GLUCOCORTICOID-INDUCED OSTEOPOROSIS

https://doi.org/10.56238/levv15n40-001

Vanessa Siqueira Batista de Oliveira[1], Allini Pereira da Silva Dantas[2], Vanessa Aline Camargo Lira Sodré[3], Raissa Gonçalves Rincon[4], Lara Medeiros de Souza[5], Leonardo Bernardes da Silva[6], Felipe da Silva Lopes[7], Bruno Graziano de Almeida Migliavacca[8], Carolina Alves dos Santos[9], Marcella Motão Ribeiro[10], Matheus Graciano Dias[11], José Francisco das Neves Júnior[12], Thalita Gomes de Sousa Fachinelli[13], Bruna Neres Moreira da Fonseca[14], Beatriz Santos Cordeiro[15].

[1] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
Email: Vanessa.siqueiraa11@gmail.com
[2] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: allini.dantas@medicina.uniceplac.edu.br
[3] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
Email: vanessasodre77@gmail.com
[4] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: Raissarincon.rr@gmail.com
[5] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
Email: lara.souza@medicina.uniceplac.edu.br
[6] Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
[7] Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: felipelopest18@gmail.com
[8] Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: brunograzianoam@gmail.com
[9] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: carolina.santos@medicina.uniceplac.edu.br
[10] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
Email: marcellamr95@gmail.com
[11] Graduating from Medicine
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: matheusmgdmed@gmail.com
[12] Graduating from Medicine
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: juniorjose1020@gmail.com
[13] Graduating from Medicine
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: thalita.fachinelli@medicina.uniceplac.edu.br
[14] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: Bruna_neres@hotmail.com
[15] Medical Graduate
Apparecido dos Santos Central Plateau University Center, Brasília, DF, Brazil
E-mail: beatriz.cordeiro1@gmail.com

ABSTRACT
Cushing's Syndrome (CS) is a disorder caused by excess cortisol in the blood, which can be exogenous (due to the use of glucocorticoids) or endogenous (due to dysfunctions in the adrenal glands or pituitary gland). This condition is associated with several morbidities, including hypertension, visceral obesity and, especially, osteoporosis, caused by the inhibition of the function of osteoblasts, responsible for bone formation. The narrative review seeks to understand the relationship between the prolonged use of glucocorticoids and the development of osteoporosis.

Keywords: Osteoporosis, Glucocorticoid, Cushing's Syndrome.

INTRODUCTION

Cushing's syndrome or hypercortisolism is a disorder that encompasses a set of signs and symptoms caused by high levels of cortisol in the blood. This hormonal excess can be caused by synthetic hormones, called exogenous CS, also called iatrogenic, or by diseases involving the adrenal gland and the pituitary gland, which is called endogenous CS. Normally, CRH (corticotrophin-releasing hormone) released by the hypothalamus stimulates the release of ACTH (adrenocorticotropic hormone) by the pituitary gland, which, when it reaches the adrenal, leads to the production of cortisol. Endogenous CS is often caused by small local tumors that lead to increased ACTH secretion (pituitary or ectopic) or an increase in adrenal production. Endogenous CS is a rare disease, reaching 1 case per 100,000 inhabitants/year (LIBERMAN, 2003).

The most common etiology of exogenous CS is prolonged or high-dose therapeutic administration of GC, which can occur with the use of practically all presentations of these drugs, such as topical, inhalational and, especially, oral routes (FAIÇAL; UEHARA, 1998).

Cushing's syndrome is associated with several morbidities, the most specific of which are: arterial hypertension, visceral obesity and osteoporosis. Bone loss is one of the most important side effects of glucocorticoid use, even at low doses and its main effect on bone is the inhibition of osteoblast function, leading to a decrease in bone formation. (FINDLING; RAFF, 2003).

Osteoporosis can be classified as primary when it results from the natural process of menopause or aging and secondary when it results from another cause such as inflammatory disease, metabolic alteration or the use of medications that result in bone loss (CHAVASSIEUX et al., 2000).

