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CORTICOSTEROIDS AND MENTAL HEALTH: A NARRATIVE REVIEW OF NEUROPSYCHIATRIC CONSEQUENCES

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Abstract: INTRODUCTION Corticosteroids, essential steroid hormones synthesized mainly in the adrenal cortex, play critical roles in regulating metabolism, immune responses, and overall physiological functions, featuring a molecular structure that facilitates their interaction with cell membranes and cellular functions. The secretion of corticosteroids like cortisol follows a diurnal and ultradian rhythm, regulated by the hypothalamic-pituitary-adrenal (HPA) axis, ensuring daily physiological homeostasis and a rapid response to stress via increased production triggered by ACTH and various stressors. While corticosteroids are invaluable in treating inflammatory and autoimmune conditions due to their anti-inflammatory and immunosuppressive properties, their therapeutic use requires careful management to balance beneficial effects against potential adverse outcomes, including metabolic disturbances, mood changes, and increased infection risk. **OBJETIVE** To analyze and describe the main aspects of the neurological and psychiatric repercussions of chronic exposure to corticosteroids in the last years. **METHODS** This is a narrative review which included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases, using as descriptors: "Corticosteroid" AND "neuropsychiatric disorders" AND "depression" AND "neuroendocrine function" AND "corticosteroid side effects" in the last years. **RESULTS AND DISCUSSION** Long-term corticosteroid therapy is crucial for managing various chronic conditions but is associated with significant psychological and psychiatric effects that adversely affect patient quality of life, including mood disturbances, anxiety, and cognitive impairments. These effects are influenced by factors such as dosage, duration of therapy, and individual characteristics like age and pre-existing mental health conditions, necessitating tailored management strategies that integrate pharmacological treatments, psychotherapy, and lifestyle modifications. The complexity of these side effects demands vigilant monitoring and comprehensive care approaches, underscored by a need for ongoing research to explore the neurobiological mechanisms involved and to develop effective interventions tailored to the diverse needs of patients across different chronic conditions. **CONCLUSION:** Long-term corticosteroid therapy significantly impacts psychological and psychiatric health, necessitating comprehensive management strategies that include pharmacological, psychotherapeutic, and lifestyle interventions tailored to individual patient needs. Factors such as dosage, therapy duration, underlying disease, and individual characteristics like age and mental health history influence the severity of these effects, highlighting the need for personalized treatment plans and regular mental health monitoring. There is a critical need for further research, including longitudinal studies and randomized controlled trials, to better understand the psychiatric effects of corticosteroids and to develop more effective intervention strategies.
Keywords: Corticosteroids; Psychiatry; Endocrinology; Depression.

INTRODUCTION

Corticosteroids, a class of steroid hormones, are potent compounds derived from cholesterol[1]. They are predominantly synthesized in the adrenal cortex, although synthetic analogues are commonly used in clinical practice. The molecular structure of corticosteroids comprises four fused carbon rings that are modified in various ways to produce hormones such as cortisol and aldosterone[2]. These compounds are vital in regulating a range of physiological functions

including metabolism and immune response. Structurally, they are characterized by their hydrophobic nature, which allows them to readily cross cell membranes and alter cellular functions[2].

The physiology of corticosteroid secretion is tightly regulated by the hypothalamic-pituitary-adrenal (HPA) axis[3]. Cortisol, the primary glucocorticoid in humans, is secreted in a diurnal pattern, with plasma levels peaking in the early morning hours and reaching a nadir at midnight[4]. This circadian rhythm is crucial for maintaining homeostasis and preparing the body for daily activities. Additionally, the secretion of corticosteroids is subject to ultradian rhythms, which dictate that their levels fluctuate significantly throughout the day, responding rapidly to the needs of the body[4].

Stimulation of corticosteroid synthesis is triggered by various physiological and psychological stimuli[5]. The basal secretion of these hormones is maintained by adrenocorticotropic hormone (ACTH) released from the pituitary gland, but levels can rise dramatically in response to stress, trauma, or illness through increased ACTH production[5]. This adaptive response enhances the body's ability to cope with stressors by modulating inflammation and affecting metabolic processes. The capability to rapidly increase corticosteroid production is essential for survival in acute stress situations[6].

Excessive corticosteroid levels in the body, whether due to endogenous overproduction or exogenous administration, can lead to a variety of signs and symptoms[7]. These include weight gain, especially in the face, back of the neck, and abdomen, hypertension, mood swings, and increased risk of infection. Chronic exposure to high levels of corticosteroids can also lead to more severe conditions such as osteoporosis, adrenal suppression, and hyperglycemia[7]. Psychiatric manifestations, such as mania, depression, or anxiety, are not uncommon and pose significant challenges in clinical management[4,8].

