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REVIEW ARTICLE

Scabies: Clinical signs, diagnosis and current treatment

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Abstract

Scabies is a parasitic infestation caused by Sarcoptes scabiei var hominis. It can spread through an indirect contact with contaminated objects as well as a direct skin-to-skin contact. In scabies, widespread itching, which gets worse at night, can be present along with a variety of lesions, including papules, vesicles, nodules and excoriations. In order to make a definitive diagnosis, mites, eggs, or faeces should be visualised by using an additional tool. Only the patient's history and physical examination are used to diagnose clinical scabies or suspected clinical scabies. It is also included in the differential diagnosis with other itchy skin diseases. Although several topical treatments such as benzyl benzoate, sulphur, and lindane are available, permethrin is still the first choice. In many countries, oral ivermectin is used as an efficient, secure, and affordable treatment for scabies despite the fact that it does not have an FDA approval for this purpose. Current studies for the treatment of scabies have been ongoing, and there are also other studies on moxidectin and isoxazoline derivative drugs. However, it is seen that some treatments fail due to various reasons such as, application errors, skipping treatment repetitions, inadequate environmental cleaning, not receiving treatment from the patient's relatives, and not providing the patient with the necessary precautions in written form. It is known that although scabies continues to be a global public health problem, it is possible to obtain good results in the treatment of it if physicians have sufficient knowledge and can manage their patients appropriately. By summarising the information that is currently available, this review aims to provide an update on the clinical characteristics, the diagnosis, the treatment, and the management of scabies.

Keywords: Scabies, Treatment, Diagnosis.

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INTRODUCTION

Scabies is a parasitosis manifested by itchy skin lesions after a direct or indirect transmission of the human mite, Sarcoptes scabiei var hominis (1–3). Scabies, which can be considered as one of the most neglected diseases by the World Health Organization, is common in overcrowded environments, particularly (2). When the adult mite burrows into the host's epidermis, the first clinical symptoms of infection are visible. In these tunnels, the fertilized adult female mite lays the eggs of the larvae that will later develop into mites. The hypersensitivity to these burrows, mites, and their byproducts leads to the clinical manifestations of scabies (1,4). An asymptomatic incubation period of 4 to 6 weeks follows the initial infestation, and the clinical symptoms begin to appear after the incubation period (5,6).

Pathogen and the Contamination

Fertilized females, which are able to move about 2.5 cm per minute on the warm body surface but cannot fly or jump, dig tunnels where they will live the remaining 4 to 6 weeks of their lives. These tunnels, which they dig between 0.5-5 mm per day, are called burrows. Every day, they lay two to three eggs in these burrows (7–10). The larvae that emerge 2 to 3 days after these eggs turn into mature mites that can mate after about 2 weeks. The males of these mature mites quickly perish while the females carry on the cycle. Transmission is usually through skin-to-skin contact. In addition, it has been demonstrated that the parasite can survive outside the skin for days. For intstance, the mite can survive for two to three days in air that is generally 21°C and with a humidity rate of 40 to 80%. Moreover, it has the ability to endure higher humidity rates and lower temperatures for longer (8). It can also spread after 15 to 20 minutes of direct contact with items like towels and clothing (11). For the transmission, there are several risk factors such as poor hygiene, malnutrition, living in crowded conditions, and sexual contact (8,12). In less than 30 minutes after infestation, the mite can penetrate the skin (8). On the other hand, when there are few mites present, there is little risk of transmission from shaking hands, hugging, or medical examinations. People who live in the same family and those who stay in communal settings are at risk under such circumstances (13). Short-term contact or even contact with dandruff can transmit crusted scabies, which includes many mites (5,9).

