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INDICATORS OF PHAGOCYTOSIS IN WOMEN WITH ACNE DURING COMPREHENSIVE TREATMENT THAT INCLUDED PRP- AND IPL-THERAPY

Dashko M., Syzon O., Voznyak I., Volbyn S., Astsaturov H.
Danylo Halytsky Lviv National Medical University

Introduction. Acne is one of the most common dermatological diseases. It may have a chronic course, leaving permanent marks, and in last years has been tending to have more and more severe clinical course with widespread skin lesions. According to recent studies, the development of acne is due to the combined effect of endogenous and exogenous factors, among which endocrine diseases, disorders of metabolic processes, reduced systemic immunity and phagocytic ability of mononuclear phagocytes and granulocytes at various stages of phagocytosis of pyogenic cocci, which contributes to more severe clinical course, and frequent relapse of this diseases. It was also proved that the intestinal microbiota plays an important role in the formation of homeostasis and immune response. The Objective of the study is to determine the evolution of phagocytosis indices in patients with acne under different comprehensive treatments, using oral antibiotics, immunotherapy (PRP-therapy), probiotics, low-dose birth control pills and IPL- therapy.
Materials and methods. We observed 93 women with acne aged from 18 to 25 years old. In 19 (20.43%) patient mild acne was diagnosed, in 41 (44.09%) – moderate acne, in 33 (35.48%) persons – severe acne, 54 (58.06%) persons suffered from acne up to 1 year, 39 (41.93%) – from 1 to 3 years. To assess the state of phagocytosis in patients with acne vulgaris, we determined phagocytic activity (PA) and phagocytic index (PI) of polymorphonuclear leukocytes, nitro blue tetrazolium recovery test (NBT test spontaneous) and NBT-test pyrogenal stimulated by recognized methods.
Results. Analysis of the studied parameters of phagocytosis at the end of treatment showed a significant increase in patients of the core group who were administered a comprehensive treatment which included oral antibiotic, probiotic, and low-dose birth control pills, PRP-therapy and IPL-therapy, as compared with the patients of other groups under study.
Conclusions. Using combined therapy for women with acne occurring against the backdrop of a sluggish process of phagocytosis and concomittant intestinal dysbiosis leads to normalization of the leading indices of phagocytosis (PI, PA, NBT tests both spontaneous and stimulated), and enchances their phagocytic activity both during capture and formation of bactericidal activity and in the final stages of phagocytosis justifying the feasibility of a combined use of antibiotics, probiotic, low-dose birth control pills PRP-therapy and IPL-therapy in the treatment of acne.
Key words: acne, phagocytosis, probiotic, PRP-therapy, IPL-therapy, low-dose birth control pills.

Introduction

Acne is one of the most common dermatological diseases. It may have a chronic course, leaving permanent marks (scars, blemishes, emotional disorders), and in recent years has been tending to have more and more severe clinical course with widespread skin lesions, formation of resistance to drugs of etiotropic treatment, leading to the chronic course, decrease or loss of patient's capacity and social activity which signifies important medical and social aspects of the problem and justifies the topicality of improving treatment studies [1, 7, 9, 14]. According to recent studies, the development of acne is due to the combined effect of endogenous and exogenous factors,

among which endocrine diseases should be pointed out, as well as disorders of metabolic processes [8, 10], reduced systemic immunity and phagocytic ability of mononuclear phagocytes and granulocytes at various stages of phagocytosis of pyogenic cocci, which contributes to more severe clinical course, and frequent relapse of this diseases [5, 9]. It was also proved that the colon microbiota plays an important role in the formation of homeostasis and immune response [3, 4]. A relationship between the conditions of the colon microbiota, indices of systemic immunity and phagocytosis and nature of clinical manifestations of acne justifying differentiated administration of probiotics and immunomodulation therapy in the comprehensive therapy were found [1, 6, 10, 13]. According to modern standards [2, 6, 8, 10], the treatment of acne is carried out in various ways: patients with mild acne are prescribed an external antibacterial and anti-inflammatory therapy (topical antibiotics, topical retinoid medicines, azelaic acid, benzoyl peroxide) only, but in case of moderate and severe forms, comprehensive treatment including systemic antibacterial, immunotropic, anti-inflammatory drugs, oral retinoid, low-dose birth control pills and other therapies are applied.

