did not develop infection) for the effects of interventions. We intended to report any adverse outcomes similarly. It has been sated that ivermectin was as effective as permethrin in the treatment of scabies. In comparison to other medications such as lindane, benzyl benzoate, crotamiton and malathion, ivermectin was more effective in the treatment of scabies. Ivermectin is an effective and cost-comparable alternative to topical agents in the treatment of scabies infection.

Key words: *Sarcoptes scabiei*, topical ivermectin, oral ivermectin

Introduction

Scabies is a contagious skin infection caused by the mite *Sarcoptes scabiei*. The mite is a tiny, and usually not directly visible, parasite which burrows under the host‘s skin, which in most people causes an intense itching sensation caused by an allergic response[1,2]. The infection in animals other than humans is caused by a different but related mite species, and is called sarcoptic mange. When a person is infested with scabies for the first time, it can take four to six weeks for the skin to react [3,4]. Signs and symptoms of scabies include a skin rash composed of small red bumps and blisters and affects specific areas of the body. Other symptoms can include tiny red burrows on the skin and relentless itching. The itch leads to frequent scratching, which may predispose the skin to secondary infections [5,6]. In its early stages, scabies may be mistaken for other skin conditions because the rash looks similar. This image compares acne, mosquito bites, and scabies. What sets scabies apart is the relentless itch. Itching is usually most severe in children and the elderly. Scabies typically spreads through prolonged, skin-to-skin contact that gives the mites time to crawl from one person to another [7,8]. Shared personal items, such as bedding or towels, may occasionally be to blame. Scabies can be passed easily between family members or sexual partners. It is not likely to spread through a quick handshake or hug. The intense itch of scabies makes it difficult to resist scratching. Frequent scratching can create open sores that are prone to infection [9,10]. Bacterial skin infections, such as impetigo, are the most common complication of scabies. Symptoms may include honey-colored, oozing blisters. This type of infection is usually treated with antibiotics. In most cases, a doctor can identify scabies based on the appearance of the rash and the description of the

itch. Sometimes a skin scraping is used to confirm the diagnosis. This involves collecting skin from the affected area and using a microscope to check the sample for mites, eggs, or fecal matter [11,12]. Scabies medications can kill the mites and eggs quickly, and patients can usually return to school or work 24 hours after starting treatment. However, the itch may persist for a few weeks. This is the result of an ongoing allergic reaction in the skin. If the itching continues for more than four weeks or a new rash appears it may be necessary to reapply scabies medication [13,14].

Review

Ivermectin. Ivermectin (22,23-dihydroavermectin B_{1a} + 22,23-dihydroavermectin B_{1b}) is a broad-spectrum antiparasitic drug in the avermectin family. The FDA approved ivermectin in November 1996. Ivermectin is a broad-spectrum antiparasitic agent, traditionally against parasitic worms [15,16]. In veterinary medicine ivermectin is used against many intestinal worms (but not tapeworms), most mites, ticks and some lices. But it is not effective for eliminating flies, flukes, or fleas. It is effective against larval heartworms, but not against adult heartworms, though it may shorten their lives [17,18]. The dose of the medicine must be very accurately measured as it is very toxic in overdosage. It is mainly used in humans in the treatment of onchocerciasis, but is also effective against other worm infections (such as strongyloidiasis, ascariasis, trichuriasis, filariasis and enterobiasis), and some epidermal parasitic skin diseases, including scabies. It is usually taken as a single dose on an empty stomach with water. If the patients are taking ivermectin to treat onchocerciasis, additional doses 3, 6, or 12 months later may be necessary to control the infection [19,20]. An estimated 6 million people worldwide have taken ivermectin for various parasitic infections. No serious drug-related adverse events have been reported. Side effects of ivermectin include fever, headache, chills, arthralgia, rash, eosinophilia, and anorexia. Many of these symptoms are thought to result from the death of parasites rather than as a reaction to the drug. Ivermectin seems to be concentrated in the liver and fat tissue, with very low levels reaching the central nervous system. No significant drug interactions have been reported [21,22]. A study of elderly nursing home patients treated for scabies infection showed an increased death rate among ivermectin-treated patients, but it was noted that this finding has not been confirmed in multiple subsequent trials [23,24]. People who have a severe or resistant form of scabies infestation, such as crusted (Norwegian) scabies, may be prescribed ivermectin in combination with medicine applied to the skin, such as permethrin. It can be especially helpful for treating HIV-infected people who have scabies. A pill form of medicine may be preferred for some people who are unlikely to use topical medicated creams or lotions properly [25,26]. Ivermectin may help get rid of or prevent scabies for people in group living situations, such as those who live in nursing homes. Ivermectin is usually not used for children younger than 5 or for pregnant women, because its safety in these children is not known [27,28].

Ivermectin *versus* placebo. No adverse events were reported in the study of ivermectin *versus* placebo [29,30].