Clinical Features

It is known that people with scabies complain about intense and all-over itching that gets worse at night. The most recognizable lesions are linear, mite-filled, and tunnel-shaped burrows, especially between the fingers (14). A wide range of lesions, including papules, vesicles, nodules, eczematizations, excoriations, and lichenifications, can also be found in addition to tunnels. The wrists, ankles, spaces between the fingers, axilla, lumbar region, aerola in women, and genital area in men are the most frequently affected areas by lesions (2,5,15). Lesions other than tunnels are caused by toxic and antigenic secretions from the mite. Itching, which is thought to be brought on by sensitivity, typically lasts between four and six weeks. Unlike adults, among infants and children, , it is crucial to have facial and palmoplantar involvement in addition to papular and nodular lesions (5,16). There is less itching with Norwegian scabies, which is typically found in immunosuppressive or mentally or physically disabled people. Along with nail hyperkeratosis, psoriasiform and hyperkeratotic, lesions are also common, particularly in the head and the neck. These people are extremely contagious and have an average of two million mites on them (5,15). Beside scabies, other possible local complications include impetigo, abscess, cellulitis, and very rarely necrotizing soft tissue infections. It can be observed in systemic complications that are more severe, such as acute poststreptococcal glomerulonephritis and sepsis brought on by secondary bacterial infections (5).

Diagnosis

Scabies is one of the dermatological diagnoses that can be both simply and challengingly recognized. Patients who have typical-distribution pruritic lesions and have recently come into contact with someone who has pruritus should be examined (17). The way to confirm the diagnosis is to see mites, eggs, or fecal residues. For this, a skin scraping from a papule or a tunnel can be examined under a microscope. An average of five suspicious lesions are scraped with a scalpel, onto which mineral oil is dripped. The scraping material is placed on the slide and covered with a lamella. Observing the mite at any stage under a microscope is accepted as diagnostic (13,14). Except this rocedure, which is rather difficult, dermatologists have the opportunity to examine a quick, non-invasive substitute by using dermatoscopy. The sensitivity and specificity of dermatoscopy are 98.3% and 88.5%, respectively, which enable the detection of the "kite sign" and the "wake-up sign" (8,18). The head, thorax, and forelimbs of the mite

combine to form the dark triangle that is the kite sign. The wake-up call is the intracorneal air spaces in the tunnel. The term "gray-edged line mark" refers to the mite faecal matter that occasionally causes the edges of the tunnel to appear dark (19). However, it is not possible to determine whether a mite is alive or not through dermatoscopy, which enables a quick and simple diagnosis. In order to find out whether a mite is alive or not, videodermatoscopy might be used (20). For the purpose of standardising the diagnosis of scabies, some criteria have been developed. (Table 1) Mites, eggs, or faeces must be visible under a microscope, dermatoscope, or any other imaging device for a definitive diagnosis of scabies. Clinical scabies or suspected scabies are diagnosed only with the patient's history and physical examination (21).

A. Confirmed scabies (at least one of the following)
A1. Visible mites, eggs, or faeces from skin samples under the light microscope
A2. Seeing mites, eggs, or faeces using a high-power imaging device
A3. Seeing the mite using dermoscopy
B. Clinical scabies (at least one of the following)
B1. Scabies tunnels
B2. Typical lesions on the male genitalia
B3. Typical distribution and lesions, as well as two history features
C. Suspected Scabies (One of the following)
C1. Typical distribution, typical lesions, and 1 history feature
C2. Atypical distribution, atypical lesions, and 2 history features
History features
H1. Itch
H2. Positive contact history
The diagnosis is made at either the A, B, or C levels. In order to make clinical and suspected scabies diagnoses, the times when differential diagnoses are less likely than scabies should be considered.

Table 1 Consensus criteria for the diagnosis of scabies, issued by the International Alliance for the Control of Scabies (21) evidence-based definitions and diagnostic methods.

Differential diagnosis

In the differential diagnosis of scabies, other itchy skin diseases such as atopic dermatitis, contact dermatitis, folliculitis, impetigo, papular urticaria, dermatitis herpetiformis, prurigo nodularis and insect bites should be taken into consideration (22).

Treatment

There are two obvious primary goals of the treatment of scabies; to destroy the parasite in the patient and to avoid environmental contamination. Regardless of whether they have complaints or symptoms, it should be the goal to treat the patient as well as anyone else with whom they have had frequent contact within the past month. Patients and their contacts with whom they receive treatment should remain isolated until the first cure of the treatment is completed (23). Beside the drug therapy, the environment where patients and contacts reside has to be cleaned. It has been demonstrated that adult mites and eggs can be destroyed by boiling them for 10 minutes at a temperature of at least 50°C or by isolating them in plastic bags for about a week (24). It is important to provide patients with the proper instructions, so they can carry out their treatments completely. Informational brochures can make it easier for the patients to follow the instructions (14).