Chronic hypercortisolism is the most frequent cause of secondary osteoporosis, mainly affecting the trabecular bone. Approximately 30-35% of patients with CS have compression fractures of the vertebrae and the risk of femoral neck fractures is increased by 50% in this population (PAULA et al., 2006).

OBJECTIVE

To conduct a broad integrative review of studies involving the effects of glucocorticoids in patients with hypercortisolism and the induction of the development of osteoporosis. In order to discuss the connection between the two pathologies. Thus, it will be possible to understand how to manage a patient currently prescribed or about to start glucocorticoid therapy in order to ensure bone health.

METHODOLOGY

This is a narrative-integrative literature review, of an exploratory nature, which, through analysis and interpretation of the existing scientific production, systematized scientific knowledge about the existence of the relationship between the use of glucocorticoids and osteoporosis.

The search was carried out in the PUBMED, ELSEVIER, MEDLINE, BVS, Scielo and LILACS databases. The keywords used for the research will be: glucocorticoids, hypercortisolism, Cushing's syndrome, osteoporosis, in Portuguese and English. The inclusion criteria were: original publications in Portuguese and English, which adopted a quantitative and qualitative approach, considering the objective of the study. The exclusion criteria were: repeated articles, reviews, theses, editorials that did not directly address the theme, and other articles that associated other techniques together.

RESULTS

Two types of bones make up the human skeleton: the cortical bone, and the trabecular bone. These are in a dynamic state, marked by a continuous process of formation and resorption, that is, bone remodeling, which is the alternation of bone formation performed by osteoblasts with resorption performed by osteoclasts occurring in a coupled manner. (LUKERT; RAISZ, 1994). And the administration of GC can affect the biology of bone formation causing a drop in bone mass. (KONIG; GRIGG, 1998).

With GC therapy, biphasic bone loss occurs, a rapid initial phase of loss, about 12-20% during the first few months, followed by a slower phase with bone loss around 2-5% annually. (LUKERT; RAISZ, 1994). Bone loss occurs in both trabecular and cortical bone. There is a predilection for trabecular bone, which is metabolically more active, so that fractures of vertebrae, ribs, and epiphyses of long bones are common manifestations of GC-induced osteoporosis (MANOLAGAS; WEINSTEIN, 1999).

GCs affect bone formation by suppressing the number, function, and half-life of osteoblasts. Histomorphometric studies have shown that these drugs reduce bone formation with a decrease in the number of osteoid matrix, a reduction in the rate of mineral apposition and trabecular thickness (LUKERT; RAISZ, 1994).

CONCLUSION

The effects of glucocorticoids on bone tissue and the induction of osteoporosis are widely described in the literature. GCs have a broad spectrum for the treatment of various diseases and most pathologies treatable with GCs require prolonged treatments, thus

leading to side effects, such as in Cushing's syndrome. Therefore, it is recommended that patients with DS who are currently prescribed or about to start glucocorticoid therapy be evaluated for risk factors for osteoporosis and counseled on lifestyle modification tactics to reduce risks, such as quitting smoking and alcohol consumption, reducing caffeine intake, participating in weight-bearing activities, and taking precautions to reduce the risk of falls.

In addition, it is necessary to initiate prophylaxis or institute treatment of osteoporosis induced by these drugs, such as the use of bisphosphonates, which are the first choice of pharmacological intervention for the prevention and treatment of glucocorticoid-induced osteoporosis, in order to minimize bone loss that occurs in these patients.

Both the American College of Rheumatology and the International Osteoporosis Foundation recommend modulating the treatment of glucocorticoid-induced exogenous osteoporosis (GIO) based on the individual fracture risk profile (calculated by FRAX) and the glucocorticoid dose used, but it is difficult to translate corticosteroid dosages into different degrees of endogenous hypercortisolism, and there are no data on the validation of the FRAX stratification method in patients with hypercortisolism endogenous. Consequently, it is unclear whether such recommendations can be adapted to patients with endogenous hypercortisolism. Thus, the correction of coexisting risk factors, which may contribute to increase the risk of fracture in patients exposed to excess glucocorticoids, and the institution of prophylaxis and treatment with bisphosphonates may lead to improved bone health.

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