DOI 10.26724/2079-8334-2020-4-74-11-15
UDC[617.711–002–02:616.995.42:595.4291]–085–08.84

P.A. Bezditko, L.I. Levchenko[1]
Kharkiv National Medical University, Kharkiv
[1]Professional Medical College of Kharkiv Medical Academy of Postgraduate Education, Kharkiv

FEATURES OF COMBINED TREATMENT IN CHRONIC DEMODECTIC BLEPHAROCONJUNCTIVITIS

e-mail: levchenko125@ukrpost.ua

The article deals with the problem of treating patients with chronic demodectic blepharoconjunctivitis. Current concepts of this pathology treatment include antibacterial, anti-inflammatory, desensitizing, immunomodulatory treatment, lacrimal substitutes. The total of 80 patients (160 eyes) was examined for chronic demodectic blepharoconjunctivitis during 2016-2018 years. The combined treatment efficacy of chronic demodectic blepharitis by means of the "Metronidazole, supercritical CO2, chamomile extract, hyaluronic acid" gel drug and phototherapy device was studied. It was found that in patients with chronic demodectic blepharoconjunctivitis after combined treatment there was a decrease in eyelid edema, eyelid edges inflammation, improved secretion of meibomian glands. The biological effects of the phototherapy apparatus for the treatment of this pathology are due to such biostimulating factors as light polarization, polychromaticity, incoherence, low energy, infrared light. Secretory-stimulating, anti-inflammatory, regenerative, immunomodulatory effects were revealed. The obtained results permit to more adequately adjust the treatment of patients with chronic demodectic blepharoconjunctivitis.

Key words: chronic blepharoconjictivitis, demodex, "Metronidazole, supercritical CO2, chamomile extract, hyaluronic acid" gel, phototherapy device.

П.А. Бездітко, Л.І. Левченко

ОСОБЛИВОСТІ КОМБІНОВАНОГО ЛІКУВАННЯ ХРОНІЧНОГО ДЕМОДЕКОЗНОГО БЛЕФАРОКОН'ЮКТИВІТА

У статті розглянуто проблему лікування пацієнтів з хронічним демодекозним блефарокон'юктивітом. Сучасні концепції лікування цієї патології включають антибактеріальне, протизапальне, десенсибілізуюче, імуномодулююче лікування, замінники сльози. Обстежено 80 хворих (160 очей) з хронічним демодекозним блефарокон'юктивітом протягом 2016-2018 років. Проведено дослідження ефективності комбінованого лікування хронічного демодекозного блефарокон'юктивіта із застосуванням препарату геля "Метронідазол, надкритичний CO2, екстракт ромашки, гіалуронова кислота", апарат для фототерапії. Встановлено, що у хворих на хронічний демодекозний блефарарокон'юктивіт після комбінованого лікування спостерігалося зменшення набряків повік, запалення країв повік, поліпшення секреції мейбомієвих залоз. Біологічні ефекти апарату фототерапії для лікування даної патології визначаються такими біостимулюючими факторами, як поляризація світла, поліхроматичність, некогерентність, низька енергетичність, інфрачервоне світло. Виявлено секретостимулюючий, протизапальний, регенераторний, імуномодулюючий ефекти. Отримані результати дають можливість більш адекватно скоригувати лікування пацієнтів з хронічним демодекозним блефарокон'юктивітом.

Ключові слова: хронічний блефарокон'юктивіт, демодекс, "Метронідазол, надкритичний CO2, екстракт ромашки, гіалуронова кислота" гель, апарат для фототерапії.

The work is a fragment of the research project "Features of the dry eye syndrome clinic and treatment in patients with diabetic neuropathy", state registration No. 0118U000922.

