Sense of alexithymia in patients with anxiety disorders comorbid with recurrent urticaria

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Aim: Alexithymia is associated with limited cognitive processing of emotions by an individual suffering from recurrent urticaria and alexithymia and makes them focus on somatic manifestations of emotional arousal and on poorly controlled compulsive reactions to negative stimulation. Alexithymia is considered to be a personality trait, which, along with other factors, predisposes individuals toward developing somatic diseases. The aim of the study was to assess the measurement of alexithymic features in patients with recurrent urticaria and to assess the types of concurrent anxiety disorders and overall anxiety level.

Methods: In order to diagnose clinical anxiety symptoms in patients, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition and the Hamilton Anxiety Rating Scale were applied. Alexithymic features were measured by means of a shortened version of the Toronto Alexithymia Scale, characterized by high discrimination power, internal coherence, and reliability.

Results: According to the Toronto Alexithymia Scale results, the greatest contributing factor was “inability to differentiate between feelings and bodily sensations”. This was observed in both males and females. Most frequently, the patients were found to suffer from generalized anxiety disorder and social phobia.

Conclusion: Alexithymia may result from the difficulty associated with expressing emotions caused by anxiety disorders. Undergoing treatment for anxiety disorders may contribute to reduced exacerbation of urticaria.

Keywords: alexithymia, anxiety, recurrent urticaria

Introduction
The alexithymia construct was created by psychiatrist Peter Sifneos. Individuals with alexithymia find it difficult to identify or describe their own emotions, recognize emotional states in others, or distinguish between emotions and bodily sensations.¹² The prevalence of alexithymia in the general population ranges between 10%–13%. Males have been reported to manifest alexithymia symptoms more frequently (12.8%–17.0%) than females (8.2%–10.0%).³ Individuals with alexithymia attribute the cause of their emotional problems to external events rather than their own inner experience. Significant exacerbation of alexithymia symptoms is reflected in a specific functioning style.⁴ Interpersonal relations of patients with alexithymia are marked with indifference toward others’ expectations, coldness, and reserve.⁵ Affected individuals also tend to have limited imagination, primarily with regard to positive events. Images arising from negative emotions are evoked more easily.⁶ Patients with alexithymia are also said to have both poor introspective and overly concrete thinking styles.⁷ As a result, verbal expression of emotions and cognitive reflection of emotional processes are impaired. This is followed by inclination of affected individuals to react to external...
events with unmoderated states of physiological arousal. Several studies indicate that alexithymia is likely a triggering and/or maintaining factor for numerous somatic diseases, including dermatological conditions, for example, chronic idiopathic urticaria (CIU), and mental disorders. Patients suffering from alexithymia are diagnosed with greater exacerbation of anxious-depressive symptoms. Other studies have revealed that individuals with alexithymia manifest changes in the activity of the sympathetic nervous system, the immune system, and the brain. Changes in the brain activity of these patients can be seen on functional magnetic resonance imaging. Emotional information from the right hemisphere is not properly transferred to language regions in the left hemisphere. This may result from a reduced size of the corpus callosum, which is regularly observed in psychiatric patients. One neuropsychological study found that the cause of alexithymia may be related to a disturbance of the right hemisphere, being that it is largely responsible for processing emotions. Furthermore, another neuropsychological study suggests that alexithymia could be caused by dysfunction in the anterior cingulate cortex. Higher autonomic reactivity is regarded as an adverse disposition that has a significant influence on stress-related mental and somatic disorders.

Alexithymia is a risk factor for the development of somatoform disorders in patients who have experienced chronic stress. The skin, being the largest body organ, forms a barrier between the organism and the environment and is constantly exposed to harmful stressors. This is where nerve endings are located, and they transmit information about touch, itch, pain, temperature, and other physical stimuli to the central nervous system. The relationship between stress, emotions, and regulation of the nervous, immune, and endocrine system activity, as well as its impact on the skin condition, is represented by the neuro-immuno-cutaneous-endocrine model (Figure 1). The model illustrates that stress induces inflammatory activation of the hypothalamic–pituitary–adrenal axis and causes the release of hormones, cytokines, and neurotransmitters. This may result in dermatitis and, for example, recurrence of CIU. The studies available show that the skin lesions that occur in the course of the disease, such as skin rash with wheals and itch, are connected with psychological problems and last at least 6 weeks. The psychological factors may involve unelaborated and suppressed emotions. They may manifest as difficulty describing emotions, for example, expressing anger. Recurrent urticaria concomitant with alexithymia may negatively affect the quality of life and increase anxiety severity.

