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Research Article

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Glucocorticoids-associated depressive symptoms on systemic lupus erythematosus patients: A drug factor or, in fact, a need for psychological care?

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ABSTRACT

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease of autoimmune nature, it can affects multiple organs and systems of unknown etiology, occurring more frequently in women of childbearing age and greater proportionality in relation to males. This study followed 57 patients suffering from SLE and assessed the possible therapeutic implications for use of glucocorticoids by these patients associated with depressive symptoms. From the data collected on the various drugs recommended for SLE patients' treatment, we found that about 80% of patients used at least one glucocorticoid. The results in our study demonstrate the relevance of depressive symptoms in SLE patients using glucocorticoids and thereby confirm that the pharmaceutical care, pharmacovigilance, and psychological care are of vital importance in conducting the safe and effective use of these drugs and in psychological support to these patients.

Keywords: Glucocorticoids; Systemic Lupus Erythematosus; Depressive symptoms

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease, which affects multiple organs and systems. It evolves with several clinical manifestations and presents with periods of exacerbations and remissions. The lesions may occur in the following tissues: cutaneous, articulation, pulmonary, cardiac, of the renal system, gastrointestinal, hematological, blood vessels, lymph nodes, eyes, endocrine changes, and can also affect the central nervous system (CNS), called the neurolupus [1].

Its etiology is still unknown, although it presents immunological links, the development of the disease is related to multifactorial aspects, genetic predisposition, hormonal, environmental, and infectious factors, which seem to be related to the loss of immunological tolerance [2].

It can occur in people of all ages, it is more frequent however in young women. Epidemiological data shows a higher frequency of the disease in women of fertile age, with an estimated frequency of the order of 5 to 10 women proportionally to each man [3], manifesting in any race, but being more prevalent in black women than white [4,5]. Epidemiological studies have been conducted in the United States and showed a prevailing average of the disease which varies from 14.6 to 122 cases per 100 thousand inhabitants [5-7].

SLE affects people of all social classes. Many of them face difficulties in obtaining a diagnosis (confirmation of the

disease) since its onset may occur with different manifestations causing visits to countless doctors until one of them suspects SLE and begins adequate treatment. This entails a level of stress and depression which only causes the disease to undergo periods of exacerbation and cause the SLE patient to be discouraged.

Glucocorticoids are widely used drugs due to their immunosuppressant and anti-inflammatory effects in the treatment of many rheumatic diseases, in addition to other inflammatory diseases [8, 9]. Cortisol is the main natural glucocorticoid circulating in humans, its synthesis is regulated by the adrenocorticotropic hormone (ACTH), secreted by the anterior pituitary in response to the release by the hypothalamus of the neuropeptide known as the corticotrophin releasing hormone (CRH), acting on receptors in different tissues, such as those present in the hypothalamus and pituitary, inhibiting the release of CRH and ACTH.

Glucocorticoids act on the cellular and physiological level and on the cardiovascular system. Several studies have demonstrated the undesirable effects of its prolonged usage, e.g., dyslipidemia and hypertension, changes in; behavior, cognitive function, memory and mood, gastrointestinal bleeding and pancreatitis; immunosuppression and activation of latent viral infections, cutaneous atrophy, erythema, hypertrichosis, perioral dermatitis, delay in healing and petechiae; cataracts and glaucoma, as well as, increased sodium retention and potassium excretion [10, 11].

It is important that orientation and pharmaceutical attention be given to the patient regarding the disease. These measures are of great importance, allowing the patient to have a better quality of life [12]. Such education aims to inform patients and their relatives: the nature of the disease, its evolution, the importance of proper diet, protection from the sun, regular physical activity (even when the disease is not active), the need to comply with the measures established by the doctor, the psychological support, which is indispensable in order to transmit optimism and motivation for the treatment, besides stimulating life projects for these people, about the risks of this pathology, the resources available for diagnosis, treatment, and the rights of the SLE patient.

EXPERIMENTAL SECTION

The SLE patients included in this study were assisted by Unified Health System (SUS), Brazil's publicly funded health care system, and attended at the General University Hospital (HGU) or at the Júlio Muller University Hospital (HUJM) located in the city of Cuiabá, the capital of the state of Mato Grosso, Brazil. The Brazilian Unified Health System represents one of the main options for the care of SLE patients all over Brazil, and, in many places, it is the only option. The patients were observed during a one year period. The participation of the patients was voluntary upon the signing of an informed consent form. All patients were guaranteed monthly treatment, and clinical, biochemical, and psychological follow-ups, conducted in groups, or individually when necessary. Based on the inferences suggested by the American College of Rheumatology, in item 19, in which it describes definitions, diagnostic criteria for peripheral syndromes of the nervous system observed in SLE [13].

The observation was conducted with 57 (fifty-seven) patients having a confirmed diagnosis of SLE, which has been performed by means of an intermediary clinical exam and by laboratorial diagnosis according to the Protocol of the Brazilian Rheumatology Society [14].

Anamnesis and initial evaluation of all patients participating in the study were performed, in order to trace a, clinical, laboratorial, and psychological profile for follow-up during the first consultation. Questionnaires were also administered for the identification of pharmaceuticals used by the patients.

As a factor of exclusion from the lupus patient study, the criterion that the patient should not be taking any kind of estrogen at the time of the initial evaluation was adopted. Patients who missed the monthly check up for two consecutive months would also be excluded from the study.

