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Principles of demodexosis treatment

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Abstract

The article presents an overview of the main modern methods of treatment of demodexosis, the main antiparasitic drugs and alternative treatment regimens, their advantages and disadvantages. The aim of the study was to compare combined method of demodexosis treatment with external treatment with 7% metronidazole. 64 patients with acne and rosacea complicated demodexosis, which were divided into two groups depends on a method of treatment (250 mg of metronidazole per os 2 times a day, externally 1% metronidazole once a day for 20 days or 7% metronidazole externally, 20 days, respectively). The effectiveness of therapy in both groups was the same. It was a significant decrease in the number of morphological elements, reduction of subjective complaints of patients after the treatment. This study represents a lack of superiority in systemic therapy of demodexosis, compared to external therapy.

Keywords: Antiparasitic Therapy; Demodex; Demodexosis; Treatment

1. Introduction

As is known, often the etiologic and pathogenetic agent in the development of papulopustular dermatoses are mites of the genus *Demodex* [1, 2]. An additional complication for antiparasitic therapy creates a special feature, depending on the extent to which, depending on the effect of the drug, the dense cuticle that covers the body of the mites is obstructed by the three layers: external - epicuticle, middle - exocuticle and inner - endocuticle. Exo and endocuticium are impermeable, thus, the body of mites is difficult to access for the action of large molecules of exogenous substances, including acaricidal drugs. Communication with the external environment of mites occurs through water or gas exchange.

To obtain the elimination of mites, antiparasitic (acaricidal) drugs are used. Over the years, metronidazole, the derivative of the nitroimidazole group, proved to be the most successful. This drug is administered by a course of 4 to 6 weeks [3]. It is established that metronidazole enhances the protective and regenerative functions of the mucous membrane of the stomach and intestines and causes a pronounced anti-oedema effect [4]. The drug has a bacteriostatic effect, the most complex processes of DNA synthesis of gram-negative anaerobic bacteria [5], and antiparasitic against *Demodex folliculorum*. In the research of D.I. Grove (1997), P.G. Nielsen (1988) proved that the suppressive effect of the drug on some indicators of cellular immunity, by authors, suppression of leukocyte chemotaxis [6, 7]. Immunomodulatory effect of the drug due to inhibition of vascular endothelial growth factors, preventing neoangiogenesis. The tolerability of the drug is generally satisfactory. Side effects include a headache, nausea, vomiting, dry mouth, urticaria, itching, leukopenia and candidiasis.

5-nitroimidazole (Ornidazole) in cycles of 8 to 10 days. The drug has both an antiparasitic effect and bacteriostatic effects, increases neutrophil activity, stimulates adrenergic structures, and enhances reparative processes [8].

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In external therapy, the most often used drugs containing metronidazole 1% in the form of ointments or gel within 14 days. Metronidazole has the authority to the nonspecific resistance of the organism and affects cell-mediated immunity [9, 10]. As an alternative therapy, topical application of 10% benzyl benzoate ointment overnight is possible [11].

In special cases with demodicosis, a treatment aimed at the pathogenesis of the disease is used. For example, in the case of acneform-type demodicosis or resistance to antiparasitic drugs, it is advisable to use systemic retinoids (isotretinoin) at a dosage of 0.1-0.5 mg/kg of body weight per day for 2-4 months [12].