The eyelids edges inflammation, which is associated with inflammation of the eyeball mucosa, is the most common chronic recurrent disease, difficult to treat [6]. Etiology is associated with micromites of the *Demodex* genus, which is found in the ducts of sebaceous, meibomian glands, in hair follicles [1,2,6,8]. Patients complain of intense itching, burning and eyelids "heaviness", fatigue of the eyes, discharge from the conjunctival cavity. Clinician observed: redness, thickening of the eyelid free margins, presence of pells and crusting □n th□m, wh□t□ □□lls □n th□ □□□l□sh□s; m□□ b□ □□□□m□n□d b□ tr□□h□s□s, □hr□n□□ □□njun□t□v□t□s, keratitis, "dry eye" syndrome [2]. In 60% of cases, this disease is complicated by the face skin lesion with mites. Products of life and decay of mites cause allergization, which enhances the inflammatory response, leads to a decrease in local immunity [5,7]. Drug treatment of demodecosis is not efficient because the mite is located deeply, the local application cannot act simultaneously on all parasites, only the most superficially located ones die [2]. Drugs containing sulfur or tar efficient for the skin demodecosis treatment cannot be used in ophthalmology due to their harmfulness. It is recommended to use various methods of treatment, including physiotherapy [4]. Therefore, a combined demodecosis treatment complex was suggested by means of applying "Metronidazole, supercritical CO2, chamomile extract, hyaluronic acid" gel on the skin twice a day and with performing phototherapy device.

The purpose of the study was to establish the efficacy of using "Metronidazole, supercritical CO2, chamomile extract, hyaluronic acid" gel in a combination with performing phototherapy device.

Materials and methods. Clinical studies were carried out during 2016-2018 at the medical centre "Evviva" of the highest category in the city of Kharkiv. The following criteria were used to select patients:

Inclusion criteria: Diagnosis established: chronic demodecosis blepharoconjunctivitis, age over 18 years, adequate attitude to the study.

Exclusion criteria: age under 18 years, presence of severe concomitant chronic diseases in the stage of exacerbation.

All patients were subjected to a general clinical examination, a standard ophthalmologic examination, a Schirmer's test. In order to detect a demodex agent in a preparation of 5-8 eyelashes, according to the traditional procedure, the ICOS mirror binocular biological microscope was used, the objective lens × 10, × 40; ocular × 10. The patients were examined on the day of visiting, on the 10th and on the 45th day of therapy. The examination scheme included: anamnesis study, collection and analysis of complaints, an objective examination with a specially designed questionnaire, assessing the severity of symptoms with a 4-point scale, according to the following criteria: itching and burning of the eyelids, fatigability, feeling of an intraocular foreign body, heaviness of the eyelids, reddening of the eyelid free margins and conjunctiva, thickening of the eyelid margins (0 – symptom absent, 1 – weak symptom, 2 – moderately pronounced symptom, 3 – strongly pronounced symptom). The dynamics of the symptoms change was estimated using observation protocols.

The total of 80 patients (160 eyes) was under supervision with laboratory confirmed demodecosis of the eyelids. Patients were divided into 2 groups: the main (n = 90) and the control one (n = 70). Patients of the control group (35 people) only underwent the standard treatment. Patients in the main group (45 people) were assigned a standard antibacterial, anti-inflammatory, desensitizing, immuno-modulatory treatment, lacrimal substitute, hygienic treatment of the eyelid margins, eye massage, and a treatment scheme applying to the eyelids skin area “Stop demodex” gel after clearing the eyelid free margins twice a day, and performing phototherapy with the “Bioptron Compact III” device. Polarized infrared light was focused on closed eyeballs for 4 to 6 minutes every day for 15 days, since it corresponds to the full life cycle of the mite (15 days); all methods of treatment affected only the imago.

Patients with generalized demodecosis were not included into the study groups. The selection of patients was performed in such a way that the groups were statistically consistent with the main statistical indices: age, gender, the presence of similar subjective complaints and objective data. The standard methods of descriptive statistics were used with the calculation of mean values, dispersion and standard mean error. To test the equality of the indices mean values in the groups under study, the Student's criterion (t-test) was used [4].

Results of the study and their discussion. The age of patients was from 28 to 62 years (average age 39.4), among them 61 women (76.25%), 19 men (23.75%). Thus, women are more likely to suffer (42 persons more (by 52.5%)). Duration of the disease made from 1 to 3 years.