The Objective of the study is to determine the evolution of phagocytosis indices in patients with acne under different comprehensive treatments, using oral antibiotics, immunotherapy (PRP-therapy), probiotics, low-dose birth control pills and IPL- therapy

Materials and methods

We observed 93 women with acne aged from 18 to 25 years old. In 19 (20.43%) patients mild acne was diagnosed, in 41 (44.09%) – moderate acne, in 33 (35.48%) persons – severe acne 54 (58.06%) persons suffered from acne up to 1 year, 39 (41.93%) – from 1 to 3 years. The control group consisted of 35 healthy individuals (donors) of the similar age. Patients were being observed during a year. The considered criteria for the study were the following: patient's age – 18 years old or more; clinical manifestations of acne, absence of chronic physical illness or exacerbation at the time of the examination. To assess the state of phagocytosis in patients with acne vulgaris, we determined phagocytic activity (PA) and phagocytic index (PI) of polymorphonuclear leukocytes, nitro blue tetrazolium recovery test (NBT test spontaneous) and NBT-test pyrogenal stimulated by the recognized methods. Statistical analysis of the results of research was carried out by the methods of statistical analysis using software (Excel, Statistica 7.0), the difference of averages was considered probable at $p < 0.05$.

Results and discussion

Before treatment, patients with acne had probable decrease in PI (by 31.7%, $p<0.001$) with the downward trend of PA (by 8.82%, $p>0.05$), characterizing the initial stages of phagocytic process, as well as probable reduction of spontaneous NBT-test (by 24.8%, $p<0.01$) and stimulated NBT test (by 22.2%, $p<0.001$), which represent the final stage of the process of phagocytosis. At the same time, women with acne had concomitant dysbiosis of the large intestine cavity of I-IV degree and interdependence between changes of parameters of systemic immunity and phagocytosis, the degree of intestinal dysbiosis and severity of clinical course of acne was established (Figure 1), justifying the administration of probiotics and immunotropic therapy for these patients.

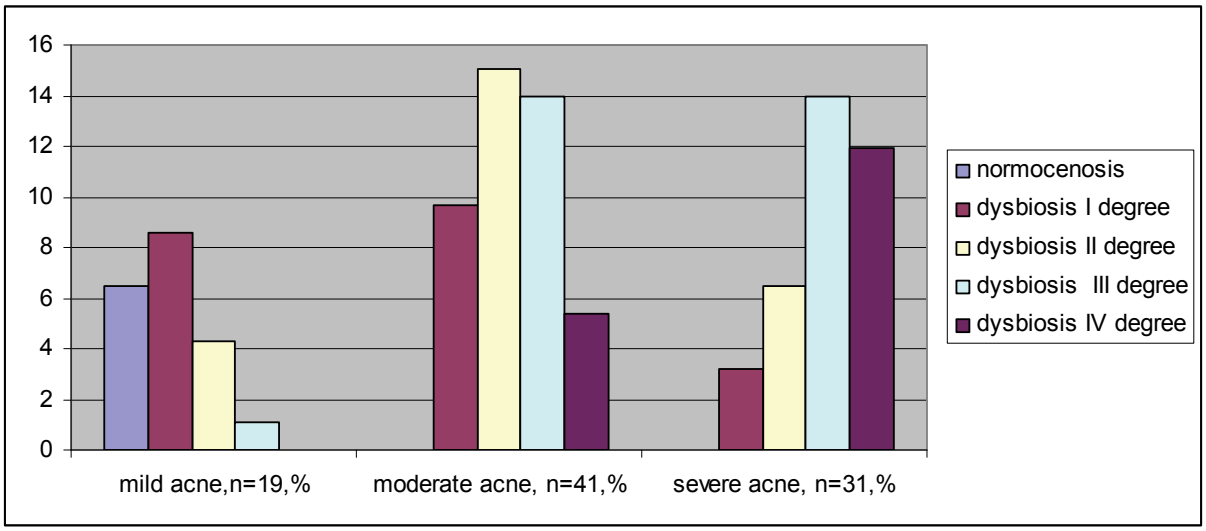

Figure 1 Distribution of patients with different severity of acne according to the degree of dysbiosis

