



Psychophysiological parameters in rosacea patients after complex therapy with Cortexin

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Abstract

Introduction: Taking into account the influence of the psycho-emotional sphere and its disorders on the pathogenetic mechanisms of rosacea, a comparative assessment of the clinical efficacy of a standard therapy and the complex therapy using Cortexin in papulopustular rosacea patients with moderate severity and concomitant neurological pathology was performed. The therapy influence on changes in the patients' psycho-emotional state was also studied.

Materials and methods: The study involved 216 papulopustular rosacea outpatients with moderate severity with a concomitant neurological pathology, aged 20 to 60 years. The patients were divided into 2 groups: 109 people (37 men and 72 women) in the study group, and 107 people (37 men and 70 women) in the control. All the patients received a treatment according to the "Standard of Medical Care for Patients with Rosacea" of the Ministry of Health of the Russian Federation. The study group patients additionally received Cortexin. The study was carried out using the Zung Self-Rating Anxiety Scale (SAS), the Taylor Manifest Anxiety Scale, the Spielberger State-Trait Anxiety Inventory, and the Eysenck Personality Questionnaire.

Results and discussion: The patients showed an increase in somatic manifestations of anxiety, levels of trait and state anxiety, and neuroticism initially before the start of treatment. The inclusion of Cortexin in the rosacea treatment reduced the somatic manifestations of anxiety more effectively than standard therapy against the background of a more considerable decrease in proportion of patients with its moderate and high levels. The severity of trait and state anxiety, neuroticism was also significantly lower against the background of the Cortexin use than with the standard treatment.

Conclusion: The Cortexin inclusion in the rosacea pharmacotherapy against the background of a concomitant neurological pathology contributes to a more pronounced correction of psychophysiological parameters, reflecting the neuroticism levels, trait and state anxiety, and somatic manifestations of anxiety, compared to standard treatment.

Keywords

rosacea, psycho-emotional state, Cortexin.

Introduction

Rosacea belongs to psychodermatological disorders (Jafferany 2007), in the genesis of which psychogenic factors play a key role. This disease has the largest proportion

(36%) in the structure of acne-like dermatoses (Wilkin et al 2002; Yutskovskaya et al. 2010; Jansen 2011). Rosacea accounts for about 5% of all dermatologic diagnoses in the Russian Federation. However, according to Russian cosmetologists, its proportion reaches 20.6%.

The pathogenesis of rosacea is multifactorial. One of the key links in the mechanisms of rosacea development is the progression of a local angioneurosis (Mimov et al. 2013; Oge et al. 2015), associated with impaired functioning of peripheral nerve endings. In addition, chronic dermatoses can cause significant mental disorders in patients.

According to the concept of "psychodermatology", rosacea belongs to a group of pathologies with predominance of psychosomatic disorders as a result of the personality's reaction to a chronic recurrent disease (Šitum et al. 2016; Sharshunova et al. 2017). The development of mental and vegetative changes, therapy resistance, and communicating discomfort limit social contacts and significantly affects the quality of patients' life. Wherein, psycho-emotional disorders are considered as the leading factor to reduce performance, social and physical activities, and they may be the most significant motivation for seeking medical care (Dalgard et al. 2015; Troitsky 2016).

The use of drugs for the correction of neurons functional state seems appropriate in the complex treatment of rosacea patients, because psychological stress with the further development of anxiety and depression can be an important etiopathogenetic factor in the occurrence of this pathology. Pharmacological leveling of the psychological sphere dysfunction corrects the psycho-emotional state, improves the general somatic state and shortens the treatment time. At the same time, there are no literature data on a complex study of the relationship between the psychophysiological indicators of character and temperament in rosacea patients, including those with a concomitant neurological pathology.

The aim of the study

To investigate the effect of complex therapy with Cortexin on the relationship between characterological and temperamental manifestations of anxiety in rosacea patients.

Materials and methods

The study was performed with the participation of 216 outpatients, aged from 20 to 60 years, which were divided into 2 groups: 109 people (37 men and 72 women) in the study group, 107 people (37 men and 70 women) in the control group. The control group consisted of the papulopustular rosacea patients with moderate severity with a concomitant neurological pathology (encephalopathy of various origins, cognitive impairment, and asthenia) in the absence of data on the Cortexin use. The study group included the patients

with a concomitant neurological pathology, who were prescribed Cortexin on the basis of a neurologist's consultation.

For a comparative assessment of a number of indicators, a group of healthy individuals participated in the study: 41 people (24 women, 17 men), aged from 18 to 65 years, without concomitant somatic and dermatological pathology.

