

## THE PHARMA INNOVATION - JOURNAL

# The Modern Aspects of Acne Rosacea Treatment by Immunotropic Medications

Nataliya Senyshyn <sup>1\*</sup>

1. Department of Dermatology of Ivano-Frankivsk National Medical University Ivano-Frankivsk, Ukraine  
[E-mail: [nata\\_if@mail.ru](mailto:nata_if@mail.ru)]

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Acne Rosacea is a topical problems of modern dermatology. Dermatitis characterized by chronically and progressive course and refractory to therapy occurs most frequently in women aged 30 to 50 years, mostly with fair skin. Treatment of Rosacea is the complex problem and characterized by a variety of pathogenic approach. 120 patients with Acne Rosacea were observed in our investigation. Additional using of immunomodulatory medication Polyoxidonium helps to restore the changed parameters of the immune status of patients with Rosacea. The positive dynamics of key indicators of cellular and humoral immune system, activated lymphocytes, imbalance of various fractions of CIC under the influence of the proposed complex treatment (basic therapy + Polyoxidonium) is accompanied by the onset of clinical and immunological remission in patients with Acne Rosacea and is a testament to the role of the above components of the immune system in the genesis of target organ damage - the skin and the formation of complications

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*Keyword:* Acne Rosacea, Treatment, Immunity, Polyoxidonium.

### 1. Introduction

At present time, acne rosacea is a topical problems of modern dermatology. Dermatitis characterized by chronically and progressive course and refractory to therapy occurs most frequently in women aged 30 to 50 years, mostly with fair skin<sup>[1,2]</sup>.

Treatment of Rosacea is the complex problem and characterized by a variety of pathogenic approach<sup>[1]</sup>. Particular difficulties arise in the treatment of pustular and papules form of acne rosacea. Traditionally, in this case prescribe metronidazole and tetracycline antibiotics<sup>[2]</sup>. Over the past years has been increasingly noted cases of failures in the treatment of acne rosacea by traditional means. The effectiveness of metronidazole is inadequate and does not always correspond to the expected results; in addition, it caused of severe hepatotoxicity, and in some

cases has the absolute contraindications. It is possible that treatment failure may be associated with emergence of resistant bacterial and parasitic flora to traditional medications<sup>[2]</sup>. This necessitates the search for more effective treatments of acne rosacea.

**2. The Aim of Study:** is investigation of the clinical and immunological efficacy treatment of rosacea by using of combination therapy with antiparasitic drugs "Ornidazole", "Spregal" and 4% permethrin ointments and immunomodulator "Polyoxidonium"

### 3. Materials and Methods:

We examined 120 people with rosacea and 30 healthy individuals (control group), the representativeness of the sample was determined by specific formulas based disparities in for full

statistically plausible scientific results. Among the patients examined were 43 male individuals (36%) and 77 females (64%) aged 30 to 59 years. In this study included 88 patients with papular and pustular stage of acne rosacea. To evaluate the efficacy of treatment we investigated the immune status, which included the tests I and II levels as required by the Memorandum WHO<sup>[8]</sup>, quantify the major populations and subpopulations of lymphocytes, determination of activated subpopulations of lymphocytes CD54+, HLA-DR+, CD25+, CD95+, circulation immune complexes (CIC) concentration of different molecular weight. All patients with acne rosacea since admission to treatment (outpatient or inpatient) received comprehensive baseline therapy. Comprehensive treatment of rosacea appointed according to the standards of treatment of dermatological patients (orders MH of Ukraine № 286 from 07.06.2004) and included: anti-parasitic drugs ("Ornidazole") treatment of

concomitant pathology of the gastrointestinal tract, desensitizing therapy, cardiovascular drugs and external treatment by "Spregal" and 4% permethrinum ointment. As Immunotropic drug used immunomodulator "Polyoxidonium" intramuscular - 6 mg a day (10 injections).