In order to optimize the treatment of acne, taking into consideration the found changes in systemic immunity indices of these patients, phagocytosis and colon microbiota, we developed a complex therapeutic method which suggests the administration of immunotherapy (PRP-therapy), probiotic Mutaflor containing Escherichia coli Nissle 1917, low-dose birth control pills that have antiandrogenic effect, oral antibiotics (including doxycycline) and IPL therapy To determine the effectiveness of the developed method of combined therapy of acne, the patients under study were divided into 3 groups, using random method, and women in the groups were of similar age and clinical forms of acne. The first comparative group included 29 women who received systemic therapy, including oral antibiotics (including doxycycline) 0.1g twice a day during 14 days, probiotic Mutaflor (1 capsule once a day during 1 month two times a year) PRP-therapy according to the admitted scheme (1 procedure per week 5-10 times) [11, 12]; the second comparative group consisted of 33 patients who were administered Mutaflor, low-dose birth control pills (for 12 month) and PRP-therapy; and the third (basic) group numbered 31 patients who were administered a comprehensive systemic therapy treatment which included oral antibiotics (including doxycycline) 0.1g twice a day 14 days, probiotic Mutaflor (1 capsule once a day during 1 month two times a year), low-dose birth control pills (during 12 months) PRP- and IPL-therapy [14], which is based on the influence of the light flow, which is able to quickly eliminate the focus of inflammation, contribute to the death of pathogenic microorganisms, reduce the synthesis of sebum, accelerate blood circulation and enhance cell regeneration. The procedures were carried out for 15-45 minutes with intervals of 2 weeks, 4-7 procedures per course. All patients also received external antibacterial and anti-inflammatory therapy: the women with mild acne – azelaic acid, benzoyl peroxide, with moderate and severe acne – additionally topical retinoid medicines. The evaluation of the results of different treatments for acne was conducted basically on the analysis of the evolution of clinical and laboratory indices of blood including those of phagocytosis, that are shown in the table.

Table I. Evolution of phagocytosis indices in patients with pyoderma after different therapies (M±m)

Indices, measurement units		Patients with acne (n=93)			Control group (n=35)
		1st group (n_1=29)	2nd group (n_2=33)	3rd group (n_3=31)	
Phagocytic activity, %	Before treatment	54.9± 1.65	54.1±2.08 p_{1-2}>0.05	55.9±2.54 p_{1-3}>0.05; p_{2-3}>0.05	62.9± 4.28
	After treatment	58.5± 1.34	57.9±1.64 p_{1-2}>0.05	62.6±1.92 p_{1-3}>0.05; p_{2-3}>0.05	
P (before/after treatment)		P>0.05	P>0.05	P<0.05	
Phagocytic index	Before treatment	4.01± 0.406**	4.08±0.264*** p_{1-2}>0.05	4.26±0.298*** p_{1-3}>0.05; p_{2-3}>0.05	6.88± 0.540
	After treatment	5.06± 0.302**	5.56±0.242* p_{1-2}>0.05	6.12±0.242 p_{1-3}<0.01; p_{2-3}>0.05	
P (before/after treatment)		P<0.05	P<0.001	P<0.001	
spontaneous NBT-test	Before treatment	9.88± 0.224**	10.1±0.598* p_{1-2}>0.05	10.0±0.709* p_{1-3}>0.05; p_{2-3}>0.05	12.5± 0.850
	After treatment	11.4± 0.244	11.9±0.672 p_{1-2}>0.05	12.6±0.624 p_{1-3}>0.05; p_{2-3}>0.05	
P (before/after treatment)		P<0.01	P<0.05	P<0.01	
stimulated NBT test	Before treatment	21.4± 0.972***	21.8±0.859*** p_{1-2}>0,05	20.8±0.698*** p_{1-3}>0.05; p_{2-3}>0.05	29.3± 0.723
	After treatment	24.2± 0.634***	24.9±0.436*** p_{1-2}>0,05	27.2±0.648* p_{1-3}<0,01; p_{2-3}<0.01	
P (before/after treatment)		P<0.05	P<0.01	P<0.001	

Notes:

1. * – The degree of probability of the indices deference relative to control group of patients:
   * – p<0.05; ** – p<0.01; *** – p<0.001
2. p_{1-2}, p_{1-3}, p_{2-4} – probability of the indices deference in patients of different groups.
3. P – probability of the indices deference in the groups of patients before and after the treatment.

According to the results of the conducted studies (Table 1), patients of the 1st comparative group, who received systemic therapy, including oral antibiotics, probiotic and PRP-therapy were likely to increase their PI by 26.18% (p<0.05), NBT-test of spontaneous and stimulated (by 15.38%, p<0.01 and 13.08% respectively, p <0.05), but preserving significant difference of PA and stimulated NBT-test with those of the control group (a decrease by 26.45%, p <0.001 and 17.41%, p<0.001 respectively). Women with acne in the second comparative group, due to the use of probiotic Mutaflor, low-dose birth control pills, PRP-therapy at the end of treatment, showed probable growth of PI rates by 36.27% (p<0.001), NBT-test of spontaneous and stimulated (by 17.82%, p<0.05 and 14.22%, p<0.01 respectively), but without probable difference to the patients of the first comparative group with preserving significant difference of PI and stimulated NBT-test with the same parameters in control group (a decrease by 19.19%, p<0.05 and 15.02%, p<0.001 respectively). However, patients with acne in the core group who received combined therapy which included oral antibiotic, probiotic, low-dose birth control pills (for 12 month) PRP- and IPL-therapy, experienced probable increase in PI and PA (by 43.66%,