The treatment of SLE patients was individualized, varying according to the degree of impairment of each patient, and, as established in Clinical Protocols and Therapeutic Guidelines of the State of Mato Grosso Health Department, the following classes of drugs have been used: antimalarial (hydroxychloroquine sulfate), glucocorticoids (prednisone, methylprednisolone, triamcinolone hexacetonide), immunosuppressants (azathioprine, methotrexate, cyclosporine, cyclophosphamide and mycophenolate mofetil).

RESULTS AND DISCUSSION

The 57 patients with SLE under observation in the study were all of the female gender. We found that close to 80% of these patients used at least one glucocorticoid (prednisone) and that a large number of them presented with emotional disturbances and disturbances of the CNS. Upon inquiry regarding when the symptoms appeared, the

answers obtained evidenced that these symptoms coincided with the prolonged use of glucocorticoids.

The most common symptoms were the presence of depressive states, lack of interest, unhappiness, despondency, lack of desire to work, or to interact with people. Furthermore, patients reported feeling despised by friends and family, devaluing themselves, feeling incapable of performing activities, useless, feelings of humiliation, some reported the onset of convulsions and deliriums. It is known that emotional factors are closely linked to this disease and that negative emotions may contribute to periods of exacerbation of SLE.

The use of glucocorticoid is not exempt of adverse effects, especially when used indiscriminately in high doses and for longer periods. Among the reported effects, mood swings are relatively well pronounced amongst patients.

Neurological and psychiatric presentations can occur among SLE patients by the disease process. 91.6% of neuropsychiatric SLE events affect CNS [15]. The CNS is considered to be one of the most compromised systems, and commonly affected in both children and adults with SLE, generating neurological symptoms, convulsions, migraines, and psychosis [16].

In patients with normal adrenal function, it produces slight euphoria, irritability, increased motor activity, and insomnia. Patients with chronic use of glucocorticoid are being associated with symptoms such as depression, hallucinations and deliriums. However, acute use may be more associated with maniacal symptoms [17, 18]. Studies show that approximately 2% of patients receiving dosages equivalent to or lower than 40mg/day developed psychiatric symptoms, while 6% of those receiving 41-80 mg / day and 18, 4% of those who received more than 80mg/day [19]. Chau and Mok [20] discuss the relationship between the probabilities of the onset of psychotic symptoms in the presence of hypoalbuminemia.

The results found in our study demonstrate the relevance of depression in lupus patients and corroborate with the results of other studies, which show that about 60% of patients present with depressive symptoms. The etiology in SLE can be attributed to numerous factors, among which are: cerebral dysfunction, the dysfunction of organs and systems, the iatrogenic effects from the use of corticosteroids and the biopsychosocial stressors. The combination of physical, social, and environmental factors and those related to drugs, puts the lupus patient at high risk of developing psychic alterations having seen the relationship between LES and the mental deterioration or sufferings [21]. Normally the depressive state occurs as a feeling of sadness and emptiness, not all patients however, report signs of sadness. Overall, many report the lack of will to perform and pleasure in performing activities in general. According to Del Porto [22], depression can be triggered by the use of certain medications in comorbidity with the disease, being that SLE and rheumatoid arthritis appear to be associated with depressive symptoms, indicating corticosteroids as pharmacological agents associated with these symptoms.

Several authors [23-25] have said that during clinical practice and during the progression of the disease, the psychosis reported by patients with SLE observed and monitored in their studies, is primary or secondary to the use of corticosteroids. Those with primary psychosis were characterized by having antiphospholipid antibodies and manifestations of the CNS. Although laboratory parameters such as the anti-P antibody are very useful for the diagnosis of SLE, this routine does not occur in the majority of cases. It is for this reason that the differentiation of corticosteroid-induced primary psychosis is important. This class of drugs when in the bloodstream binds to the plasma proteins, such as albumin, thereby becoming inactive. Elevated levels of corticosteroids in its free form could be related to hypoalbuminemia, which may justify the higher side effects in patients.

The treatment of psychological disorders is still controversial, generally the disappearance of symptoms improves or disappears with the replacement or suspension of the drug. In some patients however chronic therapy is indispensable, therefore pharmacological options should be considered to reverse the symptoms, but not so that these will result in the worsening of the clinical condition of the patient, seeing as most SLE patients have renal dysfunction, which may cause a low elimination rate of the drug thus increasing the chances of poisoning.

CONCLUSION

A review of the literature shows that several studies have demonstrated the interrelationship between the onset of side effects and the drugs involved in the treatment of SLE, including immunosuppressants and glucocorticoids. However, based on the results obtained in our study and those found in the literature it cannot be definitively concluded that these drugs are exclusively and directly responsible for the depressive states presented by the patients observed or if the association of the psychological factors to the drug factor, unique to each lupus patient causes them to have the lowest threshold for the development of depressive symptoms.

Whatever the primary factor is, the results found in our study evidence the relevance of depressive symptoms in lupus patients using glucocorticoids and therefore confirm that effective monitoring of these patients by pharmaceutical attention and psychological care are indispensable to conducting the safe and effective use of glucocorticoids. Thus, the pharmaceutical and psychological assistances should effectively be implemented to ensure conditions for the promotion, protection and recovery of the health of SLE patients.

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