

CLINICAL RESULTS OF COMPLEX THERAPY OF PATIENTS WITH ACNE - RESIDENTS OF IODINE DEFICIENCY REGION

Yu.P. Karvatska, O.I. Denysenko

Bukovinian State Medical University, Chernivtsi, Ukraine

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E-mail:
karvatska.iuliia@bsmu.edu.ua

The aim of research – the clinical results of complex therapy in patients with acne vulgaris - residents of the iodine deficiency region should be determined and analyzed considering the state of their pituitary-thyroid system, intestinal microbiota and immunological parameters.

Material and methods. The study involved 109 patients with moderate to severe acne vulgaris, who are the residents of Chernivtsi region - a region with natural iodine deficiency. Examination of the patients revealed changes in the pituitary-thyroid system, immunological parameters and intestinal biocenosis, which corresponded to the severity of dermatosis. During treatment, patients were divided into 3 groups: I comparative - 36 people who received conventional acne therapies and medicines to normalize thyroid homeostasis; group II comparative - 36 patients who were additionally prescribed probiotics, and III (main) - 37 persons who received complex treatment with the additional administration of probiotics and immunotropic drug. The effectiveness of treatment of patients was evaluated by their earliest and long-term clinical results using statistical analysis methods.

Results. It has been established that complex therapy of patients with moderate and severe acne vulgaris - residents of the iodine deficiency region with the administration alongside with the conventional acne therapy of medicines that normalize detected changes in the pituitary-thyroid system, immunotropic drug glucosaminylmuramyl dipeptide (licopid) and probiotic (laciium) reliably reduces ($p < 0.01$) in comparison with conventional acne therapy or conventional acne therapy with additional probiotics administration the terms of regress of acute inflammatory elements of acne with the achievement of the state of clinical remission of dermatosis, (respectively: by 1,54 and 1,41 times). The frequency of exacerbations acne process of patients with moderate and severe acne vulgaris during the year were also reduced (respectively: 1.59 and 1.26 times) relatively to patients in the comparison groups.

Conclusion. The complex therapy of patients with moderate to severe acne - residents of the iodine deficiency region with administration of medicines to normalize thyroid homeostasis, immunotropic drug glucosaminylmuramyl dipeptide (licopid) and probiotic (laciium) reliable improves the earliest and long-term clinical results of their treatment in comparison with conventional treatment or treatment using only the probiotic additional prescription.

Ключові слова:*вугрова хвороба, йододефіцитний регіон, комплексне лікування, клінічні результати.*

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КЛІНІЧНІ РЕЗУЛЬТАТИ КОМПЛЕКСНОГО ЛІКУВАННЯ ХВОРИХ НА ВУГРОВУ ХВОРОБУ – ЖИТЕЛІВ ЙОДОДЕФІЦИТНОГО РЕГІОНУ

Ю.П. Карвацька, О.І. Денисенко

Мета роботи – проаналізувати клінічні результати комплексного лікування хворих на вугрову хворобу – мешканців йододефіцитного регіону з урахуванням стану їх гіпофізарно-тиреοїдної системи, імунологічних показників та кишкового біоценозу.

Матеріал та методи. Спостерігали 109 пацієнтів із вугровою хворобою (акне) середнього та важкого ступеня тяжкості, які є жителями Чернівецької області – регіону з природним йододефіцитом. При обстеженні пацієнтів встановлено зміни показників гіпофізарно-тиреοїдної системи, імунологічних показників та кишкового біоценозу, які відповідали ступеню тяжкості дерматозу. Під час лікування пацієнти були розподілені на 3 групи: I порівняльна – 36 осіб, які отримали стандартне лікування акне та препарати для нормалізації тиреοїдного гомеостазу; II порівняльна – 36 пацієнтів, яким додатково призначали пробіотик, та III основна – 37 осіб, які отримали комплексне лікування із включенням пробіотика та імунотропного препарату. Ефективність лікування пацієнтів оцінювали за їх найближчими та віддаленими клінічними результатами із застосуванням методів статистичного аналізу.