#### 4. Results and Discussion

Previous studies have found the presence in patients with rosacea abnormalities in cellular and humoral immunity, phagocytic activity of neutrophils, the presence of an imbalance among the different molecular weight fractions of CIC towards the predominance of highly, probable changes in the level of cytokines in the direction of the advantages of proinflammatory activity<sup>[3]</sup>. This condition may lack clinical efficacy of the applied treatment involves complex and feasibility of use in the treatment of this dermatosis by immunomodulating drug.

**Table 1:** The content of main and activated populations and subpopulations of lymphocytes in patients with Rosacea with papules and pustular stage (M±m)

Indication	Before treatment	After treatment		Control group (n=30)
		Without Polyoxidonium (n=44)	With Polyoxidonium (n=44)	
CD 3 <sup>+</sup> cells, %	54,45±0,65	57,65±0,75* ××	61,24±0,38* ××	59,70±0,43
CD 4 <sup>+</sup> cells, %	39,95±0,95	41,05±0,85	41,37±0,52	40,80±0,82
CD 8 <sup>+</sup> cells%	27,05±0,65	27,15±0,75	26,49±0,67	26,55±0,56
CD 4 <sup>+</sup> / CD 8 <sup>+</sup>	1,47±0,08	1,51±0,07*	1,56±0,08* ××	1,55±0,04
CD 19 <sup>+</sup> cells, %	10,65±0,41	11,37±0,46	12,98±0,59*	13,20±0,56
CD 16 <sup>+</sup> cells,%	17,62±0,35	17,49±0,28	17,93±0,28	17,80±0,86
CD 25 <sup>+</sup> cells,%	17,64±0,35	13,49±0,27*××	10,27±0,20* ××	8,80±0,19
HLA-DR <sup>+</sup> cells,%	22,18±0,43	15,61±0,30*××	13,76±0,25* ××	12,30±1,27
CD 95 <sup>+</sup> cells,%	12,43±0,26	6,32±0,07* ××	4,65±0,05* ××	3,04±0,02
CD 54 <sup>+</sup> cells,%	19,68±0,40	14,97±0,29*××	12,39±0,22* ××	11,07±1,65

Notes: 1. \* - P <0.05 - the difference in the first and second groups before and after treatment. 2. × - difference in treatment compared a control group; × × - the difference after treatment between groups I and II patients. 3. n - number of patients studied.

For immunotherapy was applied "Polyoxidonium" which has immunomodulatory effects, increases the body's resistance against various infectious diseases. The mechanism of action of this medication is a direct effect on phagocytic cells and natural killer cells, and stimulation of antibody production. Along with immunomodulatory effects the drug has severe detoxification activity and increases the stability

of cell membranes to cytotoxic agents. Polyoxidonium restores immune responses in severe forms of immunodeficiency<sup>[4]</sup>. Due to the molecules on the surface of a large number of active functional groups Polyoxidonium has the ability to absorb on the surface of circulating blood in various toxic substances, immune complexes, etc., and then withdraw from the body, increases the elimination of a variety of

bacterial pathogens. As a true immunomodulator, polyoxidonium corrects only the changed parameters of immunity, thus excluded hyperactivation of the immune system. It has a high clinical and immunological efficacy both as monotherapy and in combination with basic therapy.

The addition of Polyoxidonium in the basic treatment of Rosacea in patients with papules and pustular stage of disease (Table 1) contributed to increasing of population' content of CD 3 + cells to 12.47%, normalization of immunoregulatory subpopulations, immunoregulatory index and B-lymphocytes. The relative number of CD 16 + cells in the dynamics of treatment did not change significantly and remained within the meaning of healthy individuals. This is definitely a positive thing, because the stimulation of NK - cells would result the target organ damage with the development of vascular complications. In contrast, in patients with Acne Rosacea which were treated without Polyoxidonium we observed the weak effect on activated subpopulation of T- and B-lymphocytes, - the level of CD 25 + cells, CD 95 +, HLA-DR + and CD 54 + lymphocytes decreased in the dynamics of treatment not significant, and was higher than the control group data. In the group of patients treated with basic therapy and Polyoxidonium, the number of activated lymphocyte subpopulations with  $\alpha$ -