The therapeutic use of corticosteroids has dramatically increased, particularly in the management of chronic inflammatory and autoimmune diseases[9]. These conditions, including rheumatoid arthritis, asthma, and systemic lupus erythematosus, benefit from the potent anti-inflammatory and immunosuppressive effects of corticosteroids[10]. However, the long-term use of these agents is a delicate balance to manage their beneficial effects against the potential for significant side effects, necessitating careful monitoring and adjustment of therapy[9,10].

OBJETIVES

To analyze and describe the main aspects of the neurological and psychiatric repercussions of chronic exposure to corticosteroids in the last years.

SECUNDARY OBJETIVES

1. To Identify Psychological and Psychiatric Changes Associated with Long-term Corticosteroid;
2 To Assess the Impact of Psychological Changes on Quality of Life;
3 To Analyze Factors Influencing Psychological and Psychiatric Outcomes;
4 To Explore Pathophysiological Mechanisms;
5 To Synthesize Clinical Guidelines.

METHODS

This is a narrative review, in which the main aspects the neurological and psychiatric repercussions of chronic exposure to corticosteroids in recent years were analyzed. The beginning of the study was carried out with theoretical training using the following databases: PubMed, sciELO and Medline, using as descriptors: "Corticosteroid" AND "neuropsychiatric disorders" AND

"depression" AND "neuroendocrine function" AND "corticosteroid side effects" in the last years. As it is a narrative review, this study does not have any risks.

Databases: This review included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases.

RESULTS AND DISCUSSION

Long-term corticosteroid therapy, indispensable for managing various chronic conditions, has been robustly linked to a spectrum of psychological and psychiatric effects that considerably impact patient quality of life. Mood disturbances, including depression and mania, are among the most prevalent psychiatric outcomes associated with corticosteroid use[11]. These mood alterations are thought to be dose-dependent, with higher doses increasing the likelihood of severe mood disorders[11]. Anxiety and cognitive impairments are also frequently observed, suggesting that steroids may disrupt emotional regulation and cognitive functions through interactions with glucocorticoid receptors. Moreover, prolonged exposure to high-dose corticosteroids may precipitate psychosis, a serious condition marked by delusions and hallucinations[12]. These diverse neuropsychiatric sequelae necessitate a comprehensive approach to monitoring and management, emphasizing the importance of early psychiatric consultation and tailored therapeutic strategies to mitigate these adverse effects[13].

Prolonged corticosteroid use significantly alters the psychological landscape of patients, markedly affecting their quality of life, daily functioning, and social interactions[14]. Psychological disturbances such as mood swings, depression, and anxiety not only undermine personal well-being but also impair social relationships and work efficiency[14]. Cognitive impairments linked to corticosteroids can disrupt daily activities and compromise decision-making abilities[15]. Additionally, the social stigma and isolation that often accompany psychiatric symptoms exacerbate these challenges, potentially leading to a deteriorative cycle of social withdrawal and increased dependency. This complexity necessitates a holistic approach to treatment that includes both psychological and pharmacological interventions to support patient resilience and functionality[15,16,17].

The susceptibility and severity of psychological and psychiatric effects in patients undergoing long-term corticosteroid therapy are influenced by multiple factors, including age, gender, dosage, duration of therapy, underlying disease, and pre-existing mental health conditions[18]. Age-related changes in drug metabolism and brain sensitivity can affect the neuropsychiatric outcomes of corticosteroid use, with elderly patients often showing increased vulnerability. Gender differences also play a role, with some evidence suggesting that women may experience more pronounced mood disturbances[19]. The dosage and duration of corticosteroid therapy are directly correlated with the risk of developing severe psychiatric symptoms. Additionally, the type of underlying disease necessitating corticosteroid treatment can influence psychiatric outcomes, with diseases involving the central nervous system posing a higher risk[20]. Patients with a history of mental health issues are at an increased risk of exacerbating their psychiatric conditions under corticosteroid therapy[20].

Corticosteroids influence mental health through complex biochemical and neurophysiological mechanisms that involve significant alterations in the neuroendocrine system, brain structure, and neurotransmitter regulation[21]. These agents exert their effects

primarily by interacting with glucocorticoid receptors, leading to wide-ranging impacts on gene expression that govern stress responses and emotional regulation[22]. Chronic exposure to corticosteroids can lead to volumetric reductions in key brain regions such as the hippocampus, crucial for memory and emotional processing. This atrophy may contribute to the cognitive deficits and mood alterations observed in patients[23]. Furthermore, corticosteroids affect neurotransmitter systems, including serotonin and dopamine, intimately tied to mood and behavior. Disruptions in these systems can manifest as depression, anxiety, and other psychiatric disorders[21,22,23].