Результати. Встановлено, що комплексне лікування хворих на вугрову хворобу

середнього та важкого ступеня тяжкості – жителів йододіфіцитного регіону із призначенням на тлі стандартної терапії засобів для нормалізації виявлених змін гіпофізарно-тиреїдної системи, імунотропного препарату глюкозамінілмураміддипептиду (лікопід) та пробіотика (лаціум) вірогідно ($p < 0,01$) скорочує порівняно зі стандартною терапією чи стандартною із додатковим призначенням лише пробіотика терміни регресу гострозапальних елементів вузрової висипки з досягненням стану клінічної ремісії дерматозу (відповідно: в 1,54 та 1,41 раз), а також зменшує частоту загострень вузрової хвороби впродовж року відносно пацієнтів груп порівняння (відповідно: в 1,59 і 1,26 раз).

Висновок. Застосування хворим на вузрову хворобу середнього та важкого ступеня тяжкості – жителям йододіфіцитного регіону комплексної терапії з призначенням препаратів для нормалізації виявлених змін тиреоїдного гомеостазу, імунотропного препарату глюкозамінілмураміддипептиду (лікопід) та пробіотика (лаціум) вірогідно покращує найближчі та віддалені клінічні результати їх лікування порівняно зі стандартною терапією чи додатковим призначенням лише пробіотика.

КЛИНИЧЕСКИЕ РЕЗУЛЬТАТЫ КОМПЛЕКСНОГО ЛЕЧЕНИЯ БОЛЬНЫХ УГРЕВОЙ БОЛЕЗНЬЮ – ЖИТЕЛЕЙ ЙОДОДЕФИЦИТНОГО РЕГИОНА

Ю.П. Карвацкая, О.И. Денисенко

Цель работы – проанализировать клинические результаты комплексного лечения больных угревой болезнью – жителей йододіфіцитного регіону с учетом состояния их гипотиреоидной системы, иммунологических показателей и кишечного биоценоза.

Материалы и методы. Наблюдали 109 пациентов с угревой болезнью (акне) средней и тяжелой степени тяжести, жителей Черновицкой области – региона с естественным йододіфіцитом. При обследовании пациентов установлены изменения показателей гипотиреоидной системы, иммунологических показателей и кишечного биоценоза, которые были сопоставимы со степенью тяжести дерматоза. Во время лечения пациенты были распределены на 3 группы: I сравнительная – 36 пациентов, получивших стандартное лечение акне и препараты для нормализации тиреоидного гомеостазу; II сравнительная – 36 пациентов, которым дополнительно назначали пробиотик, и III основная – 37 пациентов, которые получили комплексное лечение с включением пробиотика и иммунотропного препарата. Эффективность лечения пациентов оценивали по их ближайшим и отдаленным клиническим результатам с использованием методов статистического анализа.

Результаты. Установлено, что комплексное лечение больных угревой болезнью средней и тяжелой степени тяжести – жителей йододіфіцитного регіону с назначением на фоне стандартной терапии средств для нормализации выявленных изменений гипотиреоидной системы, иммунотропного препарата глюкозамінілмураміддипептида (лікопід) и пробиотика (лаціум) достоверно ($p < 0,01$) сокращает по сравнению со стандартной терапией или стандартной с дополнительным назначением только пробиотика сроки регресса островоспалительных элементов угревой сыпи с достижением состояния клинической ремиссии дерматоза (соответственно: в 1,54 и 1,41 раз), а также уменьшает частоту обострений угревой болезни в течение года относительно пациентов групп сравнения (соответственно: в 1,59 и 1,26 раз).

Вывод. Использование больными угревой болезнью средней и тяжелой степени – жителями йододіфіцитного регіону комплексной терапии с назначением препаратов для нормализации выявленных изменений тиреоидного гомеостазу, иммунотропного препарата глюкозамінілмураміддипептида (лікопід) и пробиотика (лаціум) достоверно улучшает ближайшие и отдаленные клинические результаты их лечения по сравнению со стандартной терапией или дополнительным назначением только пробиотика.

Ключевые слова:

угревая болезнь, йододіфіцитный регион, комплексное лечение, клинические результаты.

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Acne vulgaris, also known as acne, remains the most common inflammatory skin conditions treated worldwide [1]. Acne typically affects adolescents at a time when they are undergoing maximum physical and

social transitions, although prevalence studies suggest it is starting earlier and lasting longer, particularly in female patients [2].

The location of rash on exposed skin, frequent

formation of persistent scarring of the skin (post-acne marks) cause a negative impact on the psycho-emotional state of patients and is the cause of reduced quality of life and social activity [3, 4].