p<0.001 and 11.98%, p<0.05 respectively), spontaneous NBT-test (by 20.6%, p<0.01) as well as stimulated NBT test (by 30.77%, p<0.001) with the approximation of most of them, except NBT-test stimulated, to the values of those in the control group. Analysis of the studied parameters of phagocytosis at the end of treatment also showed a significant increase in patients of the core group compared to those of patients in other comparative groups. Thus, the rate of PI at the end of end of the treatment in patients of the main group was significantly higher both comparing to the indices of the patients in the 1st comparison group (by 20.95%, p<0.01), while stimulated NBT test relative to the 1st comparative group (by 12.39%, p<0.01) and to the 2st comparative group (by 9.24%, p<0.01). The obtained better results on the evolution of the phagocytosis indices in patients of the main group could be related to the following: direct stimulating effect of immunotherapy, low-dose birth control pills have regulatory influence on the homeostasis of woman's organism and by a decrease of microbial intestinal load on macrophages and granulocytes as a result of normalizing probiotic action on concomitant dysbiotic disturbances of the large intestine in such patients.

Conclusions

Using combined therapy with the inclusion of oral antibiotic, probiotic, low-dose birth control pills, PRP- and IPL-therapy for women with acne occurring against the backdrop of a sluggish process of phagocytosis and concomittant intestinal dysbiosis leads to normalization of the leading indices of phagocytosis (PI, PA, NBT tests both spontaneous and stimulated), and enchances their phagocytic activity both during capture and formation of bactericidal activity and in the final stages of phagocytosis, justifying the feasibility of a combined use of antibiotics, probiotic, low-dose birth control pills, PRP- and IPL- therapy in the treatment of acne. In the future we are planning to determine and analyze the evolution of other homeostasis indices in a combined treatment of patients, suffering from acne by using oral antibiotics, probiotic, low-dose birth control pills and autohemotherapy as a complex.

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РЕЗЮМЕ
ВИВЧЕННЯ ПОКАЗНИКІВ ФАГОЦИТОЗУ У ЖІНОК З АКНЕ ПІД ЧАС КОМПЛЕКСНОГО ЛІКУВАННЯ, ЩО ВКЛЮЧАЛО PRP ТА IPL-ТЕРАПІЮ

Дашко М.О., Сизон О.О., Возняк І.Я., Вольбин С.В., Асцатуров Г.Є.
Львівський національний медичний університет імені Данила Галицького

Вступ. Акне – одне з найпоширеніших дерматологічних захворювань з переважно хронічним перебігом, яке часто залишає незворотні зміни на шкірі і в останні роки має тенденцію до все більш і більш важкого клінічного перебігу з поширеними ураженнями шкіри. Згідно з останніми дослідженнями, розвиток акне зумовлений сукупною дією ендогенних та екзогенних факторів, серед яких ендокринні захворювання, порушення обмінних процесів, зниження системного імунітету та фагоцитарної здатності мононуклеарних фагоцитів і гранулоцитів на різних стадіях фагоцитозу гнійних коків, що сприяє більш тяжкому перебігу та частим рецидивам цього захворювання. Також доведено, що мікробіота кишечника відіграє важливу роль у формуванні гомеостазу та імунної відповіді.
Мета роботи. Визначити динаміку показників фагоцитозу у хворих з акне під час комплексного лікування з використанням антибіотиків, пробіотиків, низькодозованих контрацептивів, PRP- та IPL-терапії.
Матеріали та методи. Під спостереженням перебували 93 жінки з акне віком від 18 до 25 років. У 19 (20,43 %) пацієнток діагностовано акне легкого ступеню, у 41 (44,09 %) – акне середнього ступеню, у 33 (35,48 %) осіб – акне важкого ступеню; 54 (58,06 %) особи хворіли на акне менше 1 року, 39 (41,93%) – від 1 до 3 років. Для оцінки стану фагоцитозу у хворих на вульгарні вугрі визначали фагоцитарну активність (ФА) та фагоцитарний індекс (ФІ) поліморфноядерних лейкоцитів, тест відновлення нітросинього тетразолію (НСТ-тест спонтанний) і НСТ-тест стимульований за відомими методиками.
Результати та обговорення. Аналіз досліджуваних показників фагоцитозу наприкінці лікування показав достовірне збільшення досліджуваних показників у пацієнтів основної групи, які отримували комплексне лікування, що включало прийом пероральних антибіотиків, пробіотиків, низькодозованих протизаплідних таблеток, PRP- та IPL-терапії, порівняно з пацієнтами інших досліджуваних груп.