The aim of this study was to assess the anxiety level and alexithymia severity in individuals with a history of CIU and anxiety disorders, namely panic disorders (PDs), generalized anxiety disorders (GAD), and social phobia (SF). This assessment allowed identification of groups that were at the highest risk for urticaria recurrence caused by exacerbation of alexithymia.

**Patients and methods**

**Participants**

The study involved 198 subjects, 158 of whom comprised of the study group (79 females [F] and 79 males [M]). The average age was 41.4±3.5 years (range: 20–44 years of age). The study groups included SF+alexithymia (A)-M (25 participants), SF+A-F (25 participants), GAD+A-M (20 participants), GAD+A-F (20 participants), PD+A-M (17 participants), PD+A-F (17 participants), A-M (17 participants), and A-F (17 participants). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria were utilized to diagnose PD, SF, and GAD. Patients enrolled in the study came to the Crisis Intervention Centre at the Department of Psychiatry in Bydgoszcz due to anxiety symptoms. Also, all of them had alexithymia and a history of recurrent urticaria.

Before admission, the subjects had started pharmacological treatment with the following medications: selective...
serotonin reuptake inhibitor (escitalopram), serotonin–noradrenergic and specific serotoninergic antidepressant (mirtazapine), norepinephrine–dopamine reuptake inhibitor (bupropion), serotonin antagonist and reuptake inhibitor (trazodone) (Table 1), and this took place between 2012 and 2015.

Following admission to the Department of Psychiatry, the treatment was discontinued since it was ineffective. One week after treatment discontinuation, prescreening of patients was performed in order to assign them to particular study groups.

Patients who met the entrance criteria were qualified for screening. Twenty-two percent of the prescreened patients who did not fulfill the entrance criteria were considered “screen-failures”.

On examination, they had been experiencing a remission of urticaria for at least 1 year. The control group (C) involved 40 healthy subjects (20 females and 20 males) assigned according to sex and age. Individuals comprising the control group applied on their own initiative to the Department of Psychiatry in order to be enrolled in the study. They were qualified by the same psychiatry specialist. None of the test subjects were incapacitated, soldiers in compulsory military service, persons held in custody, persons in a reporting or other relationship, nor were they hospital employees. All of them had full legal capacity. The average age of the control group amounted to 40.8±3.1 years (range: 20–43 years of age). Exclusion criteria for both groups were established within the study and involved a diagnosis of mental illnesses other than indicated, organic damage to the central nervous system, detected alcohol or other psychoactive substance abuse, and treatment for infectious and chronic systemic diseases. Individuals with smoking habits and taking medications were also excluded from the study.

Study scales

Toronto Alexithymia Scale

The alexithymia construct was created by the psychiatrist Sifneos in 1972 and subsequently operationalized by Taylor et al26 as the Toronto Alexithymia Scale (TAS) along with its three subscales: difficulty describing feelings (DDF), difficulty identifying feelings (DIF), and externally oriented thinking (EOT). Currently, the TAS-20 is the most widely used self-report measure.

The DDF subscale comprises self-report items that determine the ability to cognitively express and describe feelings and emotions. The DIF subscale indicates the ability to internally distinguish and identify feelings and emotions. Finally, the EOT subscale consists of self-descriptions that refer to one’s tendency to maintain external attention directed at material objects.