Ivermectin *versus* permethrin. Twelve study compared the efficacy of ivermectin vs. permethrin cream for the treatment of scabies. Eight study demonstrated that two application of ivermectin was as effective as two applications of permethrin cream in the treatment of scabies [31–38]. Three of them stated that two application of permethrin was more effective than ivermectin cream in the treatment of scabies [39–41]. One of them stated that mass treatment of scabies with ivermectin in an endemic population is more efficacious as compared to topical permethrin application in reducing the baseline prevalence, decreasing the chain of transmission and chances of reinfection [42]. Goldust et al. [31] compared the efficacy of topical ivermectin vs. permethrin 2.5% cream for the treatment of scabies and demonstrated that two application of ivermectin was as effective as two applications of permethrin 2.5% cream at the 2-week follow-up. After repeating the treatment, ivermectin was as effective as permethrin 2.5% cream at the 4-week follow up. The main adverse event as irritation in 30 versus 20 patients treated with ivermectin and permethrin, respectively. This adverse event was not considered serious and did not affect compliance. Ranjkesh et al. [32] compared the efficacy and safety of permethrin 5% lotion with oral ivermectin for the treatment of scabies and demonstrated that two applications of permethrin with a one week interval is more effective than a single dose of ivermectin. Two doses of ivermectin is as effective as a single application of permethrin. Chhaiya et al. [33]

reported permethrin and topical ivermectin were equally effective against scabies while oral ivermectin was significantly less effective up to 2 weeks. Topical ivermectin can be used as an alternative to permethrin.

Ivermectin *versus* lindane. Six study compared the efficacy of ivermectin vs. lindane lotion for the treatment of scabies. All of them demonstrated that two application of ivermectin was more effective than applications of lindane lotion in the treatment of scabies [43–48]. Goldust et al. [43] compared the efficacy of oral ivermectin vs. lindane lotion 1% for the treatment of scabies. They demonstrated that single dose ivermectin was as effective as two applications of lindane lotion 1% at the 2-week follow-up. After repeating the treatment, ivermectin was superior to lindane lotion 1% at the 4-week follow up. Mohebbipour et al. [44] compared the efficacy and safety of oral ivermectin with topical lindane in treating scabies. This study stated that single dose application of oral ivermectin was as effective as twice application of lindane lotion 1% at one-week interval. Two doses of ivermectin proved superior to lindane lotion 1% after repeating the treatment at 4-week follow up. Two studies compared oral ivermectin (single dose of 0.15 to 0.2 mg/kg) with topical lindane (single application of a 1% 60 mL solution) and found a small number of adverse events. In the earlier study the adverse events were reported to be few, mild and transient, with 4/26 patients in the ivermectin group experiencing adverse events (headache, hypotension, abdominal pain and vomiting) compared with 6/27 in the lindane group (headache). In the later study of 100 participants only 1 reported an adverse event (severe headache) in the ivermectin group (there were no adverse events reported in the lindane group) [47,48].

Ivermectin *versus* benzyl benzoate. Six studies compared oral ivermectin (single 0.1 to 0.2 mg/kg dose) with benzyl benzoate (10% to 25% lotion) for the treatment of scabies. Four of them demonstrated that two application of ivermectin was more effective than applications of benzyl benzoate lotion in the treatment of scabies [49–52]. Two of them stated that two application of benzyl benzoate was more effective than applications of ivermectin in the treatment of scabies [40,53]. Brooks et al. [50] compared single dose oral ivermectin with topical benzyl benzoate for the treatment of paediatric scabies. They demonstrated ivermectin was better than benzyl benzoate for the treatment of paediatric scabies in developing countries. Ly et al. [53] compared the effectiveness of oral ivermectin (IV) and two different modalities of topical benzyl benzoate (BB) for treating scabies in a community setting. They demonstrated that topical BB was clearly more effective than oral IV for treating scabies in a Senegalese community. Two of these studies reported no adverse events for either all patients or just the ivermectin-treated patients. In the remaining studies, no serious adverse events were reported; adverse events in the ivermectin groups were pustular rash, cellulitis, abdominal pain and diarrhoea [51,52].

Ivermectin *versus* crotamiton. A recent study by Goldust et al. [54] investigating the efficacy of topical ivermectin vs. crotamiton cream 10% in the treatment of scabies. They demonstrated that two applications of ivermectin were as effective as single applications of crotamiton 10% cream at the 2-week follow-up. After repeating the treatment, ivermectin was superior to crotamiton cream 10% at the 4-week follow-up. This study reported 30/170 patients treated with ivermectin experienced irritation as the main adverse event (compared to 20/170 in the crotamiton group). However, this was not considered to be serious and did not affect compliance. Goldust et al. [55] compared the efficacy and safety of oral ivermectin versus crotamiton 10% cream for the treatment of scabies and they stated that ivermectin was superior to crotamiton 10% cream at the four-week follow up. The delay in clinical response with ivermectin suggests that it may not be effective against all the stages in the life cycle of the parasite.

Ivermectin *versus* malation. A recent study by Goldust et al. [56] investigating the efficacy of topical ivermectin vs. malation cream 0.5% in the treatment of scabies. This study demonstrated that two application of ivermectin was as effective as single applications of malation 0.5% lotion at the 2-week follow-up. After repeating the treatment, ivermectin was superior to malation 0.5% lotion at the 4-week follow up. They reported 40/340 patients treated with ivermectin experienced irritation as the main adverse event (compared to 20/340 in the malation group). However, this was not considered to be serious and did not affect compliance.

Conclusions

Ivermectin is an effective and cost-comparable alternative to topical agents in the treatment of

scabies infection. It may be particularly useful in the treatment of severely crusted scabies lesions or when topical therapy has failed. Oral dosing may be more convenient in institutional outbreaks and in the treatment of mentally impaired patients. Ivermectin has been used extensively and safely in the treatment of other parasitic infections. The safety of oral ivermectin in pregnant and lactating women and young children has yet to be established.

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