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Treatment options of human demodicosis

Olga Pawelczyk

Department of Microbiology, Faculty of Pharmaceutical Sciences in Sosnowiec, Medical University of Silesia, 40-055 Katowice, Poland

ORCID: 0000-0003-0091-6425

correspondence: olga.pawelczyk@sum.edu.pl

Abstract

Background: Human demodicosis is a parasitic disease caused by two species of mites, *Demodex folliculorum* and *Demodex brevis*. Cutaneous and ocular demodicosis most often occurs in people with reduced immunity. The treatment of this parasitosis can last up to several months, requires patience and regularity from the patient.

Objective: The aim of this paper is to review the therapeutic options used in treatment of ocular and cutaneous human demodicosis.

Materials and methods: This review based on available data collected in PubMed and Google Scholar databases, using the keywords: ‘*Demodex brevis*’, ‘*Demodex folliculorum*’, ‘*Demodex mite*’, ‘human demodicosis treatment’.

Conclusions: Treatment of demodicosis, which based on use of a single medicament has the lowest efficiency. In contrast, the combination therapies, in which orally administered and

topically applied medications are taken together or several types of topically applied medications are combined, have the best effectiveness.

Keywords: *Demodex brevis*; *Demodex folliculorum*; *Demodex* mite; human demodicosis treatment

1. Introduction

Human demodicosis is a parasitic disease caused by two species of mites, *Demodex folliculorum* and *Demodex brevis*. Most often cutaneous demodicosis manifest by redness, eczematous changes (lumps, vesicles and pimples), red spots and eczema. These symptoms affect facial skin areas, such as cheeks, forehead, nose, chin, eyelids and ear canal [1-2]. Parasitic mites can often be recognized in people with symptoms of rosacea, acne vulgaris, and perioral dermatitis. They impact hair follicles opening, which results in an inflammatory reaction. *Demodex* mites in the eye area can lead to inflammation of the eyelid margins, conjunctiva and eyelash loss. Symptoms of ocular demodicosis include: redness of the conjunctiva and eyelids, peeling of the eyelid epidermis, itching, burning and watery eyes [2-4]. Cutaneous and ocular demodicosis most often occurs in a situation of impaired immune response, where the attacked organism is weakened, has reduced immunity or metabolic disorders. Hormonal factors, diet and using cosmetic creams also contribute to the above-mentioned disease [4-5]. Increased intensity of human *Demodex* infection and skin lesions can also be observed in people with AIDS, people after chemotherapy or with immune system deficiency [6]. The occurrence of dermatological changes depends on the number of *Demodex* mites on the skin [5].

2. Etiological agents and symptoms of human demodicosis

Demodex folliculorum is the most often reported parasite of hair follicles and Zeiss glands of eyelid margin. Its presence is observed on the face, mainly in the nasolabial folds, around the eyes and around the mouth, but can also live on the forehead, nose, chin and in the external auditory canal [1-2, 7]. This species mechanically irritates the hair bulb by moving in the hair follicles. Additionally, by secreting metabolites *D. folliculorum* mites can chemically enhance the effect of irritation, which leads to inflammation and dilation of the blood vessels. As a result of base epithelium stimulation, the hair changes its growth direction and falls out [8]. Another species, *D. brevis* is reported less frequently than *D. folliculorum* [9]. It most often inhabits the sebaceous glands located in the eyelids (Meibomian glands), but can be also present in other places of the human body, mainly around the face [7]. When attached to the sebaceous glands of the hair follicles and Meibomian glands it disrupts the lipid secretion, which can lead to dry eye syndrome [4, 8]. A significant factor that increases the pathological effect of these mites on the human skin is their excretion of metabolites along with *Bacillus oleronius* bacteria. These gram-negative, symbiotic bacteria produce antigens that stimulate the human immune system and leading to subsequent inflammation of the hair follicle [4]. In conjunction *Demodex* mite movement and excretion of the *B. oleronius* highly contributes to the transfer of bacteria to places more susceptible to them. This process has a significant importance in course of rosacea and causes the symptoms of this parasitosis to become more severe [10]. Demodicosis symptoms intensify during spring and summer, while reduce in winter because of changes in skin lipid metabolism [4]. This can be correlated with sebum and epidermal cell changes of the host, which are the main nutrition for the mites. *Demodex* mites have the highest activity in the evening, mainly during the night [8, 11]. Demodicosis is spreading directly by contact with the host or indirectly via personal belonging like cosmetics, sheets or towels. In the case of infants, infection can occur while in contact with the mother skin, where demodicosis is present [12-13].

The aim of this paper is to review the therapeutic options used in treatment of ocular and cutaneous human demodicosis.