The study was carried out under the supervision of the Regional Ethics Committee Kursk State Medical University of the Ministry of Health of Russia (Minutes No. 3 of March 16, 2020).

The patients of both study groups received treatment according to the "Standard of Medical Care for Patients with Rosacea" of the Ministry of Health of the Russian Federation: Ornidazole (1g × 2 times a day for 10 days) and Ascorutin (0.1g × 3 times a day for 21 days). The patients also applied Metrogyl Gel (2 times a day for 28 days) to the skin. The study group patients additionally received Cortexin (GEROPHARM LLC, Russia) at a dose of 10 mg intramuscularly No. 10.

The study was performed using psychological tests before and after patients' treatment. Somatic manifestations of anxiety were assessed using the Zung Self-Rating Anxiety Scale (SAS). The level of trait anxiety, independent of a specific situation, was determined using the MAS scale (Taylor's Manifest Anxiety Scale). The level of anxiety at the examination time was studied by the state anxiety scale – Spielberger's State-Trait Anxiety Inventory (STAI). The levels of extraversion, introversion, and neuroticism were determined in patients using the Eysenck's Personality Questionnaire.

The obtained data was processed on a personal computer using the IBM Statistical Package for the Social Sciences Base ver. 22, taking into account the significance of the distribution-free tests and the significance of normal and intermediate tests. Significance of differences was assessed using paired and unpaired Student's t-test, Z-test with Yates's continuity correction and Fisher's exact test. Differences were considered statistically significant at $p < 0.05$.

Results and discussion

The levels of somatic manifestations of anxiety were equal, with a predominance of patients with low or moderate levels of anxiety in both groups before treatment (Table 1).

At the end of the standard treatment, the number of patients with a low anxiety level increased 2.6 times ($p < 0.05$), and their proportion in this group was 45%. The proportion of patients with a moderate anxiety level

Table 1. Indicators of Somatic Manifestations of Anxiety in Patients with Rosacea.

Groups	Before treatment						After treatment					
	Low anxiety level		Moderate anxiety level		High anxiety level		Low anxiety level		Moderate anxiety level		High anxiety level	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Standard treatment (n=107)	18	17	47	44	42	39	49	45*	40	37	18	18*
Complex treatment with Cortexin (n=109)	18	17	48	44	43	39	85	78*	18	16 ^{1*}	6	6 ^{1*}

Note: * – $p < 0.05-0.01$ compared to the indicators of the group before treatment, ¹ – $p < 0.05-0.01$ compared to the indicators of patients who received standard treatment.

decreased by 15% and did not achieve significant differences compared to their number before treatment. A significant decrease (2.2 times, $p < 0.05$) was registered in the proportion of patients who rated their condition as highly anxious.

Complex therapy with Cortexin had a more pronounced corrective effect on the somatic manifestations of anxiety. The number of patients with a low anxiety level increased 4.7 times ($p < 0.01$) and their proportion in the group was 85% in comparison with the before-treatment state. Wherein, there was a significantly considerable decrease in the number of patients with a moderate (2.8 times, $p < 0.05$) and high (6.5 times, $p < 0.01$) anxiety levels. The proportions of patients with medium and high anxiety levels were significantly less (2.3 and 3 times, respectively, $p < 0.05$) after complex therapy with Cortexin in comparison with the patients who had received standard treatment. At the same time, the proportion of patients with a low level of somatic manifestations of anxiety was also greater than that after standard treatment (1.7 times), but those differences were not significant. Consequently, at the end of the standard treatment, there was an increase in the number of patients with a low level of physiological discomfort caused by anxiety against the background of a decrease in the number of highly anxious patients as well as a slight decrease in the proportion of patients with moderate levels. The inclusion of Cortexin in the treatment of rosacea more effectively reduces physical discomfort caused by anxiety, primarily because of a more significant decrease in the proportion of patients with its medium and high levels than with standard treatment.

In order to explain the development mechanisms of anxiety manifestations identified in rosacea patients using the SAS, studies of trait and state anxiety were performed.

The level of trait anxiety, which does not depend on a specific situation, in rosacea patients before treatment was 2.6 times higher ($p < 0.01$) compared with healthy subjects according to the results of the Taylor's test (Table 2). Anxiety levels were the same in both groups of patients before treatment. There was a decrease in this indicator by 33% ($p < 0.01$) at the end of the standard treatment, and the decrease reached 67% ($p < 0.01$) after complex therapy with Cortexin. This circumstance caused a significantly lower level of trait anxiety at the end of treatment (2 times, $p < 0.01$) in patients after treatment with Cortexin in comparison with standard one. These results are consistent with the data obtained when assessing the somatic anxiety manifestations of using the SAS scale.