Moeorver, topical medications should be applied to all parts of the body, such as between the fingers, inside the nails, the navel, and the genital area, and should stay on the skin for 8 to 12 hours. During the procedure of topical medications, the drug should be applied to cool and dry skin and followed by clean clothes.

In order to consider the course of action as successful, one week after the last cure of the treatment, the number of active lesions and nighttime itching should have decreased. However, it can not be ignored that itchiness might persist for 2 to 4 weeks following a successful treatment. For this kind of persistent itching, moisturisers or topical corticosteroids can be used (6).

Alternatives for the treatment

Scabies has a variety of treatment alternatives that can be selected based on the patient, the severity of the disease, the accessibility and the cost of the treatment, and the doctor's experience and personal preferences. Whatever the alternative is, the treatment should be given not only to patients with a definite diagnosis but also in all suspicious cases and at every stage of the diagnosis (25).

Topical or systemic drugs are classified as acaricidal and ovicidal. Permethrin, when used as the first line of the treatment, has been reported in several studies to have a higher cure rate than other options like sulphur, benzyl benzoate, malation, crotamiton, and lindane (6). It was believed that topical ivermectin was the most effective treatment for itching relief and that oral ivermectin combined with topical permethrin was the most effective treatment for curing the condition (2).

For first-line therapy, many recommendations still call for the safe, easily accessible, and ovacidal 5% permethrin (26,27). When permethrin is unavailable, 10–25% benzyl benzoate and 2–10% sulphur can be used as substitutes (5). Despite not having FDA approval, oral ivermectin is frequently used to treat scabies because it is safe and well tolerated (28). Due to the fact that ivermectin is not ovocidal, a second treatment should be administered between the second and the third days of egg emergence and the seventh and fifteenth days, when fertilised female mites begin to lay new eggs.

Sulfur and permethrin are safe to be used in children older than two months and pregnant women (29,30). In the use of permethrin for pregnant women, nursing mothers and children under the age of two, it is recommended to use it for two cycles at one week intervals and for a maximum of two hours (31). Although the use of Ivermectin remains contraindicated in pregnant women and children weighing less than 15 kg, there has been a recent ongoing research on children weighing 5 to 15 kg. (1,32) Some trustworthy institutions use ivermectin as a treatment when necessary, despite the fact that its contraindication in pregnancy is based on animal studies at doses significantly higher than those used in humans. It is regarded as secure while nursing (33).

DRUGS

Drugs applied topically

Permethrin, benzyl benzoate, sulphur, crotamiton, malathion, and lindane are the topical medications that are most frequently used to treat scabies, respectively (5).

Permethrin

A strong insecticide and synthetic pyrethoid, permethrin is ranked first among treatment options in many countries. Permethrin 5%, which is FDA-approved for the use on adults and children older than two months, has a high level of efficacy and tolerability (5,34). Permethrin has a strong acaricidal effect and low mammalian toxicity because it is poorly absorbed through the skin, rapidly metabolised by skin esterases, and excreted in the urine. For two weeks, the cream is applied once per week to the entire body, allowing for eight hours of skin contact (14). Permethrin, which has almost no allergic side effects and can be used safely in cosmetic purposes, can be applied to the whole body, including the head, in babies. The only drawback for the drug is that it is more expensive than other topical medications for scabies (34,35).

Sulphur

The earliest treatment for scabies is sulphur, which is still in use. Beside having an unpleasant smell, it can stain clothing, and it can also lead to irritant dermatitis. In general, 6% ointment form is preferred, though mixtures between 2–10% can alos be used. Following a bath, the entire body is covered in ointment, which is then used for three nights straight. Sulfur is most easily applied in ointment form. Additionally, due to its low cost, sulphur might be the first choice in severe epidemic situations (7,14). It is a risk-free option to treat children, infants, and pregnant women (1,16).

