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DISCOVERY SCIENTIFIC SOCIETY

Stress, anxiety, depression and psychiatric/psychological methods in treatment of Chronic Spontaneous Urticaria

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ABSTRACT

Introduction: In Chronic Spontaneous Urticaria (CSU), onset of symptoms can be triggered by various factors, including psychological stress. Furthermore, disease activity itself can cause stress and disturbance of sleep, which become contributing factors to development of depression and anxiety. *Purpose*: The objective is to discuss the role of psychiatric and psychological methods as part of CSU treatment. The review analyses studies researching a correlation of CSU with psychiatric conditions and the use of psychiatric/psychological methods in CSU. *Materials and Methods*: Authors conducted a literature search using the PubMed database to identify relevant studies published between January 2015 and June 2025. The following keywords were used in various combinations: "chronic spontaneous urticaria", "stress", "anxiety", "depression", "psychological treatment", and "psychiatric methods". Main results: Anxiety and depression are more prevalent in CSU population, and their severity seems to correlate with urticaria activity; sleep disturbance is a possible mediator of this correlation. Psychiatric/psychological methods can decrease CSU activity, but there is not enough evidence to strongly support this claim. *Conclusions*: Low sleep quality, anxiety and depression are more common in CSU patients, and there is a possible causal relationship between them, with sleep disturbance as a potential mediator. There is not enough evidence to strongly endorse psychiatric/psychological methods for the prevention/alleviation of CSU symptoms. Clinicians treating patients with CSU should be aware of the increased risk of psychiatric comorbidity and consider diagnostic and treatment options regarding those conditions. Further research is needed.

Keywords: Chronic Spontaneous Urticaria, anxiety, depression, stress, psychiatry

1. INTRODUCTION

Characteristics and classification of urticaria

Urticaria is a condition characterised by the onset of itchy wheals (hives) and/or angioedema. A differential diagnosis should include other clinical conditions that

may present with those symptoms: anaphylaxis, autoinflammatory syndromes, urticarial vasculitis, or bradykinin-mediated angioedema including hereditary angioedema (HAE) (Hon et al., 2019; Zuberbier et al., 2022).

Urticaria is classified depending on duration, as:

- acute, if the occurrence of wheals and/or angioedema lasts for 6 weeks or less;
- chronic, if the occurrence of wheals and/or angioedema lasts (continuously or intermittently) for more than 6 weeks.
- Chronic Urticaria (CU) is further classified depending on triggering factors, as:
- Chronic Inducible Urticaria (CIndU), if there is a definite trigger, meaning symptoms always occur when the trigger is present and never occur when the trigger is absent;
- Chronic Spontaneous Urticaria (CSU, also known as Chronic Idiopathic Urticaria), if symptoms appear due to known or unknown causes, without a definite trigger.

Lack of definite triggers is a defining trait of CSU, but there can be non-definite triggers (like drugs, food, infections, and stress). Non-definite trigger is a factor that can cause a disease activity, but its presence does not always induce wheals and/or angioedema, and the signs and symptoms also occur without it, spontaneously (Zuberbier et al., 2022).

Pathophysiology of CSU

The complete pathophysiology of Chronic Spontaneous Urticaria is still unclear; however, it is well established that the activation of skin mast cells and their mediators (histamine, cytokines, platelet-activating factor, and others) are key parts of the mechanism (Bansal and Bansal, 2019; Hon et al., 2019; Ferreira et al., 2021; Zuberbier et al., 2022; Tomaszewska et al., 2023).

This activity causes dilatation and augmented permeability of the postcapillary venules and lymphatic vessels, as well as cell recruitment to urticarial lesions, resulting in edema. Wheals develop when these changes occur primarily in the upper and mid dermis, while angioedema develops when changes occur primarily in the lower dermis and the subcutis (Zuberbier et al., 2022).

Activation of sensory nerves is one of the components of this mast cell-driven reaction. While the mechanism is not well established, Siiskonen and Harvimaa (2019) propose a hypothetical model for the communication between mast cells and sensory nerves activated by psychological stress, resulting in neurogenic inflammation in the skin. The reciprocal communication between mast cells and sensory nerves might result in an increase in mast cell numbers and nerve fibers, creating a vicious circle and causing exacerbation of neurogenic inflammation and pruritus.

Currently used treatment methods

One of the main available CU management options is the avoidance of triggering factors. This approach is helpful for reducing the disease activity, but can highly interfere with patients' life. Furthermore, it is less effective for CSU than CIndU, because triggers in CSU are not definite (Zuberbier et al., 2022).

The other options are symptomatic pharmacological therapies to prevent mast cell mediator release and/or their effects. Modern 2nd generation H1-antihistamines are used as 1st line treatment of urticaria, with an option of increasing the dose to up to fourfold. If this treatment doesn't achieve sufficient results, omalizumab may be added as a 2nd line treatment. If high doses of 2nd generation H1-antihistamines and omalizumab aren't effective, ciclosporin treatment is considered the next step. However, it should be used with caution, because of a higher risk of adverse effects. Glucocorticosteroids (GCS) may be considered as a short course of rescue systemic GCS in case of acute exacerbation, but long-term use is not recommended (Zuberbier et al., 2022; Kolkhir et al., 2024).