The level of state anxiety in the groups of rosacea patients before treatment was 2 times ($p < 0.01$) higher than that of healthy subjects. There was a decrease in the severity of this type of anxiety by 18% at the end of the standard treatment, which did not achieve significant differences in comparison with the indicators in this group before the start of treatment ($p > 0.05$). In patients who received complex treatment with Cortexin, the decrease in state anxiety was significantly more pronounced (by 29%, $p < 0.05$) at the end of therapy. At the same

Table 2. Changes in Indicators of the Psycho-emotional Sphere in Rosacea Patients ($M \pm m$).

Indicator	Healthy subjects	Standard treatment		Complex treatment with Cortexin	
		Before treatment	After treatment	Before treatment	After treatment
Extraversion	11.71±1.26	9.26±0.93	11.08±0.93	9.22±1.24	11.44±0.21
Introversion	9.48±0.84	16.19±1.78 ²	14.01±0.84	15.24±1.81 ²	14.82±1.13
Neuroticism	9.91±0.81	24.26±2.39 ²	16.58±1.19 ²	24.38±2.32 ²	9.96±1.26 ^{*1}
Trait anxiety	16.32±0.45	41.96±2.32 ²	28.30±1.40 ²	42.12±2.23 ²	14.02±1.31 ^{*1}
State anxiety	25.61±0.28	52.46±1.39 ²	43.03±1.53	52.31±0.43 ²	37.12±1.51 ^{*1}

Note: * – $p < 0.05-0.01$ compared to the indicators of the group before treatment, ¹ – $p < 0.05-0.01$ compared to the indicators of patients who received standard treatment, ² – $p < 0.05-0.01$ compared to the indicators of the healthy subjects.

time, in this group of patients at the end of treatment, the level of anxiety was also significantly lower in comparison with the indicators of patients after standard therapy (by 13%, $p < 0.05$).

Consequently, the reduction in the initially elevated level of state anxiety in rosacea patients with standard treatment does not reach statistically significant values. At the same time, complex therapy with Cortexin has a more pronounced effect on the reduction of this psychophysiological indicator, contributing to the achievement of significantly lower levels. So the patients become more balanced in specific situations of interaction with external factors.

Along with the study of anxiety levels in rosacea patients, we performed an investigation of some psychophysiological characteristics of temperament using the Eysenck's test. It was found that the indicators of extraversion in both clinical groups before treatment did not differ significantly from those in healthy individuals. There were no significant differences either between the two clinical groups in this case. The level of extraversion did not change significantly at the end of both standard and complex treatment with Cortexin. At the same time, introversion was significantly more pronounced before the start of treatment in clinical groups in comparison with healthy individuals: in the group receiving standard treatment – by 70% ($p < 0.05$), and in the group receiving therapy with Cortexin – by 71% ($p < 0.05$). However, this indicator, as well as extraversion, did not change significantly at the end of treatment in both groups.

The data obtained indicate that patients with rosacea are characterized by an increase in the index of introversion (isolation, lack of communication, preference for solitude, individualism). The absence of significant shifts in the levels of extraversion and introversion after treatment is consistent with the existing ideas about the consistency of temperament properties, the characteristics of which are these indicators.

However, at the same time, there were quite pronounced changes in the personality psychophysiological indicator – neuroticism. Its level in both groups of patients before treatment exceeded the values of healthy subjects by an average of 145% ($p < 0.01$). This fact suggests an increased level of neuroticism is a temperament property predisposing to rosacea development.

In contrast to extraversion and introversion, there was a significant change in this personality indicator in both groups at the end of treatment. So, its values decreased by 32% ($p < 0.05$) after standard treatment, and the decrease was even more pronounced at the end of complex therapy with Cortexin, amounting to 59% ($p < 0.01$). Also, significant differences were registered between the levels of neuroticism in these two groups: its level in the group was by 40% lower ($p < 0.05$) after treatment with Cortexin. The data on the nature of changes in the levels of neuroticism in rosacea patients we received indicate that these patients have a higher level of lability and reactivity of the nervous system in comparison with healthy subjects. A decrease in neuroticism parameters after standard treatment indicates the normalization of nervous processes and, as a consequence, personality psychophysiological parameters, the change in which occurred due to rosacea manifestation. A more significant decrease in neuroticism while taking Cortexin reflects the effect of the drug on neuroticism initial level, this level being due not to the effect of the disease, but to the basic characteristics of temperament in the period even before the development of rosacea. Considering the fact that neuroticism is the temperamental basis for anxiety manifestation, a change in neuroticism at the initial level could cause a more pronounced correction of anxiety after treatment with Cortexin.