Benzyl benzoate

Benzoic acid, an ester of benzoic acid and benzyl alcohol obtained from the balsam of Peru and tolu, has a neurotoxic effect against mites. Although it is used as a 25% emulsion, in children 12.5% emulsions might be preferred. Within 24 hours of contact time, it has to be applied three times without bathing. The medication, which is very effective if used properly, can irritate areas with thin skin, such as the face and the scrotum. Due to its side effects, the medication, which should not be used by those who are pregnant, nursing, or who have children under the age of two, has begun to lose importance. However, it can still be preferred in cases resistant to other treatments and in developing countries due to its cost advantage (6,14,34).

Crotamiton

Crotamiton (crotonyl-N-ethyl-o-toluidine) 10% is available as a cream or lotion, though some researchers do not advise the use of crotamiton due to the conflicting efficacy and toxicity data. To achieve the best results, it is recommended to be applied for five days, twice daily after taking a bath (5,7,36).

Malathion

It is an organophosphate insecticide that permanently inhibits the acetylcholinesterase enzyme. For the treatment

of scabies, it is no longer advised due to its harmful side effects (5,14).

Lindane

It is also known as lindane gamma benzene hexachloride, which is an insecticide. It affects the central nervous system (CNS) of the mite and results in excitability, convulsions, and death. It is absorbed through the mucous membranes, is transported throughout the body, reaches high concentrations in lipid-rich tissues, is metabolised, and is then eliminated through the urine and faeces (34,37). Applying 1% lindane cream or lotion for 6 hours, then repeating it after a week is sufficient (14). While the advantages are ease of administration and non-irritation, the disadvantages are the risk of causing CNS toxicity, causing convulsions and death, though rarely (2,5). Accidental ingestion results in lindane toxicity, which can cause convulsions, breathing problems, nausea, vomiting, headaches, and even death. It can affect the course of some hematological diseases such as aplastic anemia and thrombocytopenia (38,39). It is not popular in many countries due to the possibility of neurotoxicity, but for developing countries, it might be a less expensive and more practical option than permethrin (5,14).

Oral antiscabietic agent

Ivermectin

Ivermectin is an avermectin dihydro derivative that is similar to macrolides, but does not have antimicrobial properties. Its main mechanism of action is the stimulation of gamma amino bituric acid from presynaptic nerve endings and increasing its binding to postsynaptic nerve endings, thereby reducing impulse transmission in nerve-muscle synapses (14,40). Ivermectin, which is rapidly absorbed and excreted through the faeces, is relatively safe in terms of side effects and should not be used in those with ivermectin allergy, CNS disease, women who are pregnant and nursing women and children under 15 kg (2,7,9). Ivermectin, which is highly efficient, safe to use and economical, is used to treat scabies in many countries but has not received a FDA approval yet (47). A second dose should be administered 1-2 weeks after the initial 0.2 mg/kg dose because it is not ovacid (5,6).

The management of special forms of scabies

While 2–10% sulphur can be used in infants, 5% permethrin is only suitable for babies older than two months (34). Ivermectin and lindane should not be used for infants. Infants and children older than two months can use 5% permethrin and 12.5% diluted benzyl benzoate emulsion (7). Ivermectin and lindane are not advised during pregnancy or lactation, though 6% sulphur might be preferred in those situations (34). A chronic form of scabies known as nodular scabies manifests as nodular lesions in the genital area, axillae, and male genitalia. Intralesional steroid should be used in the treatment along with the scabies treatment (41). Norwegian scabies requires prolonged and repeated topical and systemic treatments which last, on average, three weeks. In this way, it will be possible for the medications to work beneath thick crusts while reducing the high mite load (6,42). Oral ivermectin is given in three, five, or seven standard doses. In addition to systemic therapy, it is advised to use a topical keratolytic agent containing 5–10% salicylic acid or urea, and permethrin or benzyl benzoate, two to three times per week for one to two weeks (8,43). It should not be forgotten that the nails should be cut short and brushed with an anti-scabicide agent (15,16). Also, in the highly contagious Norwegian scabies, hospitalisation and treatment can be planned to ensure isolation (5).

