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The vicious circle mechanism in atopic dermatitis: psychological distress as cause and effect of atopic dermatitis

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Abstract

Introduction and purpose:

Atopic dermatitis (AD) is chronic inflammatory skin disorder. It typically begins in infancy or childhood and might persist into adulthood. AD is characterized by dry, itchy, eczematous skin. The lesions can vary in intensification from mild to severe according to patient age or body region. AD requires ongoing management to control the symptoms. Skin manifestations along with the demand of treatment and care regimens significantly impact quality of life (QOL) in patients with AD. Individuals suffering from this condition are more prone to developing mental health disorders, which are often linked to emotional stress they experience. Exposure to stress exacerbates AD and stimulates skin changes, which in turn leads to intensification of treatment regimens. This cause-and-effect chain can be considered as a vicious circle mechanism. The aim of the review is to highlight the phenomenon by examining current literature on this topic in order to raise the awareness of healthcare professionals regarding this subject as well as implement appropriate and complete support for patients struggling with AD.

A brief description of the state of knowledge:

The pathophysiology of AD is multifactorial. Numerous studies explore the impact of stress on the deterioration of AD symptoms and delve into its pathogenic concepts. Simultaneously, researchers highlight increased psychological distress in AD patients, which surpass that observed in many other chronic conditions.

Summary:

Psychological factors play a significant role in AD. It demands considering mental health

screening and support as a part of clinical practice, treating AD patients. Further research is necessary to provide efficient and comprehensive interventions.

Keywords: atopic dermatitis; mental health; psychological distress; quality of life

Introduction and purpose

Atopic dermatitis (AD) ranks among the prevalent chronic inflammatory skin conditions globally. Reports from the USA and Europe indicate its impact on roughly 20% of children and 7-10% of adults, although these percentages vary across different countries [1]. AD is marked by symptoms such as pruritus, eczema-like skin lesions, and dry skin. Its causes are multifaceted, including genetic predisposition, impairment of epithelial barrier function, immune system irregularities, psycho-neurogenic inflammation and environmental factors [2][3]. Stress triggers many various biological reactions in organism, including neuroimmune response, what result in influence AD symptoms [4]. In our review we focus on psychological distress in terms of its mutual interaction with atopic dermatitis. According to research findings, stress can be seen as both a contributing factor and a consequence of AD. On the one hand, researchers indicate a connection between AD and psychological stress, showing that it can intensify symptoms of AD, influencing different neuroendocrine mediators, potentially activating local neurogenic inflammation and disrupting the skin's barrier function. On the other hand, studies demonstrate that individuals with AD tend to experience higher levels of psychological stress compared to those without the condition [5,6]. The effect surpasses many other chronic illnesses in terms of its impact on mental well-being [7]. The patients' quality of life in atopic dermatitis is estimated to be lower than that in individuals with epilepsy or diabetes [8,9].

The aim of this review is to shed light on the phenomenon by exploring body of literature, in order to enhance the awareness among healthcare professionals about this matter. Through examination of current research, this review seeks to contribute to a deeper understanding of AD, empowering healthcare practitioners to provide more effective and targeted assistance to patients facing challenges associated with this condition.

Challenges posed by atopic dermatitis.

Numerous adults with AD noted that the disease constrained their lifestyle (51.3%), led to avoidance of social interactions (39.1%), and affected their activities (43.3%). A quarter reported having fair or poor overall health (25.8%) and around 16.7% expressed some level of dissatisfaction with their life. These effects occurred both in people with low intensity of disease symptoms and in those with moderate and severe AD. However, among individuals experiencing moderate and severe forms of AD, it was more common [10].