Acne is a chronic multifactorial disease of the sebaceous glands, which is based on sebum hyperproduction, pathological desquamation and inflammation of sebaceous follicles due to activation of skin microorganisms (*Propionibacterium acnes*, *Staphylococcus*, etc.), which is facilitated by exogenous triggers, genetic predisposition, endocrine and immune disorders, metabolic disorders, etc. [5-7].

Optimization of acne vulgaris treatment is an urgent problem of modern dermatology at the present stage due to the high prevalence of this dermatosis and the tendency to its more severe clinical course with frequent prolonged relapses, torpid to conventional acne therapy [8, 9].

As established by modern research, changes in the pituitary-thyroid system play an important role in the development and course of chronic dermatoses, as thyroid hormones have a wide range of effects on metabolic processes, including skin [10]. Especially relevant is the detection and correction of changes in the pituitary-thyroid system in patients with acne vulgaris, living in regions with natural iodine deficiency at high risk of thyroid pathology, which includes Chernivtsi region - a biogeochemical region with natural iodine deficiency [11].

It has also been established that important pathogenetic factors of the aggravated clinical course of acne vulgaris are changes in the immune system and intestinal microbiota, which justifies the appointment of immunotropic and probiotic drugs in their complex therapy [9, 12].

The aim of the study

To determine and analyze the clinical results of a comprehensive method of treatment of patients with acne vulgaris - residents of the iodine deficiency region, taking into account the state of their pituitary-thyroid system, immunological parameters and intestinal biocenosis.

Material and methods

The study included 109 patients with acne vulgaris aged 18 to 25 years, of whom 58 (53.2%) were female and 51 (46.8%) were male, who are permanent residents of Chernivtsi region - a region with natural iodine deficiency. Moderate stage of acne vulgaris was diagnosed in 83 (76.1%) patients while 26 (23.9%) patients had severe stage of skin process. In all patients the dermatosis had a chronic persistent course, in most (65.8%) patients the duration of acne vulgaris was more than 3 years, of which every second patient (50.7%) had frequent (3-4 times a year) recurrences of dermatosis.

Examination of patients with acne vulgaris - residents of the iodine deficiency region revealed changes in the pituitary-thyroid system, immunological parameters and intestinal biocenosis, which corresponded to the severity of dermatosis, which justify correction of thyroid homeostasis, administration of immunotropic drugs and

probiotics [13, 14]. All patients with acne vulgaris with changes in the thyroid function were consulted by an endocrinologist, depending on the nature of changes in the thyroid function, they were prescribed differentiated treatment: in case of hypofunction - L-thyroxine (euthyrox), in case of hyperfunction - antithyroid drugs (mercazolyl, tyrosol) - iodine preparations and observation by a surgeon [14].

During treatment, patients were divided into 3 comparable groups: I comparative group - 36 patients who were prescribed conventional therapy and (according to indications) medicines to correct the detected changes in the pituitary-thyroid system; II comparative group includes 36 patients who alongside with the conventional acne therapy were prescribed medicines to correct the detected changes in the pituitary-thyroid system (according to indications) and additional use of probiotics (Iaciум - 1 sachet 2 times a day for 14 days) and III (main) group includes 37 patients who were prescribed complex treatment with combined and differentiated administration medicines to correct the detected changes in the pituitary-thyroid system (according to indications), cephalosporin antibacterial drugs, probiotics (Iaciум - 1 sachet 2 times a day for 14 days) and immunotropic drug (likopid - for moderate acne vulgaris - 2 mg twice a day for 10 days, for severe forms - 10 mg once a day 10 days).

Evaluation of the results of various methods of therapy of acne patients with moderate and severe clinical course was performed on the basis of analysis of the earliest and long-term results of their treatment.

Statistical processing of the research results was carried out by methods of statistical analysis using licensed programs "Microsoft Excel" and "Statistica", the difference between the averages at $p < 0.05$ was considered probable. Non-parametric Friedman analysis of variance with the definition of chi-square (χ^2) was used to assess the relationships between the indicators, and the relationship between the indicators was considered probable if the value of the chi-square (χ^2) exceeded the critical value [15].

Results and discussion

Evaluation of the results of various methods of treatment of patients with acne vulgaris - residents of the iodine deficiency region with moderate and severe clinical stages of the disease, who were prescribed conventional treatment and (according to indications) means to correct the detected changes in the pituitary-thyroid system (I comparative group), patients with additional use of probiotics (II comparative group) and patients which were prescribed complex therapy with combined administration of thyroid drugs (according to indications), probiotics and immunotropic drug (III comparative group) was done on the basis of the analysis of the earliest and long-term result of their treatment.