In the course of treatment, a positive clinical effect was observed in all 80 patients (160 eyes) of the main and control groups. No cases of allergies or side effects have been reported. The presence of the mite was confirmed by microscopy of eyelashes in all the patients under examination. The most common complaints were itching and burning in the area of the eyelid free margins (100%), fatigue, a feeling of an intraocular foreign body, and the eyelids heaviness.

The following objective clinical features were observed in patients before treatment: redness of eyelid free margins and conjunctiva, thickening of the eyelids (160 eyes – 100%) in the main and control groups. According to our data, during the combined treatment of patients, a positive trend was observed.

Among the patients in the main group on the 10th and 45th day of treatment, there was a faster decrease in the intensity of the disease symptoms compared to the control group (table 1). Regression is presented in points for the 45 days period.

Table 1

Comparative assessment of subjective symptoms changes in patients of the main and control groups at different terms in points

Subjective complaints in points	Main group			Control group		
	Days of treatment		Regression, points	Days of treatment		Regression, points
	10-th	45-th	-2.1	10-th	45-th	-1.2
Eyelids itching and burning	-1.5	-3.6		-0.7	-1.9	
Eyelids fatigue	-2.1	-2.9	-0.8	-1.7	-1.9	-0.2
Foreign body sensation	-2.9	-3.7	-1.2	-1.6	--1.9	-0.3
Eyelids heaviness	-1.8	-2.5	-0.7	-1.5	-1.8	-0.3

It was found that more rapid regression was in patients of the main group on the 45th day of observation compared to the control group, indicating the necessity of treatment during 1.5 months. During the whole treatment period in the main group, the regression in complaints was more rapid: of the eyelids itching and burning (by 0.9 points), that of fatigue (0.6 points), the intraocular foreign body sensation (by 0.9 points), the eyelids heaviness (by 0.4 points).

The dynamics of objective features is presented in the figure. According to our data, after 10 days of treatment in the main group, the eyelid redness decreased by 38/90 cases (42.2%), in the control group - by 4/70 cases (42.2%); after 45 days in the main group eyelid redness decreased by 56/90 cases (62.2%), in the control group-by 41/70 cases (58.6%). The findings were correlated with an objective ophthalmologic examination.

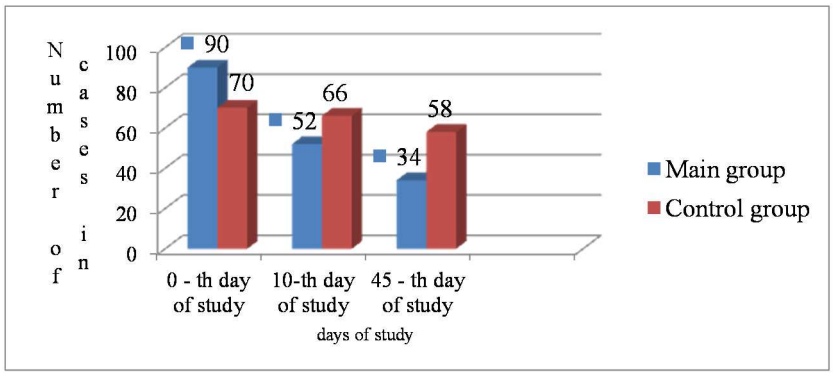

Fig.1. Comparative assessment of the eyelid margins redness change in absolute numbers

According to our data, among the patients in the main group, on the 10-th and the 45th days of treatment, a faster decrease in the intensity of redness and thickening of the eyelids was observed in comparison with the control group (table 2). Also, more rapid features regression in patients of the main group remained on the 45th day of observation compared to the control group, which confirms the necessity of treatment during the 45 days period. During this period, in the main group, in comparison with the control one, regression of the eyelid margins redness was faster (by 0.8 points), as well as the eyelid margins thickening (by 0.2 points).