The maximum score for a shortened version of the TAS-20 is 100. The subscale maximum scores are 25 (DDF), 35 (DIF), and 40 (EOT). The TAS-20 total score for alexithymic patients is 61 or more (Table 2).26

Hamilton Anxiety Rating Scale

The Hamilton Anxiety Rating Scale (HAM-A) was one of the earliest established rating scales to measure the severity of anxiety symptoms. Since then, it has been commonly utilized in clinical and research settings. It is a 14-item scale in which each item is specified by a series of symptoms. The HAM-A measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints connected with anxiety). Despite its general application in

<table>
<thead>
<tr>
<th>Group</th>
<th>M</th>
<th>SF+ A-M</th>
<th>GAD+ A-M</th>
<th>PD+ A-M</th>
</tr>
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<tr>
<td>% of TAS-20 total (≥61 points)</td>
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</table>

<table>
<thead>
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<th>Group</th>
<th>M</th>
<th>SF+ A-F</th>
<th>GAD+ A-F</th>
<th>PD+ A-F</th>
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</thead>
<tbody>
<tr>
<td>% of TAS-20 total (≥61 points)</td>
<td>10</td>
<td>12</td>
<td>22</td>
<td>24</td>
</tr>
</tbody>
</table>

Abbreviations: TAS-20, Toronto Alexithymia Scale; A-M, alexithymia males; A-F, alexithymia females; SF+ A-M, social phobia + alexithymia males; SF+ A-F, social phobia + alexithymia females; GAD+ A-M, generalized anxiety disorder + alexithymia males; GAD+ A-F, generalized anxiety disorder + alexithymia females; PD+ A-M, panic disorder + alexithymia males; PD+ A-F, panic disorder + alexithymia females; M, male; F, female; A, alexithymia.
clinical trials, the scale is said to have some drawbacks related to poor ability to differentiate between anxiolytic and antidepressant effects and between somatic anxiety and somatic side effects. Also, no standardized probe questions are given by the HAM-A. However, levels of interrater reliability for the scale have been reported to be satisfactory.

Each item is scored on a 0–4 scale, where 0 stands for “not present” and 4 for “severe”. The total score ranges from 0 to 56 with <17 indicating mild severity, 18–24 mild-to-moderate severity, and 25–30 moderate-to-severe severity. The eligibility cutoff score for patients with GAD was 22.

Statistical analysis

A number of quantitative traits were subject to a descriptive statistical analysis. The analysis was aimed at obtaining measures, such as the arithmetic mean (x̄), standard deviation (SD), and middle quartiles (Q2 = Me).

The Shapiro–Wilk test was adopted to examine the normal distribution of variables. Regarding variables with normal distribution, the comparison of two mean values in the study groups was conducted by means of the Student’s t-test, and it followed verification of homogeneity of variance with the Fisher–Snedecor test. Two groups of variables without normal distribution were contrasted by means of the Mann–Whitney U-test. The chi-square test was utilized to examine the significance of differences between the fractions and some dichotomous features. Therefore, for statistical hypotheses verification, parametric and non-parametric statistical tests were applied with a significance level of P≤0.05.

In addition to the descriptive analysis, one- and multifactor analyses of variance were carried out.

Ethics

This study received approval of the Bioethics Committee of the Medical College in Bydgoszcz. All information about the research was given to each study participant who then provided written informed consent for enrollment. All the subjects included in the study were interviewed, and their mental status was evaluated by a psychiatry specialist, the first author of this paper.

Results

The first comparison regarded the control group and the group of patients with alexithymia (A-M, A-F). Statistically significant differences in the mean were found (P<0.001). It was observed that in both cases of males and females, all diagnostic scales indicated a lower value of mean test results for the controls versus the group of patients with alexithymia (A). With regard to sex, greater differences were observed in males than females.

Females with alexithymia (A-F) were reported to have higher mean values on the TAS-20 scale and its subscales (DDF) versus males with alexithymia (A-M). With reference to the EOT and DIF subscales, as well as the HAM-A, similar mean values were revealed between males and females (Table 3; Figure 2).

A significance test for differences between the A and PD+A groups revealed diverse results. The PD+A group was reported to have a slightly higher score than the A group. This was observed for the TAS-20 (P=0.008), DIF (P=0.001), and EOT (P=0.033). However, differences for the HAM-A and DDF were not statistically significant (P>0.05).