Indicators of the average duration of regression of acute inflammatory elements of acne elements in patients with acne vulgaris - residents of the iodine deficiency region with the use of different therapies are presented in table 1.

As can be seen from the data given in table 1, the

Table 1

The duration of regression of acute inflammatory elements of acne patients – residents of the iodine deficiency region, provided different therapies

Indexes	Patients with acne (n=109)		
	I group (n ₁ =36)	II group (n ₂ =36)	III group (n ₃ =37)
The average duration of regression of acute inflammatory elements of acne (days)	29,5±0,46	26,9±0,34 p ₁₋₂ <0,001	19,1±0,36 p ₁₋₃ <0,001 p ₂₋₃ <0,001

Note: p - is the probability of the difference in patients in different groups.

treatment of acne patients with administration alongside the conventional therapy medicines to normalize thyroid homeostasis (according to indications) and probiotic (Iacium); (II comparative group) compared with patients which were prescribed the only conventional acne therapy appears to be more effective due to reliable reduction of regression terms of acute inflammatory elements on average to 26,9±0,34 days compared with patients treated by the standard method (29,5±0,46 days, p<0,001).

At the same time, the use of complex therapy with combined and differentiated administration of thyroid drugs (according to indications), cephalosporin antibacterial medicines, probiotics (Iacium); and immunotropic drug (Ikipid) (III - the main group) appears the most frequent regression of acute inflammatory acne elements that courses reliable (p<0,001) reduction of treatment term of these patients 19,1±0,36 days.

Thus, a comparative analysis of the earliest clinical results of the different therapy methods in patients with acne vulgaris showed that the best results were in patients of the main group.

The consequences of different methods of treatment of patients with acne vulgaris were also assessed by the percentage reduction in the number of rash elements on the skin: the state of clinical recovery was determined in case of complete resolution or reduction of the rash by more than 76%, significant improvement - reduction of the rash by 50% - 75%, improvement - reduction of the amount of rash to 50%, without clinical effect - while maintaining the same amount of rash, deterioration - increase in the number of rash elements on the skin. Clinical results of different methods of treatment of patients with acne vulgaris - residents of the iodine deficiency region, determined three months after the start of their treatment, are presented in table 2.

Table 2

Clinical results of various methods of treatment of acne patients – residents of the iodine deficiency region

Indexes	Patients with acne (n=109)					
	I group, (n ₁ =36)		II group, (n ₂ =36)		III group, (n ₃ =37)	
	Absolute numbers	%	Absolute numbers	%	Absolute numbers	%
Clinical recovery	9	25,0	13	36,1	19	51,4
Significant improvement	11	30,6	10	27,8	12	32,4
Improvements	14	38,9	12	33,3	6	16,2
Unchanged	2	5,5	1	2,8	-	-
Deterioration	-	-	-	-	-	-
Total	36	100,0	36	100,0	37	100,0

As can be seen from the data in table 2, the use of conventional and thyrotropic treatment in patients with acne vulgaris caused clinical recovery in only 1/4 (25.0%) of patients, a significant improvement occurred - in 1/3 (30.6%) of improvement - more than 1/3 (38.9%) of patients and 2 patients treatment did not give a positive effect. It has been also found that the use of conventional and thyrotropic (according to the indications) treatment

and probiotic (Iacium) (II comparative group) improves the clinical outcome of treatment of acne patients from iodine deficiency region. Similar indicators in this group of patients were respectively: 36.1%, 27.8%, 33.3% and 2.8%.

At the same time, the best results of acne vulgaris treatment were found in patients of the main group due to the use of a complex therapy with combined and

differentiated administration of means for correction thyroid homeostasis (according to indications), cephalosporin antibacterial medicine, probiotic (laciум) and immunotropic drug (likopid): clinical recovery more than half of patients (51.4%) and significant improvement - in 32.4%, which was a total of 83.8%, and improvement - only in 16.2% of patients in this group. No cases of deterioration were reported in any of the groups of patients with acne under treatment.

The results of the study of long-term outcome of treatment of acne patients - residents of the iodine deficiency region with moderate and severe clinical course of dermatosis, who were prescribed different

therapies of dermatosis are presented in table 3.