There are 78 different signs and symptoms of AD with significant diversity by world region and patient age, which were detailed by Yik Weng Yew et al. in global systematic review and meta-analysis [11]. Skin manifestation can have different morphology (e.g. erythema, lichenification, erosions, scaling, oozing/weeping, prurigo nodules) and may affect many body regions (skin under the knees, in the elbow creases, head, neck, hands and feet) [11,12]. Lesions are also characterized by diverse age of onset [13,14], persistence [15] and symptoms. The most common is itching, although skin pain [16] and sleep disturbances [17, 18, 19] might also occur. These elements may lead to emotional and social distress, stigmatization [20], disruptions in function and limited activities of daily living. Itch along with dryness and redness of inflamed skin are the most burdensome symptoms of AD. They are observed in about half of the adults dealing with this condition. Second most challenging symptoms are skin pain and sleep disturbances. They occur in 10% of adult patients. Among individuals with moderate and severe AD the statistics are slightly different. They indicate blisters, bumps, red and inflamed skin, sleep disturbances, pain, open sores or oozing as the most onerous [10].

Atopic dermatitis is linked to notably reduced quality of life (QOL). This is reflected in measures such as Dermatology Life Quality Index (DLQI) [10], Children's DLQI (CDLQI) [21], Skindex [22] or itch-related QOL (ItchyQOL [23]). Poorer quality of life is more prominent as the severity of AD signs and symptoms increase [24, 25]. Collectively, these data illustrate that atopic dermatitis is a disease that is very burdensome in everyday life.

Both mild and particularly moderate to severe AD significantly affect the quality of life for patients. Furthermore, AD lead to a greater loss of quality-adjusted life years compared to other autoimmune disorders, diabetes, food allergies, or heart disease. This is due to a combination of its high prevalence and substantial influence on quality of life [26].

Psychological distress as a cause of atopic dermatitis

Currently, the activation of both the central and peripheral cutaneous hypothalamic–pituitary–adrenal (HPA) axis is recognized as the molecular mediator of psychological stress, leading to significant impacts on neuroimmune reactions and skin barrier function. Dysregulation of the HPA axis was observed in individuals with AD. Prolonged exposure to psychological stress could be detrimental to both inflammation and skin barrier function [27].

Research involving both animals and humans has presented considerable proof indicating that the impact of perceived stress on inflammation in organs such as skin, is noteworthy [28]. Atopic dermatitis (AD), serving as a paradigmatic chronic inflammatory skin condition, has been pivotal in enhancing our understanding of the fundamental neuroendocrine-immune interactions. Several studies investigating the connection between increased stress and worsened inflammation in humans have shown the participation of the hypothalamus-pituitary-adrenal axis (HPA) and the sympathetic axis (SA) in forming its unique immune profile. This profile is characterized by the prominent production of pro-allergic cytokines like interleukin (IL)-4 and IL-5, driving humoral and eosinophilic inflammation and dominating the initial lesion. Subsequently, cytokines associated with cellular adaptive immunity, such as tumor necrosis factor-alpha (TNFα) and interferon-gamma (IFNγ) elevate [29,30,31,32,33,34,35]. Furthermore, a considerable body of research, primarily conducted in animal experimental models using inbred mice, demonstrated the involvement of neurotrophin- and neuropeptide-dependent neurogenic inflammation in the stress-induced exacerbation of allergic flares [36,37,38,39]. This innate immune response contributes to approximately 50% of stress-induced worsening of skin inflammation in mice with experimentally induced allergic dermatitis [40,41]. These foundational research findings support the notion that maladaptive neuroendocrine-immune interaction serves as a potent factor in stress-induced worsening of AD.

Psychological distress as an effect of atopic dermatitis.

Severe itching, frequent sleep disturbances, stigmatization, social isolation, reduced quality of life and neuroinflammation have a potential to elevate the level of anxiety, depression or

suicidal thoughts in individuals with AD. Studies linked sleep disturbances in AD to various adverse outcomes such as headaches [42], shorter height in children [43], decreased quality of life in both children and adults [10, 18, 19, 44], heightened risk of fractures and other injuries as well as higher risk of cardiovascular diseases in adults [45]. Tiredness and disruptions in sleep patterns could potentially heighten the likelihood of, or have a shared underlying mechanism with, anxiety or depression. The sleep disruptions observed in AD may be linked to persistent itching, inflammation [46, 47], and the extent of atopy [48]. Additionally, AD might enhance the expression of neuroimmune factors, including sensitivity induced by neuropeptides [49] and inflammatory cytokines, contributing to the subsequent onset of mental health disorders [50, 51]. Further research is essential to fully understand the precise connections between AD, anxiety, depression.