Висновки. Застосування комплексної терапії у жінок з акне, що протікає на фоні уповільненого фагоцитозу та супутнього дисбактеріозу кишечника, призводить до нормалізації основних показників фагоцитозу (ФІ, ФА, НСТ-тесту як спонтанного, так і стимульованих), а також підвищує їхню фагоцитарну активність як під час захоплення і формування бактерицидної активності, так і на завершальних стадіях фагоцитозу, що обґрунтовує доцільність комбінованого застосування антибіотиків, пробіотиків, низькодозованих протизаплідних таблеток, PRP- та IPL-терапії при лікуванні акне.

Ключові слова: акне, фагоцитоз, пробіотик, PRP-терапія, IPL-терапія, низькодозовані контрацептиви.

АВТОРСЬКА ДОВІДКА

Дашко Маріанна Олегівна
К.мед.н., доцент кафедри дерматології та венерології
Львівського національного медичного університету імені Данила Галицького
Адреса: вул. Пекарська, 69, м. Львів, Україна, 79010
Тел.: +380 (67) 769 19 77
E-mail: mariannadashko@gmail.com
Dashko Marianna
Candidate of Medical Sciences (PhD), Associate Professor of the department of dermatology and Venereology of Danylo Halytsky Lviv National Medical University
Address: str. Pekarska, 69, Lviv, 79010
Tel.: +380 (67) 769 19 77
E-mail: mariannadashko@gmail.com
Сизон Орися Орестівна
Д.мед.н., професорка, завідувачка кафедри дерматології та венерології
Львівського національного медичного університету імені Данила Галицького.
Адреса: вул. Пекарська, 69, м. Львів, Україна, 79010
Тел.: +380 (95) 440 79 75
E-mail: syzon-orysya@ukr.net
Syzon Orysya
Doctor of Medical Sciences, Professor, Head of the Department of Dermatology and Venereology of Danylo Halytsky Lviv National Medical University
Address: str. Pekarska, 69, Lviv, Ukraine, 79010
Tel.: +380 (95) 440 79 75
E-mail: syzon-orysya@ukr.net
Возняк Ірина Ярославівна
К.мед.н., доцент кафедри дерматології та венерології
Львівського національного медичного університету імені Данила Галицького
Адреса: вул. Пекарська, 69, м. Львів, Україна, 79010
Тел.: +380 (67) 701 84 83
E-mail: voznyaki@gmail.com
Vozniak Iryna
Candidate of Medical Sciences (PhD), Associate Professor of the department of Dermatology and Venereology of Danylo Halytsky Lviv National Medical University
Address: str. Pekarska, 69, Lviv, Ukraine, 79010
Tel.: +38 (067) 701 84 83
E-mail: voznyaki@gmail.com
Вольбин Світлана Володимирівна
К.мед.н., доцент кафедри дерматології та венерології Львівського національного медичного університету імені Данила Галицького
Адреса: вул. Пекарська, 69, м. Львів, Україна, 79010
Тел.: +38 (063) 788-15-88
E-mail: volbynsvitlana@gmail.com

Volbyn Svitlana
Candidate of Medical Sciences (PhD), Associate Professor of the department of Dermatology and Venereology of Danylo Halytsky Lviv National Medical University
Address: str. Pekarska, 69, Lviv, Ukraine, 79010
Тел.: +38 (063) 788-15-88
E-mail: volbynsvitlana@gmail.com
Асцатуров Геннадій Євгенович
К.мед.н., доцент кафедри дерматології, та венерології
Львівського національного медичного університету імені Данила Галицького
Адреса: вул. Пекарська, 69, м. Львів, 79010
Тел.: +380 (50) 549 78 47
E-mail: h.astsaturov@gmail.com
Astsaturov Gennadiy
Candidate of Medical Sciences (PhD), Associate Professor of the department of Dermatology and Venereology of Danylo Halytsky Lviv National Medical University
Address: str. Pekarska, 69, Lviv, Ukraine, 79010
Tel.: +380 (50) 549 78 47
E-mail: h.astsaturov@gmail.com

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