Table 3 The mean scores for the scales in particular diagnostic tests

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group</th>
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<th>C-F</th>
<th>M vs F</th>
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<td></td>
<td>Av</td>
<td>SD</td>
<td>Me</td>
<td>Av</td>
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<tr>
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<td>32.50</td>
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<tr>
<td>DDF</td>
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<tr>
<td>DIF</td>
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<td>14.50</td>
<td>13.60</td>
</tr>
<tr>
<td>EOT</td>
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<td>12.00</td>
<td>18.15</td>
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<tr>
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<td>6.00</td>
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</tr>
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<td>A-F</td>
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<td>1.80</td>
<td>15.00</td>
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<td>6.24</td>
<td>22.00</td>
<td>20.18</td>
</tr>
<tr>
<td>EOT</td>
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<td>4.69</td>
<td>26.00</td>
<td>25.06</td>
</tr>
<tr>
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<td>19.00</td>
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<td>28.32</td>
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<tr>
<td>EOT</td>
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<td>5.55</td>
<td>28.00</td>
<td>27.88</td>
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<tr>
<td>HAM-A</td>
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<td>2.22</td>
<td>21.00</td>
<td>20.88</td>
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<td>GAD+A-M</td>
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<td>GAD+A-F</td>
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<td>3.47</td>
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<td>HAM-A</td>
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<tr>
<td>EOT</td>
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<td>HAM-A</td>
<td>21.35</td>
<td>3.14</td>
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<td>20.53</td>
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Abbreviations: TAS-20, Toronto Alexithymia Scale; DDF, difficulty describing feelings; DIF, difficulty identifying feelings; EOT, externally oriented thinking; HAM-A, Hamilton Anxiety Rating Scale; C-M, control group males; C-F, control group females; A-M, alexithymia males; A-F, alexithymia females; SF+A-M, social phobia + alexithymia males; SF+A-F, social phobia + alexithymia females; GAD+A-M, generalized anxiety disorder + alexithymia males; GAD+A-F, generalized anxiety disorder + alexithymia females; PD+A-M, panic disorder + alexithymia males; PD+A-F, panic disorder + alexithymia females; Av, average; SD, standard deviation; Me, median; M, male; F, female.
Differences in the mean results between males and females with PD+A were also interesting. The differences for all the studied parameters (TAS-20, DDF, DIF, EOT, and HAM-A) were insignificant. However, when comparing the results between A and PD+A groups among males and females, a different observation was made (Table 3; Figure 3). For females, significant differences between A and PD+A groups were reported only on the DDF subscale ($P<0.001$). For males, significant differences were found on the DDF ($P=0.040$), DIF ($P<0.001$), and EOT ($P=0.016$) subscales.

In the case of contrasting patients with alexithymia (A) with subjects suffering from SF+A, the differences in the mean were statistically significant for the TAS-20 test ($P<0.001$). The differences in the mean on the three subscales of the TAS-20 scale (DDF, DIF, EOT) revealed statistical significance as well.

It was only the HAM-A scale, for which the Mann–Whitney U-test showed insignificant differences in the mean values ($P=0.261$).

Males with SF concomitant with alexithymia (SF+A-M) were reported to have higher mean values on the TAS-20 scale and its subscales (DDF, DIF) when compared to females.

Comparable mean results in the group of males and females with SF+A were found on the EOT subscale (Table 3; Figure 4).

Having compared patients with alexithymia (A) with subjects suffering from GAD+A, statistical significance was revealed with regard to the differences in the mean ($P<0.001$) on the TAS-20 scale and its EOT subscale as well as on the HAM-A ($P<0.05$). It was only the subscales DDF ($P=0.141$) and DIF ($P=0.053$), for which the Mann–Whitney test showed insignificant differences in the mean values.

Nevertheless, since the significance level of the difference observed on the DIF subscale is close enough to the accepted threshold of $P=0.05$, its result should be considered nearly significant.

Both males and females with GAD concomitant with alexithymia (GAD+A) were reported to have higher mean values on the TAS-20 scale and its EOT subscale, as well as on the HAM-A scale when compared to the control group (Table 3; Figure 5).

In addition to the earlier analyses, single- and multi-factor analyses of variance were conducted. Statistically significant differences were revealed in all study groups for all performed tests. It was found that sex was a significant factor responsible for these differences only in the case of the TAS-20 scale, the DIF subscale, and the HAM-A scale (Table 4).