chain of IL-2 receptor decreased compared with data before treatment to 83.75% ( $p < 0.05$ ), exceeding the data controls 11.87 % ( $p > 0,1$ ). The level of HLA-DR + cells decreased for 68.46% ( $P < 0.05$ ); it was higher than in the normal rate for 11,87% ( $p > 0,1$ ). Similar were the content and dynamics of CD 95 + and CD 54 + lymphocytes. In the comparison group who did not receive immunotropic drug also was recorded dynamics of reduction in the number of activated cells, however, their degree was not enough. Thus, the reduction of T-lymphocytes, which are markers of early and late (T + B lymphocytes) activation was accompanied by the simultaneous characteristic of this regimen, reducing the number of CD 54 + cells, and thus not only reduced the number of activated lymphoid cells of peripheral blood but migrating lymphocytes through the endothelium of ICAM-1 in inflammation in the skin, which is particularly important and relevant in connection with presence of angiopathy in this condition. Immunotropic positive effect of the treatment regimen is expressed and activated in reducing the number of CD 95 + lymphocytes, due to decreased serum concentrations of TNF- $\alpha$  by anti-inflammatory, antibacterial, antiparasitic, antifungal and antioxidant action of Polyoxidonium. The additional prescription of Polyoxidonium had the positive effect for circulating immune complexes level (Table 2).

**Table 2:** The dynamics of concentration of circulating immune complexes during treatment

Indication	Before treatment	After treatment		Control group (n=30)
		Without Polyoxidonium (n=44)	With Polyoxidonium (n=44)	
CIC high-molecular., U	29,41±1,02	38,17±0,73* $\times\times$	47,20±1,20* $\times\times$	51,70 ± 3,12
CIC middle-molecular., U	58,10±1,45	50,43±1,20* $\times$	39,15±1,23* $\times\times$	34,54 ± 2,02
CIC, small-molecular., U	57,26±1,41	43,29±1,28* $\times$	26,45±0,94* $\times\times$	10,94 ± 1,13

Notes: 1. \* -  $P < 0.05$  - the difference in the first and second groups before and after treatment. 2.  $\times$  - difference in treatment compared a control group;  $\times\times$  - the difference after treatment between groups I and II patients. 3. n - number of patients studied

In patients, who received only basic therapy with ornidazole, after treatment (Table 2) we observed the elevated levels of pathogens medium and

small molecular CIC, which exceeded normal ranges for 46.0% and 295.7%, and of reducing high molecular complexes for 26.17%, which is

evidence of the presence of autoimmune reactions in patients with Acne Rosacea. Additional using for basic therapy of Polyoxidonium led to normalization of CIC large sedimentation constant of  $>19S$  for 60,49% ( $p < 0,05$ ). Along with increasing concentrations of CIC large a decrease in the concentration of pathogenic CIC medium and small size of the sedimentation constant 11-19S and  $<11S$ , accompanied imbalance in different size fractions of CIC. Thus, the content of pathogenic medium size CIC decreased for 48.40% ( $P < 0.05$ ), and the small size of CIC – for 116.48% ( $p < 0,01$ ).

### 5. Conclusion

Thus, our investigation showed the high efficacy of Polyoxidonium, which helps to restore the changed parameters of the immune status of patients with Rosacea. The positive dynamics of key indicators of cellular and humoral immune system, activated lymphocytes, imbalance of various fractions of CIC under the influence of the proposed complex treatment (basic therapy + Polyoxidonium) is accompanied by the onset of clinical and immunological remission in patients with Acne Rosacea and is a testament to the role of the above components of the immune system in the genesis of target organ damage - the skin and the formation of complications.

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