Table 2

Comparative assessment of objective symptoms changes in patients of the main and control groups at different terms in points

Objective data in points	Main group			Control group		
	Days of treatment		Regression, points	Days of treatment		Regression, points
	10-th	45- th		10-th	45-th	
Redness of eyelid margins	-1.9	-4.3	-2.4	-1.1	-2.7	-1.6
Thickening of eyelid margins	-2.3	-3.6	-1.3	-1.6	-2.7	-1.1

According to the results of the Schirmer's test (less than 15 mm) (table 3), dry eye syndrome (DES) was observed in 160/160 (100%) cases prior to treatment. It can be seen from the table that after treatment for 45 days, there was a significant improvement in the Schirmer's test results in patients of the main group. In patients with a mild DES stage, the mean value of the Schirmer's test significantly increased by 17.9% ($t = 4.8$; $p < 0.05$); in patients with a moderate DES stage by 24.2% ($t = 5.2$; $p < 0.05$), and in patients with severe DES stage-by 32.6% ($t = 2.4$; $p < 0.05$). According to our data, in 6/90 patients (7%) of the main group, after 45 days of treatment, the mean values of Schirmer's test were normal, while in all patients of the control group after treatment, the DES was maintained, indicating the efficacy of the suggested combination treatment. A significant difference between the mean values of the Schirmer's test was observed when compared to the control group after 45 days treatment ($t > 2.0$; $p < 0.05$). In the control group, there was no significant positive dynamics in the mean values of the Schirmer's test after treatment.

Based on the analysis of Schirmer's test results in the main group, it is evident that after 45 days of treatment, the number of patients with the mild DES stage increased by 9/90 (10%), that with the moderate stage, decreased by 9/90 (10%), with the severe stage - decreased by 6/90 cases (6.7%). The number of patients with mild DES in the control group after 45 days of treatment decreased by 2/70 (2.9%), with the moderate stage increased by 2/70 cases (2.9%), that with the severe stage remained unchanged. This indicates a better treatment effect in patients with the main group for 45 days compared to the control group. All patients were prescribed lacrimal substitutes drugs.

Table 3

Mean values of the Schirmer test in patients with demodectic blepharoconjunctivitis

Groups under study	Before treatment			After treatment		
	DES stages			DES stages		
	mild (9-14 mm)	moderate (5-8 mm)	severe (<5 mm)	mild (9-14 mm)	moderate (5-8 mm)	severe (<5 mm)
Main group (90eyes)	11.2±0.3 (33 eyes)	6.6±0.3 (40 eyes)	3.1±0.5 (17 eyes)	13.2±0.2 (42 eyes)	8.2±0.1 (31 eyes)	4.1±0.3 (11 eyes)
Control group (70 eyes)	11.4±0.4 (35 eyes)	6.4±0.3 (24 eyes)	3.2±0.3 (11 eyes)	10.9±0.3 (33 eyes)	6.7±0.3 (26 eyes)	3.1±0.3 (11 eyes)
p	>0.05	>0.05	>0.05	<0.05 (t=4.8)	<0.05 (t=5.2)	<0.05 (t=2.4)

The presence of a clinically significant amount of demodex mites was confirmed by microscopy in 100% of cases prior to treatment. After 10 days in the main group, its number decreased by 40 (44.5%) cases, in the control group - by 10 (14.3%) cases; after 45 days in the main group it decreased by 62 (68.9%) cases, in the control group-by 26 (37.1%) cases, indicating a positive dynamics of treatment in patients of the main group (table 4).

Table 4

Dynamics of the mite presence in patients of the main and control groups in different terms, n (%)

Terms	Main group	Control group
0-th day	90 (100%)	70 (100%)
10-th day	50 (55.5%)*	60 (85.7%)*
45-th day	28 (31.1%)*	44 (62.9%)*

Note: * p≤ 0.01

It was established that after 10 days in the main group, the clinically significant number of mites was reduced by 44.5% of cases (in the control group-by 14.3% of cases); after 45 days in the main group, it reduced by 68.9% of cases (in the control group-by 37.1% of cases), which reliably indicates the positive dynamics of treatment in patients of the main group. The best effect was observed in patients of the main group for 45 days of treatment, therefore it is necessary to carry out the suggested combined treatment for 1.5 months.