Two-factor analysis of variance included groups assigned according to both the type of disorder and sex. Statistically significant differences between the groups were revealed
Figure 3 The mean result of diagnostic tests for females and males with alexithymia, as well as alexithymia concurrent with panic disorder.

Abbreviations: TAS-20, Toronto Alexithymia Scale; DDF, difficulty describing feelings; DIF, difficulty identifying feelings; EOT, externally oriented thinking; HAM-A, Hamilton Anxiety Rating Scale; A, alexithymia; PD+A, panic disorder + alexithymia; M, male; F, female.

Figure 4 The mean result of diagnostic tests for females and males with alexithymia, as well as alexithymia concurrent with social phobia.

Abbreviations: TAS-20, Toronto Alexithymia Scale; DDF, difficulty describing feelings; DIF, difficulty identifying feelings; EOT, externally oriented thinking; HAM-A, Hamilton Anxiety Rating Scale; A, alexithymia; SF+A, social phobia + alexithymia; M, male; F, female.
for the TAS-20 scale and its EOT subscale, as well as for the HAM-A scale. However, the differences between these groups for the DDF and DIF subscales were reported to be insignificant.

Discussion

CIU, commonly referred to as the occurrence of extensive itchy wheals lasting at least 6 weeks, belongs to significant diseases among other dermatoses that are said to be related to psychological factors. For the etiology of the disease to be defined, it may be important to closely consider the inability to express or elaborate emotions.\textsuperscript{21,29} It has been proved that CIU is caused by personality-based difficulties relating to emotional regulation with an emphasis on the feeling of anxiety.\textsuperscript{30} This deficit may be the reason for manifesting the experienced emotions through bodily symptoms, such as pruritus, angioedema, and urticarial vasculitis.\textsuperscript{31,32}

In this paper, the authors present the study results of individuals with a history of CIU, who additionally reported the symptoms of alexithymia or alexithymia concomitant with GAD, PD, or SF.

The obtained results indicate the presence of statistically significant differences in the mean ($P<0.0001$) when comparing the C and A groups on the TAS-20 and HAM-A scales. This is reflected by higher values on the TAS-20 scale and its subscales (DDF, DIF) versus the female group. However, the anxiety level measured by the HAM-A was comparable in these groups. Having contrasted the groups with SF$^+\text{A}$ and A, statistically significant differences in the mean were observed both on the TAS-20 scale and all its subscales. Also, alexithymia in the male group with SF$^+\text{A}$ showed higher values on the TAS-20 scale and its subscales (DDF, DIF) than in the female group. The anxiety level measured by the HAM-A was statistically insignificant in these contrasted groups. Having compared the groups with GAD$^+\text{A}$ and A, statistically significant differences in the mean were observed both on the TAS-20 scale and its subscales, as well as on the HAM-A scale. The highest level of alexithymia was observed in females from the GAD$^+\text{A}$ group on the TAS-20 scale and its EOT subscale. The most substantial anxiety level

Table 4 ANOVA for the TAS-20 (DDF, DIF, EOT) and for the HAM-A

<table>
<thead>
<tr>
<th>ANOVA</th>
<th>TAS-20</th>
<th>DDF</th>
<th>DIF</th>
<th>EOT</th>
<th>HAM-A</th>
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<td>0.929</td>
<td>0.001</td>
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</table>

Abbreviations: ANOVA, analysis of variance; TAS-20, Toronto Alexithymia Scale; DDF, difficulty describing feelings; DIF, difficulty identifying feelings; EOT, externally oriented thinking; HAM-A, Hamilton Anxiety Rating Scale.
measured by the HAM-A was detected in females from the GAD+A group.

The obtained results prove that males suffering from alexithymia concomitant with SF (SF+A-M) and females with alexithymia concomitant with GAD (GAD+A-F) were reported to have more elevated levels of alexithymia on the TAS-20 scale. In the case of males comprising the SF+A group, alexithymia presented more strongly with DIF and DDF. In turn, in the case of females from the SF+A group, alexithymia exerted the greatest influence on the operational thinking style (EOT), and it disturbed cognitive functions. Individuals suffering from alexithymia without concomitant anxiety disorders, such as SF, GAD, and PD, had alexithymia with more substantial values on the TAS-20 scale and its subscales (DDF, DIF) with regard to males versus females. However, the anxiety level in this group (A) measured by the HAM-A scale was comparable between male and female groups.