Current treatment options

New treatment researches emerge as a result of the difficulties in the applicability of multiple treatment regimens. A single dose of moxidectin, which has a similar effect to ivermectin but a longer half-life, offers a significant amount of efficacy (44). Moxidectin has been given FDA approval for the diagnosis of onchocerciasis in people over the age of 12, but its effectiveness in treating scabies has not been sufficiently established yet (44,46). In addition to moxidectin, studies have been conducted on promising oral drugs that are isoxazoline derivatives, about which the FDA has issued a neurotoxicity warning (47,49). Continued research is being done to create a scabies vaccine (49).

In addition to its antimicrobial property, tea tree oil has a scabicidal activity (50). Beside tea tree oil, there are some other substances that exhibit a scabicidal activity including Tinospora cordifolia and Ligularia virgaurea (51,52).

The reasons for the failure of the treatment

There have been several scientifically proven reasons for failures of the treatment such as application mistakes, missed treatments, incompatibility between the patient and his environment, sloppy cleaning of the patient's living space, the failure of the patient's relatives in receiving treatment, and failure to provide the patient with the necessary precautions in written form (53). The

topical drug must be applied completely to all body areas below the neck. In order to eliminate the failure of the treatment, the following malpractice scenarios should be avoided: failing to trim the nails before application; failing to ensure that the drugs are in contact with the skin for an adequate amount of time; failing to administer keratolytic treatment for crusted scabies; and failing to administer to the infant's head area. Otherwise, the disease might reoccur (13,16,26). To maintain the effectiveness of the prescribed medications, they should be administered undiluted. Contacts must also be treated in order to prevent reinfection, which is another treatment failure (16). Drug resistance is a significant factor in treatment failure, but it must be eliminated first, along with all other resistance-causing factors. Various combination therapies can be tried to prevent the resistance. Resistance to permethrin, ivermectin, and benzyl benzoate has been reported in the literature (54,55). Although it is thought to be resistant to permethrin, the genetic mutation that blocks the pharmacodynamic effect of permethrin has been shown only in dog mites. It is possible that repeated permethrin applications can induce elimination enzymes that will reduce the effectiveness of the drug on mites, which in this case might explain the permethrin resistance (56,57). In addition, it has been determined that permethrin cannot maintain its effect for a long enough time in children and people with impaired skin barrier (8). It has been demonstrated that mites can extend their survival after exposure to permethrin by increasing the transcription of glutathione-s-transferase (58). Genetic resistance to ivermectin is thought to be influenced by a polymorphism in the p-glycoprotein gene (59). Following the treatment, dying mites release antigens that continue the inflammatory response. In this situation, it causes symptoms like itching to last for a while and could be mistakenly interpreted as a failure of the treatment (60). Additionally, a psychogenic itch and an isolated delusion might occur in some patients (61).

Conclusion

Scabies is a condition that does not pose a life-threatening risk, but has a profound impact on a person's quality of life. Clinical examinations or assisting tools like a dermatoscope and a microscope are used to diagnose the disease. Permethrin is the first choice for topical treatment and is available in options such as benzyl benzoate and sulfur. Ivermectin is administered in two courses separated by 1-2 weeks during the systemic therapy. The most effective treatment in terms of cure is the use of oral ivermectin together with topical permethrin. Topical treatment and keratolytic agents should be given in addition to the systemic ivermectin treatment in highly contagious Norwegian scabies. Sulfur can be used in pregnants, lactating and infants younger than two months. Topical permethrin can be preferred in infants and children older than 2 months. It is believed to be resistant to topical permethrin. However, before it is considered that there is a resistance to the drug, it should be questioned whether the patient has been fully and completely treated, whether the contacts have received treatment, and whether the environment has been cleaned. For the treatment of the patient and the prevention of transmission, attention must be paid to environmental cleanliness along with the complete treatment of the patient and her or his contacts. It is crucial to keep in mind that it is possible to obtain successful results in scabies, which continues to be a problem in our country and a global problem all over the world, especially in developing countries. The successful results can be reached if physicians have sufficient knowledge about the treatment and if they are able to manage their patients appropriately.

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