The results of the study correlate with the detailed summary reports of Koo H. [8]. Demodex were found in 84% of patients with ocular discomfort [8]. In our study it was found in 100% of cases in patients with this pathology, which indicates the relevance of studying the problem of demodicosis. The available treatments, which are described in the literature, are not always effective. Summarizing the data obtained, it should be noted that there are no serious side effects, which indicates the safety of the combined treatment of chronic demodicosis blepharitis with the use of the "Metronidazole, supercritical CO2, chamomile extract, hyaluronic acid" gel drug and phototherapy device. It was found that in patients with chronic demodicosis blepharoconjunctivitis after combined treatment there was a decrease in eyelid edema, inflammation of the edges of the eyelids, improved secretion of meibomian glands. At the same time, the results indicate an increase in side effects in patients without this combination therapy, especially on the skin and mucous membranes, as these systems respond to drugs with sulfur or tar in the body [1]. The secretory-stimulating, anti-inflammatory, regenerative, immunomodulatory effects of the combined method of treatment of chronic demodicosis blepharoconjunctivitis were revealed, which is confirmed by the objective data of the Schirmer's test. This is consistent with the literature of a number of authors, but they did not perform combination therapy with light therapy. [1,6]. The obtained results make it possible to more adequately adjust the treatment of patients with chronic demodicosis blepharoconjunctivitis [2,4].

Conclusions

1. Clinical observations of patients using the new combined method of chronic demodectic blepharoconjunctivitis treatment have shown its high efficacy, absence of complications and side effects, its ease of use, availability and safety.

2. The combination of applying "Metronidazole, supercritical CO2, chamomile extract, hyaluronic acid" gel and the physiotherapeutic method phototherapy device treatment prevents the excessive reproduction of the demodex mite, which leads to rapid elimination of the chronic demodectic blepharoconjunctivitis features, was observed in patients of the main group; the complaints regression was observed in eyelids itching and burning was faster (by 0.9 points), fatigue of the eyelids (by 0.6 points), foreign body sensation (by 0.9 points), the eyelids heaviness (by 0.4 points), redness of the eyelid margins (by 0.8 points), thickening of the eyelid margins (by 0.2 points). This indicates the clinically proven efficacy of the suggested combined treatment method.

3. The secretion-stimulating effect of phototherapy device treatment has been established, which is confirmed by a significant increase in the mean values of the Schirmer's test in patients with the mild DES stage by 17.9% ($t = 4.8$; $p < 0.05$), in patients with the moderate DES by 24. 2% ($t = 5.2$; $p < 0.05$), in patients with the severe DES stage-by 32.6% ($t = 2.4$; $p < 0.05$; in 7% of the patients in the main group after 45 days treatment, mean values of the Schirmer's test were normalized, all patients in the control group did not demonstrate changes.

4. It was found that the number of patients with the mild stage of the main group has grown after treatment by 10% (control group-by 2.9%), those with the moderate stage reduced by 10% (control group-increased by 2.9%), patients with the severe stage reduced by 6.7% (control group-unchanged).

5. It was established that after 10 days in the main group, the clinically significant number of mites was reduced by 44.5% of cases (in the control group-by 14.3% of cases); after 45 days in the main group, it reduced by 68.9% of cases (in the control group-by 37.1% of cases), which reliably indicates the positive dynamics of treatment in patients of the main group.
6. According to our data, the best effect was observed in patients of the main group for 45 days of treatment, therefore it is necessary to carry out the suggested combined treatment for 1.5 months.