Antiparasitic properties are also possessed by permethrin (a group of pyrethroids). Pyrethroids will bind to lipid structures of nerve cell membranes, disrupting the operation of sodium channels, which regulate the polarization of membranes. Repolarization of the membrane is difficult, which paralyzes the parasite. An important point is that the molecules of pyrethroids are able to penetrate the mites' cuticle and concentrate in the hemolymph. Permethrin 5% cream is applied twice a day for 15-30 days [13, 14]. However, it must be remembered that the permeability of different areas of the skin is not the same. Drugs most actively penetrate the skin in the face area, where the thickness of the stratum corneum is minimal, so the spread of side effects in the form of erythema and simple contact dermatitis is possible. Acaricidal activity is also provided by preparations of ivermectin, lindane 1%, crotamiton 10% [3, 11]. Ivermectin is a synthetic derivative of compounds possessing antiparasitic activity, known as avermectins. The drug is effective against endoparasites having a tropism to the skin (*Strongyloides stercoralis*, *Ancylostoma braziliense*, *Cochliomyia hominivorax*, *Dermatobia hominis*, *Filaria bancrofti*, *Wucheria malayi*, *Onchocerca volvulus*, *Loa-loa*) and ectoparasites (*Sarcoptes scabies*, *Pediculus humanus*, *Demodex folliculorum* and *Cheyletiella* sp.) [15].

Ivermectin is recommended to be used systemically or topically in the form of 1% cream. In studies, it has been proven that ivermectin has an antiparasitic and anti-inflammatory effect. Clinical improvement with external 1% ivermectin cream was observed after 12 weeks of therapy [16]. Orally, the drug is administered at a dose of 200 mg/kg body weight twice with a break of 7 days [17]. The use of 1% Lindane also causes many doubts due to its neurotoxicity, therefore in some countries, the drug is banned, and in some, its use is limited [18]. As for the drug crotamiton 10%, it is applied to the skin at night for two to three days and is often used in children's practice [19, 20].

From the physiotherapy techniques, the positive effect of the use of intense pulsed light (IPL), discovered in 1992 and having a wavelength of 515 to 1200 nm [21], was proved. IPL radiation suppresses secretion of sebaceous glands, with their subsequent involution, which leads to resorption of lymphocytic infiltrates and death of mites [22].

Cryotherapy is an anti-demodectic action, and to achieve a more stable therapeutic effect it is recommended to use cryotherapy in combination with external preparations containing metronidazole [23].

Despite the fact that according to various authors, currently, the "gold standard" and the most effective way of treating demodicosis is the systemic application of the antiparasitic drug metronidazole, the drug itself has many side effects and has a number of contraindications. Taking into account the fact that in medicine the search for new medicinal products that have the least negative effect on the body remains an actual topic, we evaluated the effectiveness of external therapy of demodicosis in comparison with the systemic use of drugs.

The aim of this study is to compare the traditional regimen for the treatment of facial demodicosis (250 mg of metronidazole per os 2 times a day, externally with 1% metronidazole 1 time per day for 20 days) with the effectiveness of external therapy (metronidazole 7% days).

2. Material and methods

The study was conducted in compliance with the provisions of the Helsinki Declaration (1964) on Medical Ethics. The study protocol was approved at the meeting of the Ethical Committee of the Russian Medical Academy of Continuous Professional Education. All patients who participated in the study signed the "Informed consent of the participant in biomedical research".

The study included 64 patients with acne and rosacea complicated by demodicosis. The diagnosis of acne and rosacea was established on the primary admission on the basis of the clinical picture of the diseases. In this case, the main complaints of the patient were taken into account, which was distributed among the following groups: rashes, pain, burning, redness, itching, pigmentation, the presence of crusts/excoriations, telangiectasia, fatty shine. When assessing the local status (status localis), the following primary and secondary morphological elements were identified: papules, pustules, open comedones, milium, telangiectasia, crusts, redness, pigmentation, fatty shine. All patients included in the study were examined for mites of the genus *Demodex* by scraping the skin of the face, squeezing the contents of the

sebaceous glands before and after treatment. The diagnosis of "Demodecosis" was established when more than 5 individuals of ticks were detected per 1 cm². The study included men and women over the age of 18 with no somatic complications.

All patients were divided into two equal groups, depending on the chosen method of treatment. The first group (n=32; 50%) received 250 mg of metronidazole per os 2 times a day, externally 1% metronidazole once a day for 20 days, the second group (n=32; 50%) received 7% metronidazole externally within 20 days. The method of treatment was chosen randomly.

Statistical processing of data was carried out by the software package SPSS 21. The interrelation of categorical indicators was established by the exact method of Fisher.