Outside of those possibilities, there are no strong recommendations for other treatment options. Nevertheless, clinical experience indicates that some of them may be useful in specific contexts. Antidepressants, pseudoallergen-free diet, H2-antihistamines, immunosuppressive drugs, leukotriene receptor antagonist, and sulfones are considered widely used alternative treatments. Psychotherapy is among the less frequently used options (Zuberbier et al., 2022).

2. REVIEW METHODS

Authors conducted literature search using databases including PubMed, Scopus, and Web of Science, covering publications from January 2015 to June 2025. The search strategy combined terms related to "chronic spontaneous urticaria", "stress", "anxiety", "depression", "psychological treatment", and "psychiatric methods".

Studies were included if they met the following criteria:

- Original research articles published in English;

- Studies involving adult or pediatric populations diagnosed with chronic spontaneous urticaria (CSU) or chronic urticaria (CU);
- Studies assessing psychological comorbidities (e.g., anxiety, depression, stress, sleep disturbance) or evaluating psychiatric/psychological treatment strategies.

As illustrated in the diagram (Figure 1), a number of articles were excluded after full-text screening. The reasons for exclusion were lack of original data, focus on other forms of urticaria (e.g., inducible urticaria), and absence of psychological or psychiatric outcome measures. After applying inclusion and exclusion criteria, a total of 25 studies were included in the final analysis.

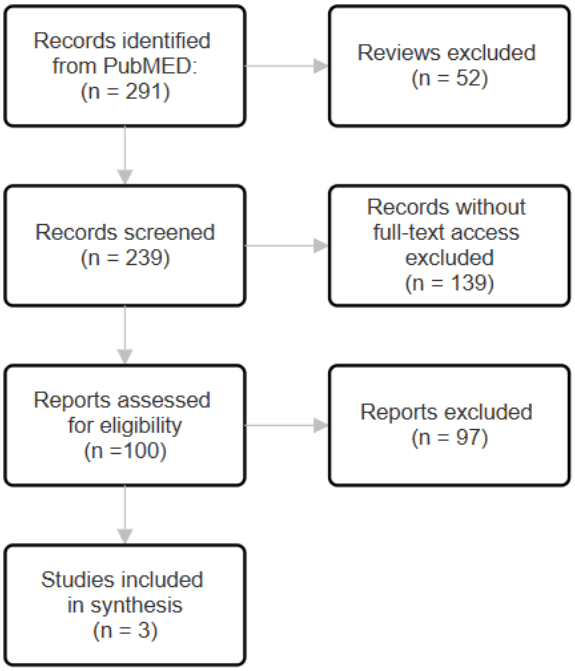

Figure 1. Flow diagram.

3. RESULTS & DISCUSSION

Correlation of CSU with stress, low sleep quality, anxiety, and depression

In the 2013 meta-analysis, Ben-Shoshan et al. systematically reviewed studies from 1 January 1935 to 1 January 2012 in order to assess the contribution of psychological factors to CSU. Among other results, they concluded that the patients had a higher prevalence of anxiety, depression, and stress (Ben-Shoshan et al., 2012).

In the 2020 meta-analysis, Huang et al. systematically reviewed studies from January 2000 to January 2019, and concluded that CU is associated with higher risks of anxiety and depression (Huang et al., 2020).

For our study, we analysed 10 studies from the last decade (January 2015 and June 2025) including cumulatively 1056 patients with CSU or CU and 2217 patients in control groups. CU and CSU patients were grouped together, because CSU patients are statistically majority (80-90%) of CU patients, and CSU share many characteristics with CIndU (Hon et al., 2019; Zuberbier et al., 2022).

Although in some of the analysed papers, studying the correlation of stress/low sleep quality/anxiety/depression with CSU wasn't the primary purpose, our analysis focused on the results regarding this topic. There were only two studies taking measuring the stress levels directly. One showed no significant difference between the CSU patients and the healthy control group, while the other showed that stress tended to be lower in the CSU patients compared to the asthma patients (Schut et al., 2019; Choi et al., 2020).

Most of the reviewed studies show that anxiety and depression are more prevalent among CSU patients compared to the control groups. There is some indication of a connection between urticaria activity and depression/anxiety scores, but this has not been consistently confirmed by all studies. Three studies suggested that low quality of sleep caused by urticaria activity might be a mediator

causing an increased rate of anxiety and depression (Ograczyk et al., 2017; Arslan and Çelik, 2024; Huang et al., 2021; Bangera et al., 2023; Choi et al., 2020; Memet et al., 2021; Abdel-Meguid et al., 2024; Sánchez-Díaz et al., 2023; Tat, 2019).

Psychiatric/psychological methods of CSU treatment

Pharmacological therapies

Although psychiatric drugs are not recommended as the main line of CSU treatment, some clinicians use antidepressants as an alternative or adjunctive treatment of CSU (Eskeland et al., 2017; Memet et al., 2021; Zuberbier et al., 2022).