References

1. Zheltikova TM. Demodekoz: mify i realnost'. Semeynaya meditsina. 2012; 1: 36-38. [in Russian]
2. Ivanova NV, Voronova NN, Anisova SYu, Ivanova MI. Klinicheskaya effektivnost sredstv «STOP DEMODEX» v kompleksnom lechenii bolnykh demodekoznym blefarokonyuktivitom. Krymskiy zhurnal ehksperimentalnoy i klinicheskoy meditsiny. 2012; 2(1-2): 42-45. [in Russian]
3. Petri A, Sebin K. Naglyadnaya meditsinskaya statistika. Ucheb. posobiye. Moskva: GEOTAR-Media. 2015. [in Russian]
4. Polunin GS, Makarov IA. Fizioterapevticheskie metody v oftalmologii. Moskva: Meditsinskoe informatsionnoe agenstvo. 2012. [in Russian]
5. Khilkevich ND, Kachuk MV, Muzychenko AP, Kruk NV, Vetohina EL. Demodekoz kak dermatologicheskaya problema. Voyennaya meditsina. 2012; 3: 151-155. [in Russian]
6. Chuprov AD, Malygina EK. Sovremennyi vzglyad zarubezhnykh avtorov na diagnostiku i lechenie blefaritov demodekoznoy etiologii. Prakticheskaya meditsina. 2018; 3(114): 200-203. [in Russian].
7. Yutskovskiy AD, Yutskovskaya AYa, Kusaya NV. Osobennosti immunnogo statusa u patsiyentov s demodekozom kozhi. Dermatovenerologiya. 2011; 3: 33-36. [in Russian].
8. Koo H, Kim TH, Kim KW, Wee SW, Chun YS, Kim JC. Ocular surface discomfort and Demodex: effect of tea tree oil eyelid scrub in Demodex blepharitis. J. Korean Med. Sci. 2012; 27(12): 1574-1579.

Стаття надійшла 21.12.2019 р.

DOI 10.26724/2079-8334-2020-4-74-15-19
UDC 616.895.1-616.895.6, 618.175

O.O. Belov, A.L. Kostyuk, V.M. Andriichuk, I.Yu. Kostyuk
National Pirogov Memorial Medical University, Vinnytsya

FEATURES OF MENSTRUAL AND GENERATIVE FUNCTION DISORDERS IN DEPRESSIVE DISORDERS OF ENDOGENOUS NATURE

e-mail: oleksbelov@gmail.com

Menstrual and generative dysfunction in 104 women with depressive disorders was studied. Decreased generative function with small number of pregnancies and births, decreased or nullbirth and sexual life; at this immaturization of generative function worsens with deepening of depression. Women with depressive disorders have a significant incidence of dysmenorrhea (83% in total), the prevalence of which also increases with the severity of depression. The most common disorders are opsomenorrhea (41%), amenorrhea (33%) and oligomenorrhea (20%). The prevalence of premenstrual syndrome among women with depression was 57%; it varies from 48% in mild depression to 90% in severe.

Key words: depressive disorders, dysmenorrhea, generative function

О.О. Белов, А.Л. Костюк, В.М. Андрійчук, І.Ю. Костюк

ДЕПРЕСИВНІ РОЗЛАДИ І ПОРУШЕННЯ МЕНСТРУАЛЬНО-ГЕНЕРАТИВНОЇ ФУНКЦІЇ

Досліджено порушення менструально-генеративної функції у 104 жінок, хворих на депресивні розлади. Встановлено зниження генеративної функції з малою кількістю вагітностей і пологів, зниженням або відсутністю лібідо і статевого життя; при цьому реалізація генеративної функції погіршується з поглибленням депресії. Жінкам, хворим на депресивні розлади, притаманна значна ураженість дисменореями (в цілому 83%), поширеність яких також зростає по мірі важкості депресії. Найбільш поширеними розладами при цьому є опсоменореї (41%), аменореї (33%) та олігоменореї (20%). Поширеність серед жінок, хворих на депресію, передменструального синдрому склала 57%; вона варіює від 48% при легкій депресії до 90% при важкій.

Ключові слова: депресивні розлади, дисменорея, генеративна функція.

The work is a fragment of the research project "Research of reproductive potential and problems maintaining the health of women", state registration No. 0116U000258.

Depressive disorders are one of the most pressing medical and social problems. Depression is recognized by the WHO as the third leading cause of illness worldwide; it is predicted that by 2030 this disease will come to the fore, and the elimination of the effects of depression will be the main source of medical costs [6, 9]. Depressive disorders are accompanied by severe somatovegetative disorders, an important place among which is occupied by disorders of menstrual and generative function [2, 4, 10].