3. Results

Of all the patients included in the study, patients with acne were 38 (59.37%), rosacea - 26 (40.62%). The distribution by sex, age and diagnosis are presented in table 1.

Table 1 Distribution by sex, age and diagnosis of respondents included in the study

Sex	Patients with Demodex mites				Total 64 (100%)
	Male (n=18; 28.13%)		Female (n=46; 71.88%)		
Diagnosis	Acne	Rosacea	Acne	Rosacea	
Age	23±5,5	44±10,4	29±6,4	51±17,6	

All patients were divided into two groups depending on the chosen treatment regimen. The patients were re-visited after 20 days of continuous therapy. Subjectively, both treatment regimens were tolerated well, no side effects were observed, no patient was excluded from the observation group. Evaluation of the effectiveness of therapy was based on complaints of patients and clinical picture. As can be seen from table 2, after treatment statistically reliably decreased complaints of patients on rashes, burning, pain, itching and redness. Moreover, in patients of the second group, complaints of oily skin gloss decreased, which is an additional advantage of topical therapy. The results are shown in table 2.

Table 2 Complaints of patients before and after treatment

Patients' complains	Percentage of patients			
	I group		II group	
Rashes	100	65*	100	70*
Hurt	75	30*	68	34*
Burning	64	30*	59	40
Redness	70	40*	69	40*
Itch	54	10*	70	20*
Pigmentation	36	17	42	25
Presence of crusts/ excoriations	39	20	45	30
Teleangiectasias	58	40	60	40
Oil shine	65	40	70	40*

(* p≤0.05)

Analysis of clinical manifestations after the therapy showed the presence of the following morphological elements in the first and second groups significantly decreased: papules, pustules, perifocal erythema, excoriation (p≤0.05) compares to the initial data (table 3).

Table 3 Frequency of occurrence of primary and secondary morphological elements before and after treatment in patients of two groups

Morphological elements	Percentages of elements			
	I group		II group	
	Before treatment	After treatment	Before treatment	After treatment
Papules	100	42	72	49
Pustules	80	31	64	40
Comedones	85	40	85	46
Milium	59	20	40	15
Teleangiectasias	40	15	58	15
Perifocal erythema	55	19	74	35
Excoriations	46	10	67	20
Pigmentation	73	50	89	64
Oil shine	64	25	74	55

When the scraping was repeated for the presence of Demodex mites, the following data were obtained in the two groups, the order in table 4.

Table 4 Detection of Demodex mites after treatment

	I group n=32; 50%	II group n=32; 50%
Detection of Demodex mites	19; 30%	20; 32%

Demodex mites after treatment in two groups were found approximately in an equal number of cases (30% and 32% of cases, respectively).

Estimating the results of treatment, it can be stated that the effectiveness of therapy in both groups was the same. Analysis of the clinical picture showed a positive dynamics of therapy, which manifested itself in a significant decrease in the number of morphological elements that characterize the severity of inflammation. The effectiveness of the therapy was confirmed by the reduction of subjective complaints of patients after the treatment, and, in patients who received only external therapy, complaints about the oily shine of the skin decreased, which is an additional advantage. Thus, clinical observations demonstrated a lack of superiority in systemic therapy of demodectosis, compared to external therapy using a preparation containing 7% metronidazole in the form of a cream or cream gel, as confirmed by statistical analysis.

4. Conclusion

Our study showed that the use of an external agent containing 7% metronidazole for 20 days in patients with demodectosis is comparable in effectiveness to systemic treatment with metronidazole 250 mg per os for 20 days. External application of 7% metronidazole makes it possible to avoid systemic administration of the drug, which reduces the risk of side effects of therapy.

Compliance with ethical standards

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Disclosure of conflict of interest

The author declares the absence of a conflict of interest.

Statement of ethical approval

The study protocol and all procedures were approved by the Ethical Committee of the Russian Medical Academy of Continuous Professional Education.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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