The management of psychological and psychiatric side effects of corticosteroid therapy presents a multifaceted challenge. Pharmacological interventions often prioritize the use of selective serotonin reuptake inhibitors (SSRIs) and mood stabilizers, which have shown efficacy in mitigating mood disturbances and depressive symptoms commonly associated with corticosteroid use[24]. Psychotherapy and counseling are integral, providing a supportive framework that addresses the cognitive and emotional aspects of coping with chronic illness[25]. Lifestyle modifications, including regular physical activity and dietary adjustments, are recommended to enhance overall mental health and mitigate some of the mood instability induced by steroids[26]. A comprehensive approach that integrates these strategies tailored to individual patient needs and conditions is crucial for improving quality of life and treatment adherence[25,26,27].

The psychological impact of long-term corticosteroid therapy varies significantly across different chronic conditions, reflecting the complex interaction between the underlying disease pathology and the pharmacological effects of corticosteroids[28]. In autoimmune diseases like systemic lupus erythematosus, patients often experience mood swings and increased anxiety, potentially exacerbated by the immune-mediated effects on the central nervous system[29]. Conversely, in chronic respiratory conditions such as asthma or COPD, the psychological burden is primarily linked to the stress of chronic symptom management and the side effects of steroids, including mood lability and cognitive changes[30]. These variations underscore the necessity for disease-specific psychosocial assessments and tailored mental health interventions to adequately address the diverse psychological needs of these patient populations[30].

Effective management of psychological and psychiatric effects in patients undergoing long-term corticosteroid therapy is essential, requiring vigilant monitoring and comprehensive intervention strategies[31]. Healthcare providers should regularly assess mental health status using validated tools. Preventive strategies should include patient education about potential side effects, timely psychiatric referrals, and consideration of corticosteroid-sparing alternatives when feasible[32]. Management may involve behavioral therapies and, if necessary, pharmacological interventions such as antidepressants or mood stabilizers[33]. Regular follow-up appointments should be scheduled to adjust treatment plans based on psychiatric evaluations, enhancing patient quality of life and treatment adherence[30,32,34].

Significant gaps remain in the research concerning the long-term psychological and psychiatric effects of chronic corticosteroid therapy[35,36]. Notably, longitudinal studies are scarce, and the long-term mood and cognitive impacts of such treatments are not well-documented[37]. Future research should focus on prospective cohort studies to assess the incidence and progression of

psychiatric symptoms over time in patients under prolonged corticosteroid therapy[38]. Additionally, there is a critical need for randomized controlled trials (RCTs) to evaluate the efficacy of various preventive and therapeutic strategies, such as cognitive-behavioral therapy and mindfulness-based stress reduction, in patients receiving corticosteroids[39]. Investigating the role of genetic predisposition to steroid-induced psychopathology could further refine patient risk profiles and personalize treatment approaches[40]. Enhancing our understanding of the neurobiological mechanisms underpinning steroid-induced psychiatric disorders through advanced imaging techniques could also illuminate new therapeutic targets[41,42].

CONCLUSION

The psychological and psychiatric impacts of long-term corticosteroid therapy are substantial and multifaceted, affecting a wide range of patients with chronic conditions. The adverse effects, including mood disturbances, anxiety, cognitive impairments, and, in severe cases, psychosis, are influenced by numerous factors such as dosage, duration of therapy, underlying medical conditions, and individual patient characteristics including age and pre-existing mental health status. The neurophysiological and biochemical mechanisms underlying these effects involve alterations in neuroendocrine function, changes in brain structure, and disruptions in neurotransmitter systems, particularly involving glucocorticoid receptors which play a pivotal role in stress response and emotional regulation.

Effective management of these side effects requires a holistic, multidisciplinary approach that includes not only pharmacological interventions, such as the use of SSRIs and mood stabilizers, but also psychotherapy, patient education, lifestyle modifications, and regular monitoring of mental health status. It is crucial for healthcare providers to implement comprehensive strategies that are tailored to the specific needs of each patient, taking into consideration the type of chronic condition being treated and the unique psychosocial challenges that come with it.

Despite significant advances in our understanding of the psychiatric sequelae of corticosteroid therapy, there remain considerable gaps in research, particularly in long-term studies and in trials evaluating the efficacy of various therapeutic and preventive strategies. Future research should focus on longitudinal studies to better understand the progression of psychiatric symptoms in corticosteroid-treated patients and explore the potential genetic predispositions to these effects. Additionally, more randomized controlled trials are needed to assess the effectiveness of non-pharmacological interventions such as cognitive-behavioral therapy and mindfulness practices. Enhanced understanding of the neurobiological mechanisms through advanced imaging and genomic studies could also offer new insights into personalized treatment approaches, ultimately improving patient outcomes and quality of life for those requiring long-term corticosteroid therapy.

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