In 2017 systematic review, Eskeland et al. studied the effectiveness of antidepressants in different inflammatory skin disorders, including chronic urticaria. They analysed 13 original studies regarding CU – all of them showed positive results after antidepressant therapy. Seven of these studies researched the effects of doxepin: one of them was a randomized controlled trial (comparing doxepin to hydroxyzine), three were double-blind, placebo-controlled crossover trials, and the remaining three were case studies. Authors concluded that doxepin may be of value in the treatment of CU, but it is not clear if antidepressants have a purpose in the treatment of CU without psychiatric comorbidity, and larger controlled trials are needed to provide further evidence (Eskeland et al., 2017).

Non-pharmacological therapies

Researchers suggest two kinds of non-pharmacological psychiatric/psychological methods of treating CSU patients: psychotherapy/psychological interventions; (Ograczyk et al., 2017; Choi et al., 2020; Schut et al., 2020; Memet et al., 2021; Zuberbier et al., 2022); self-administered relaxation techniques. (Ben-Shoshan et al., 2013; Oland et al., 2018; Tomaszewska et al., 2023)

Psychotherapy/psychological interventions

Lindsay et al., (2015) tested whole-person treatment approach (WPTA) sessions with a clinician trained in psychotherapy. Three CSU patients with poor response to standard drug treatment participated in the study. After a course of 10 sessions, there was a significant reduction in disease activity and drug use of those patients. The effects were sustained 2 years later in follow-up.

In the article, Vojvodic et al., (2019) presented a case study of a 32-year-old female patient. Anxiety and CSU symptoms appeared after the life circumstances triggered a memory of the patient's traumatic experience. The urticaria seemed to be connected to her mental state, as it manifested within 10 seconds of becoming anxious. Patient was diagnosed with generalised anxiety disorder (GAD) with consideration of post-traumatic stress disorder (PTSD). The dermatological diagnosis was CSU with no proposed treatment.

The patient refused proposed selective serotonin reuptake inhibitors (SSRI) treatment for GAD, so the treatment consisted only of psychotherapeutic interventions in the form of rational emotive behavioural therapy (REBT) once per week over 4 months. By the end of the treatment, the patient reported remission of symptoms of both GAD and urticaria.

In the article, Konstantinou et al., (2025) presented a case study of a 35-year-old female patient. The patient was treated for CSU, starting in 2014, for several years with standard treatment of ebastine (2nd-generation antihistamine), escalating to omalizumab, cyclosporine A and oral corticosteroids. The treatment was effective, but it caused side effects (hirsutism) and control wasn't stable long term – symptoms were coming back during periods of stress, even with chronic doses. In 2021, the patient was diagnosed with generalized anxiety disorder (GAD), treated with cognitive behavioral therapy (CBT) and escitalopram (SSRI). After this treatment, there was significant improvement in CSU control, allowing patient to discontinue ebastine in 2021, and subsequently omalizumab in 2022. One month after the discontinuation CBT and escitalopram treatments were also stopped, followed by CSU relapse, and reestablishing of urticaria control after resuming CBT and escitalopram. In 2024, upon pregnancy, escitalopram was discontinued again, resulting in CSU exacerbation, which ended after escitalopram reintroduction.

All three studies showed promising results (Table 1), but since the sample sizes were small, and there were no control groups, the strength of the evidence is low.

Table 1. Summary of studies with psychotherapy/psychological interventions.

CSU patients	Psychiatric/psychological methods used	Subsequent CSU control	Source
3	WTPA sessions	Reduction in disease activity and drug use, sustained 2 years later	(Lindsay *et al.*, 2015)
1	REBT	Remission of CSU	(Vojvodic *et al.*, 2019)

1	CBT and escitalopram	Remission of CSU, relapsing after treatment discontinuation	(Konstantinou *et al.*, 2025)

Self-administered relaxation techniques

In three studies, authors suggest teaching patients self-administered techniques that help reduce stress, including Jacobson training (progressive muscle relaxation), visualization, and mindfulness training (Ben-Shoshan et al., 2013; Oland et al., 2018; Tomaszewska et al., 2023). Techniques mentioned above are generally considered beneficial in stress reduction. However, to the best of our knowledge, there are currently no available papers studying the effectiveness of those stress-reducing techniques in the management of CSU (Khoury et al., 2013; Wilczyńska et al., 2019).

4. CONCLUSION

Studies indicate that low sleep quality is correlated with CSU activity and can be caused by it. Anxiety and depression are more common in CSU population, and their severity seems to be associated with urticaria activity. Sleep disturbance is suggested as a mediator causing an increase in anxiety and depression. These correlations should be taken into account while treating patients with CSU in order to improve patients' quality of life. Methods such as psychotherapy, relaxation techniques, and antidepressants might help treat some CSU patients. There is a possibility that psychiatric/psychological methods might be important not only as symptomatic treatment, but also as causal treatment for CSU, but there is not enough evidence to strongly support that claim. Further research (case reports, retrospective studies, and clinical trials – studying larger population samples, containing control groups, using a placebo) is needed to study this topic properly.

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Conflict of interest

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Data and materials availability

All data associated with this study will be available based on reasonable request to the Corresponding Author.

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