3. Review of therapeutic methods for human demodicosis

3.1. General information – therapy and prevention

The treatment of demodicosis is difficult and can last up to several months. The therapy requires patience and regularity from the patient. Unfortunately, there no established guidelines for the treatment, hence an error/trial method is used, where many patients react differently to a given medicament. The lack of guidelines results in individual therapy for the patient [14-15].

The therapy primarily aims to stop the development of the parasite life cycle, otherwise the symptoms may recur due to repopulation of mites. The basic preventive, as well as treatment supportive method is a proper hygiene, which can limit *Demodex* infection. Hence, washing and cleaning products in the form of soaps, shampoos or specialist wipes for daily care are recommended [15]. Elimination of parasites from the environment is facilitated by washing bed linen in a high temperature [3]. The main therapeutic process most often consists of applying medicaments intended for external use like: 2% metronidazole ointment or gel, 1% cream with metronidazole, 1-2% mercury ointment (containing yellow mercury oxide), 2% erythromycin ointment, 5% cream with permethrin (Infectoscab), 4% pilocarpine, sulfur ointment, 10% crotamiton, 0.5-1% silver nitrate, 20% tea tree oil and camphor oil or cholinesterase inhibitors [3, 15-16]. Ointments may additionally contain zinc sulfate, boric acid, petrolatum and paraffin, which act as excipients [14]. A positive effect was noticed when using peeling with 50% tea tree oil and shampoos with this ingredient [12]. Local skin therapy based on the use of Demoxoft gel and eyelid wash, which contains aloe extract, tea tree oil and Spanish sage oil [4, 14, 17]. In order to increase the effectiveness of local therapy, it is also recommended to take oral medications, for example: propolis and/or echinacea extract, which can stimulate regenerative processes, reduce inflammation, strengthen immunity, have antibacterial and anti-exudative effects [15]. Systemic treatment involves oral administration of tetracycline or doxycycline [8, 18]. It is also possible to take ivermectin orally with topical application of permethrin cream. In addition, metronidazole can be administered orally, but according to some clinicians claim that the best effects are achieved after topical application of 2% metronidazole ointment or gel. Therapeutic effects may also be enhanced by metronidazole therapy combined with ivermectin [8, 19]. Many patients are resistant to treatment due to the location of *Demodex* mites inside the sebaceous glands and hair follicles, which reduces effectiveness of therapy [15]. In treatment of Meibomian gland demodicosis (MGD) the therapeutic effect is achieved by inducing the flow of Meibomian gland secretion. This can be accomplished by increasing the surrounding temperature to reach the melting point of secretion by using warm compresses around the eye area. Such compresses are made using cloths, which is heated and applied to the affected areas. When the cloth cools down it should be changed to new one to keep the temperature effect for 5 to 10 minutes [8]. Another way, of the heat therapy is by using infrared lamps or specialist heating glasses [4]. In beauty salons, a 50% water-alcohol solution of mandelic acid is used for demodicosis treatment. The solution gently exfoliates the epidermis, unblocks the sebaceous glands and hair follicles, and also has low antibacterial properties.

Mandelic acid solutions have a positive effect on people with rosacea, whose symptoms are exacerbated by *Demodex* mites accompanying *B. oleronius* [10]. The keratolytic effect, that the mandelic acid has, prevents *Demodex* mites from colonizing the skin and can be used on very sensitive skin. Cosmetic care with mandelic acid solution in many cases can be combined with dermatological treatment - antibiotic therapy and local therapy, such as metronidazole ointment or metronidazole taken orally. The exfoliation procedure does not interfere with pharmacological therapy and only improves the effectiveness of the overall treatment [11].

3.2. Patients with demodicosis – clinical studies

Gao et al. [20] conducted a study to assess the effectiveness of eyelid massage using a 5% tea tree oil ointment in patients with eyelid demodicosis caused by *D. folliculorum*. In the study, the patients previously had a daily eyelid skin massage using the chlortetracycline hydrochloride ointment for four weeks. During that time no positive effect of the therapy was observed. Therefore, the 5% tea tree oil ointment was used for a daily eyelid skin massage for the next four weeks. The treatment resulted in decrease in number or complete elimination of *Demodex* mites. Salem et al. [21] conducted a study to assess the efficacy of oral ivermectin therapy in a combination of oral ivermectin and metronidazole therapy. The results of the study showed that in the case of ivermectin therapy, 45% of patients experienced complete remission of symptoms, 33.3% of patients noted significant improvement, while 21.7% of the patients had no improvement. In the group treated with a combination of ivermectin and metronidazole, 71.6% of patients were completely cured, while 26.7% showed significant improvement, and only 1.7% no effect. In the case of ivermectin alone, a decrease in mite numbers was observed in all groups in the first two weeks, however some patients with rosacea and blepharitis experienced a recurrence in parasite numbers. Krajewska et al. [22] assessed the efficacy and safety of popular medicaments - Demoxoft Lipogel and Demoxoft Solution. Both were developed in Poland proved effective on *Demodex* mites. The active ingredients in Demoxoft Lipogel are Spanish sage oil, freeze-dried aloe, terpinen-4-ol obtained from tea tree oil, olivem 1000, D-panthenol, hyaluronic acid and Fucoert®. Demoxoft Solution contains: D-panthenol, hyaluronic acid, aloe extract, fucogel and olivem 300. Therefore, Demoxoft Lipogel has ingredients that act directly to eliminate the *Demodex* mites, while Demoxoft Solution is used to moisturize dry eyelid skin, soothe irritations and stimulate the regenerative processes of the epidermis. Patients used Demoxoft Solution daily in the morning and evening for eyelid washing, while Demoxoft Lipogel was used daily at night, applying a small amount on eyelids. After two weeks of therapy, the symptoms decreased and by the end of the treatment in 26% of