The previously conducted studies on alexithymia with regard to anxiety disorders failed to involve patients with other concurrent diseases, for example, idiopathic urticaria. They focused on patients with alexithymia and anxiety disorders.33,34 Thus, the study results presented in this article are considered pioneering by the authors.

Cucchi et al35 claimed that patients with PDs revealed a higher level of alexithymia than healthy individuals. The study by Dalbudak et al36 showed exacerbation of alexithymia on the TAS-20 general scale and its DDF subscale in students with an elevated anxiety level and diagnosed SF. Moreover, Koyuncu et al37 claimed that 32.9% of patients with SF suffered from alexithymia. Additionally, individuals suffering from SF were more predisposed to developing depression. In patients with depression and concomitant SF, the alexithymia level was higher than in subjects with SF alone.37 Also, alexithymia disturbed social functioning in this group of subjects, as well as being responsible for secondary exacerbation of SF.4 Therefore, the results of this study indicate that concomitance of two psychiatric disorders (SF and depression) makes alexithymia more severe. What is more, De Berardis et al40 observed that individuals with GAD and alexithymia expressed by an increased DIF subscale frequently had suicidal thoughts.

Majoehr et al41 found that there exists a relationship between alexithymia and anxiety-based dissocial personality disorders. The authors concluded that alexithymia and dissocial personality disorders may predispose an individual to panic attacks. In patients with dissocial personality disorders, alexithymia manifested as “DIF”. Patients who were observed to have the symptoms of dissocial personality disorders were reported to have an increased level of alexithymia, particularly represented on the subscales of the TAS-20 scale, which involved DIF and, to a lesser extent, “DDF”. The results of the study confirm a strong relationship between alexithymia and dissocial personality disorders in patients with PD.40

Very few studies have been found in the literature on the presence of alexithymia in patients with past CIU.41,42

The study by Zachariae et al revealed that patients suffering from urticaria and posttraumatic stress disorder (PTSD) were observed with higher alexithymia levels than the controls. Their defense mechanism was classified as defensive, and it involved conscious self-image management along with elevated manifest anxiety.43

Another study by Conrad et al40 found that there exists a relationship between intensified itch in patients with CIU and a tendency to suppress negative emotions, such as anger. Moreover, these authors also marked the relationship between exacerbation of depression and exacerbation of itch in psoriasis.30

These studies also indicate a possibly higher dysregulation of the hypothalamic–pituitary–adrenal axis taking part in the neurohormonal response with respect to anxious-depressive disorders. The axis is also responsible for exacerbation or recurrence of symptoms related to many somatic diseases, including dermatological conditions, such as CIU, the pathogenesis of which is linked to immune and neurohormonal factors.44

On the basis of the studies conducted by the authors of this paper, it was revealed that GAD and SF exacerbate alexithymia symptoms in patients with past CIU and with GAD+A and SF+A. PDs do not exacerbate alexithymia in patients experiencing remission of CIU or in subjects with PD+A. The studies proved the need for psychotherapeutic treatment directed toward overcoming difficulties with expressing feelings in patients from GAD and SF groups and with concomitant alexithymia. Moreover, in the group of patients with GAD+A, it is crucial to provide psychotherapeutic and/or pharmacological treatment aimed at reducing anxiety severity and to treat anxiety disorders, taking into account psychological factors. Psychotherapeutic and/or pharmacological treatment for anxiety disorders and alexithymia in patients with past CIU may prevent recurrence of urticaria.45

Conclusion

Anxiety disorder, SF, and GAD are factors that exacerbate alexithymia symptoms in patients with a history of CIU.
Limitations
The study groups were composed of patients with a history of recurrent urticaria; yet, they were experiencing a remission of the disease at the time of enrollment. Therefore, urticaria severity was not evaluated by means of the Urticaria Severity Score. Moreover, when assigning patients to particular groups according to the type of disorder, the authors did not include patients with PTSD since it was impossible to select subjects with the same duration of PTSD symptoms.

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