Thus, according to the results of the study, we have established a pronounced change in anxiety in rosacea patients after complex treatment with Cortexin. In particular, there was a reduction in the somatic manifestations of anxiety, primarily due to a more significant, than with standard treatment, decrease in the proportion of patients with its medium and high levels.

Taking into account the important role of anxiety state for psycho-emotional stress development, which is the most important rosacea trigger (Olisova et al. 2012; Coda et al. 2013; Sorokina and Korsunskaya 2013; Potekaev et al. 2016), we also studied trait and state anxieties along with the self-assessment of physical discomfort from anxiety in order to increase the objectivity of the data obtained. The initially established increased level of trait anxiety in rosacea patients indicates a high degree of psycho-emotional stress, and it is consistent with the literature data (Khairutdinov 2014; Liu et al. 2014). Trait anxiety decreased more significantly after complex therapy with Cortexin, which indicates an increase in the effectiveness of rosacea treatment with using this drug.

The level of situation-dependent state anxiety was also significantly increased in rosacea patients before treatment, and therapy with Cortexin caused its significant decrease, i.e. it increased emotional balance. However, the degree of state anxiety reduction was significantly lower than that of anxiety, which may be a consequence of the psychophysiological nature of this character trait.

The results obtained in the study of temperament individual properties, using the Eysenck's test, indicate their relatively low variability. Introversion was more pronounced in rosacea patients in comparison with healthy

individuals. The levels of extraversion and introversion did not change in either group after treatment, which is line with the existing ideas about the consistency of temperament properties, the characteristics of which are these indicators. At the same time, in the results of Eysenck's test, it should be noted a change in the personality psychophysiological indicator of neuroticism, which is characterized by worry, excitability, anxiety, and self-doubt. This fact indicates that an increased level of neuroticism may be a personality trait predisposing to rosacea development. Significant differences were established when comparing neuroticism levels between the groups of patients at the end of treatment. The nature of changes in the neuroticism levels indicates an initially higher lability and reactivity of the nervous system in rosacea patients, the correction of which against the background of Cortexin use could improve the general well-being of patients.

The established effects from the drug may be based on its pharmacological action aimed at restoring the balance between the excitatory amino acids neurotransmitters and their inhibitory antagonists. In addition, the drug effects can be realized by changing the activity of enzymes that regulate the functional state of dopamine and acetylcholine receptors, under the influence of mineral substances that are its active ingredients (Chéret et al. 2013; Yu et al. 2014; Shavlovskaya 2016; EuroLab 2017). The direct effect of Cortexin on the metabolic processes of neurons is also known (Arlt et al. 2013; Gomazkov 2015; Zarubina et al. 2015, EuroLab 2017). A decrease in various aspects of anxiety manifestations in the studied patients may also be due to positive changes in the cognitive sphere in the form of improved memory and increased attention. In general, the data obtained are consistent with the ideas currently existing in psychodermatology about the role of neuropsychic mechanisms in the development of dermatoses (Olisova et al. 2012; Sorokina and Korsunskaya 2013; Liu et al. 2014; Egeberg et al. 2016).

Conclusion

Based on the results of a psychophysiological study, it can be concluded that the inclusion of Cortexin in the pharmacotherapy of rosacea with a concomitant neurological pathology contributes to a more pronounced correction of psychophysiological parameters, reflecting the levels of neuroticism, trait and state anxieties, and somatic manifestations of anxiety than with standard treatment. It was found that the revealed effects of the drug may be based on a change in neuroticism as a temperamental basis of anxiety at an individual's initial levels, not associated with the disease effect, because of an improvement in the functional state of neurons due to the complex pharmacological action of Cortexin. The consequences of these effects were more significant changes in the characterological indicators of patients: a decrease in psycho-emotional stress and an increase in emotional balance. In addition, the inclusion of Cortexin in rosacea treatment more effectively

reduces physical discomfort from anxiety, especially in patients with its moderate and high levels. It can be assumed that to achieve the described psychophysiological changes in rosacea, not the anxiolytic effects of tranquilizers, but nootropic, neuroprotective and tissue-specific influences are required to a greater extent.

Conflict of interest

The authors have no conflict of interests to declare.

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