patients, no *Demodex* mites were observed in microscopic examination of the samples, while for 53% of patients the population size decreased significantly. There were no side effects noticed after using Demoxoft products and they were well tolerated by the patients. The therapy had been continued until complete recovery. Anane et al. [23] described a case study of a woman with demodicosis, who was treated with a combination of ointment with 2% yellow mercuric oxide and metronidazole orally. At the end of the therapy, the woman had no symptoms and no *Demodex* mites were noted in the material collected for the study. In another study, researchers Rodriguez et al. [24] also positively assessed the effectiveness of 2% mercuric oxide ointment used in patients with chronic blepharitis. After a few weeks, reduction of the symptoms was noted with a decrease in the number of mites around the eyelid area. The therapy had a 50% effectiveness after six months of treatment. The biggest disadvantage is the toxic effect of the mercuric oxide ointment (2% yellow mercuric oxide), as well as intolerance and allergy that may occur during its use. For this reason, it has been withdrawn from the pharmaceutical market in Poland. It can only be prepared in a pharmacy based on a physician prescription. However, the mercuric ointment should be applied very carefully on the eyelids and cannot have contact with the eyeball. Furthermore, it should be washed off the next morning and the eyelids should be thoroughly cleaned [24]. The case of a young man described by Raszeja-Kotelba et al. [25], in whom the presence of *D. folliculorum* was detected in the eyelids, shows that oral treatment with doxycycline, local treatment with metronidazole in gel and 2% ichthyol in zinc ointment also have positive effect on the treatment of demodicosis. The patient was treated ophthalmologically for two years, but without success, the periods of remission were short and the symptoms quickly returned. Only after a 2-month of therapy with oral doxycycline together with topical application of metronidazole in gel and 2% ichthyol in zinc ointment resulted in elimination of the *Demodex* infection and no symptoms were observed.

3.3. *In vitro* tests results

In vitro studies conducted by Sędzikowska et al. [26] showed that among the substances tested for their toxic effect on *Demodex*, the most effective were Spanish sage, tea tree and peppermint oils. This is probably due to the high concentration of terpenes, which have a lethal effect on these mites. Lavender, camphor, eucalyptus and fennel oils were slightly less effective probably because of lower terpenes concentrations. The study also tested the effectiveness of metronidazole and mercuric oxide, which, as mentioned earlier, are often used in treatment of demodicosis. The study showed, that apart from sea buckthorn oil, metronidazole was the weakest of all substances tested. This is probably related to the fact that metronidazole does not

have a direct effect on mites, only on the bacteria accompanying demodicosis infections, hence it has a positive effect on reducing the symptoms of secondary infection. Mercury oxide was also very weak, but slightly better than metronidazole. This allows to conclude that essential oils containing a high concentration of terpenes will be the most effective in the treatment of demodicosis [27].

4. Conclusions

In summary, metronidazole is the most widely used substance in treatment of human demodicosis, but very often its therapeutic process is combined with oral therapy or with other local medicaments. The combination of oral therapy of metronidazole with ivermectin or local skin therapy using metronidazole with oral doxycycline and 2% ichthyol in zinc ointment allows to obtain satisfactory therapeutic effects. Moreover, the use of 2% ointment with yellow mercury oxide topically and with metronidazole orally, ether peeling and eyelid hygiene fluid allows for more beneficial therapeutic effects, than use of the individual topical therapy with ointment. In addition, the treatment of demodicosis with medicaments containing essential oils and high concentration of terpenes is highly effective, because of their acaricidal effect. In addition, cosmetic procedures with mandelic acid support the treatment and healing of lesions caused by *Demodex*, afterwards preventing recurrence of the disease. Treatment of demodicosis based on the use of a single medicament has the lowest efficiency and effectiveness. In contrast, a combination therapies, in which orally administered and topically applied medications are taken together or several types of topically applied medications are combined, have the best effectiveness.

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