According to the clinical results, the prescription of only conventional therapy of acne patients (I comparative group) from iodine deficiency region with moderate and severe clinical dermatosis did not lead to significant changes in the long-term outcome of their treatment (table 3). At the same time, the prescription alongside the conventional treatment the means to correct thyroid homeostasis (according to the indications) and probiotic (laciум) (II comparative group) appears to be more effective and lead to reliable prolongation of dermatosis remission (on average 1.47 times, $p=0.004$) with only a tendency to decrease relapses (1.11 times, $p=0.096$).

Table 3

Comparative data of long-term results of different therapies of acne patients – residents of the iodine deficiency region

Indexes	Patients with acne (n=109)					
	I group (n ₁ =36)		II group (n ₂ =36)		III group (n ₃ =37)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Duration of remission (months)	3,08±0,11	2,91±0,12	3,03±0,13 $p_{1-2}=0,77$	2,72±0,13 $p_{1-2}=0,29$	2,92±0,16 $p_{1-3}=0,42$ $p_{2-3}=0,59$	1,76±0,09 $p_{1-3}<0,001$ $p_{2-3}<0,001$
	P=0,30		P=0,096		p<0,001	
Number of exacerbations per year (cases)	2,75±0,21	3,01±0,19	2,81±0,25 $p_{1-2}=0,85$	4,13±0,37 $p_{1-2}=0,009$	2,97±0,33 $p_{1-3}=0,58$ $p_{2-3}=0,70$	5,70±0,43 $p_{1-3}<0,001$ $p_{2-3}=0,005$
	P=0,036		P=0,004		p<0,001	

At the same time, the best long-term results of therapy were noted in patients of the main group, who received alongside the conventional treatment with combined and differentiated use of means to correct thyroid homeostasis (according to indications), cephalosporin antibacterial drug, immunotropic drug (likopid) and probiotic (laciум). This therapy lead to reliable prolongation of clinical remission of dermatosis (on average 1.92 times, $p<0.001$), which also made a significant difference with a similar indexes in patients of I and II comparative groups (increase, respectively: 1.89 times, $p<0.001$ and 1.38 times, $p=0.005$), as well as a decrease in the number of relapses (1.66 times, $p<0.001$) with a reliable difference with a similar rate in patients of I and II comparative groups (decrease, respectively: 1.54 times and 1.41 times, $p<0.001$).

It has been also established by the method of odds ratio (OR), that the developed comprehensive treatment of patients with acne vulgaris from iodine deficiency region with moderate and severe clinical stage of dermatosis reduces the risk of exacerbations of acne during the year by 1.57 times compared with patients of I comparative group - OR = 1.57 (95% CI 0.13-18.40) and 1.49 times relative to the II comparative group - OR = 1.49 (95% CI 0.12-17.89).

Conclusion

The complex therapy of patients with moderate to severe acne - residents of the iodine deficiency region with administration of medicines to normalize thyroid homeostasis, immunotropic drug glucosaminylmuramyl dipeptide (licopid) and probiotic (laciум) reliable improve the earliest and long-term clinical results of their treatment in comparison with conventional treatment or treatment with only the probiotic additional prescription.

Prospects for further research

The perspective is to study the long-term dynamics of the pituitary-thyroid system and immunological parameters, intestinal biocenosis in patients with acne - residents of the iodine deficiency region due to the use of complex therapy with drugs to normalize the detected changes in thyroid homeostasis, immunotropic drug glucosaminylmuramyl dipeptide (licopid) and probiotic (laciум).

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Відомості про авторів:

Карвацька Ю.П. – к.мед.н., доцент кафедри дерматовенерології, Буковинський державний медичний університет, м. Чернівці, Україна.

Денисенко О.І. – д.мед.н., професор, завідувачка кафедри дерматовенерології, Буковинський державний медичний університет, м. Чернівці, Україна.

Сведения об авторах:

Карвацкая Ю.П. – к.мед.н., доцент кафедры дерматовенерологии, Буковинский государственный медицинский университет, г. Черновцы, Украина.

Денисенко О.И. – д.мед.н., профессор, заведующая кафедрой дерматовенерологии, Буковинский государственный медицинский университет, г. Черновцы, Украина.

Information about authors:

Karvatska Yuliia P. – Candidate of Medical Sciences, Associate Professor of the Department of Dermatovenereology, Bukovinian State Medical University, Chernivtsi, Ukraine.

Denysenko Olga I. - Doctor of Medicine, Professor, Head of the Department of Dermatovenereology, Bukovinian State Medical University, Chernivtsi, Ukraine.

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Рецензент – проф. Пашковська Н.В.

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