Recent systematic reviews and meta-analyses delved into the connection between AD and mental health issues, specifically depression, suicidality, and anxiety. Heightened likelihood of AD was observed in adults with depression and anxiety, children with depression, and adults and adolescents with suicidality [52]. The second review, comprising 36 studies with adequate data, disclosed that 20.1% of individuals with AD experienced depression, in contrast to 14.8% in those without AD [53]. In the United States, around 1 in 5 adults with AD met criteria for major depressive disorder or received a depression diagnosis in the preceding year [54]. Moreover, individuals with AD displayed elevated rates of clinical depression, numerically higher antidepressant usage, and significantly increased rates of suicidality in adults. Depression was notably prevalent in cases of moderate to severe AD, with a higher occurrence in adults. Children with AD also exhibited a higher prevalence of parental depression [53].

Some studies suggested that diverse AD treatment approaches ameliorated depressive symptoms. The outcomes suggest a direct association between depressive symptoms in AD and disease severity, implying modifiability with enhanced AD treatments [55, 56, 57].

AD was linked to higher overall rates of depressive symptoms (22.2% vs 14.5%), encompassing feelings of hopelessness, fatigue, poor appetite, negative self-perception, difficulty concentrating, and contemplation of death [53,54].

Subsequent population-based study of 2893 adults with vs without AD in the United States revealed heightened prevalences of abnormal anxiety and depression subscores in adults with

AD. Notably, a considerable percentage (13%-55%) of adults with AD and abnormal anxiety or depression scores reported lacking formal diagnoses [58].

These collective studies suggest that anxiety and depression are symptomatic of AD, correlating with disease severity and potentially amenable to treatment, yet clinicians frequently overlook these aspects.

Cognitive behavioural therapy (CBT) as a promising tool for patients with atopic dermatitis.

Erik Hedman-Lagerlöf et al. conducted a randomized controlled trial with the involvement of 102 patients with AD from Sweden. Research participants underwent internet-delivered CBT, lasting 12 weeks. The results of this study turned out to be very promising. Individuals who received CBT online experienced a considerably greater weekly reduction in symptoms related to atopic dermatitis, compared to the control group. Subsequent analyses revealed that internet-delivered CBT also brought about significant decreases in itch intensity, perceived stress, sleep difficulties, and depression. Moreover, these improvments were sustained even at the 12-month follow-up [59]. In 2022, a review was conducted on the role of CBT in the treatment of skin dermatoses, including atopic dermatitis. Data regarding the effectiveness of CBT in atopic dermatitis was especially powerful, contrasted to other skin conditions [60]. Due to this data, CBT has a chance to become a significant part of treatment for patients with AD.

Summary

Atopic dermatitis and psychological distress mutually influence each other, diminishing the quality of life in patients struggling with this condition. It is essential to continually raise awareness among healthcare workers regarding this topic so they could help patients more effectively. Management of atopic dermatitis should not only include pharmacological therapy but also offer psychological support, providing the patients an access to psychological resources in order to reduce emotional stress and develop healthy and powerful coping mechanisms e.g. by using CBT. Consequently, patients can achieve improved control of the symptoms on a daily basis, thereby increasing their quality of life. It is also important to acknowledge that anxiety and depression can be symptoms of AD per se. Due to this, more intensive approach to AD treatment, potentially involving the use of systemic agents may be necessary. Dermatologists should consider a multidisciplinary psychodermatological

approach in trating AD patients. This topic must be further explored in order to supply the utmost and comprehensive care standards for those who suffer from atopic dermatitis.

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