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Original Article

Biometric, histomorphometric, and biochemical profile in atorvastatin calcium treatment of female rats with dexamethasone-induced osteoporosis☆

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ABSTRACT

Objective: To assess the effects of atorvastatin calcium in the treatment of dexamethasone-induced osteoporosis.

Methods: Osteoporosis induction consisted of the administration of an intramuscular dose of 7.5 mg/kg of body weight of dexamethasone, once a week for four weeks, except for the control animals (G1). The animals were divided into the following groups: G1 (control group without osteoporosis), G2 (control group with untreated osteoporosis), G3 (control group with osteoporosis treated with sodium alendronate 0.2 mg/kg) and G4 (group with osteoporosis treated with atorvastatin calcium 1.2 mg/kg). Serum alkaline phosphatase, bone alkaline phosphatase, and biometric and bone histomorphometric assessments were performed after 30 and 60 days of treatment onset.

Results: In relation to the biometric and histomorphometric analyses, at 60 days of treatment, G4 presented bone density (Seedor index), bone trabecular density, and cortical thickness of 0.222 ± 0.004 g/cm, $59.167 \pm 2.401\%$, and $387{,}501 \pm 8573$ μm, respectively, with a positive and statistically significant difference ($p < 0.05$), in relation to G2. At 30 and 60 days of treatment, G4 presented statistically significant serum levels of alkaline phosphatase alkaline phosphatase ($p < 0.05$) that were higher than all groups (7.451 ± 0.173 μg/L and 7.473 ± 0.529 μg/L, respectively).

Conclusion: Treatment with atorvastatin calcium demonstrated the ability of this drug to increase osteoblastic activity and bone tissue repair activity, acting differently from alendronate sodium, which demonstrated predominantly antirebsorptive activity.

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Perfil biométrico, histomorfométrico e bioquímico no tratamento com atorvastatina cálcica de ratas com osteoporose induzida com dexametasona

Palavras-chave:
Glicocorticóide
Difosfonatos
Alendronato
Fosfatase alcalina
Histomorfometria óssea

RESUMO

Objetivo: Avaliar os efeitos da atorvastatina cálcica no tratamento da osteoporose induzida com dexametasona.

Métodos: A indução da osteoporose consistiu na administração de dexametasona na dose de 7,5 mg/kg de peso corporal, por *via* intramuscular, uma vez por semana durante quatro semanas, à exceção dos animais do grupo controle (G1). Os animais foram distribuídos nos seguintes grupos: G1 (grupo controle sem osteoporose), G2 (grupo controle com osteoporose sem tratamento), G3 (grupo controle com osteoporose tratado com alendronato de sódio 0,2 mg/kg) e G4 (grupo com osteoporose tratado com atorvastatina cálcica 1,2 mg/kg). Após 30 e 60 dias do início do tratamento dos animais, foram feitas as dosagens dos níveis séricos de fosfatase alcalina, fosfatase alcalina óssea, avaliação biométrica e histomorfométrica óssea.

Resultados: Em relação às análises biométricas e histomorfométricas, aos 60 dias de tratamento o G4 apresentou densidade óssea (índice Seedor), densidade trabecular óssea e espessura da cortical de 0,222 ± 0,004 g/cm, 59,167 ± 2,401% e 387,501 ± 8,573 μm, respectivamente, com diferença positiva, estatisticamente significativa ($p < 0,05$), em relação ao grupo G2. Aos 30 e 60 dias de tratamento, o G4 apresentou níveis séricos de fosfatase alcalina óssea estatisticamente significativos ($p < 0,05$) e superiores a todos os grupos (7,451 ± 0,173 μg/L e 7,473 ± 0,529 μg/L, respectivamente).

Conclusão: O tratamento com atorvastatina cálcica demonstrou a capacidade desse fármaco de aumentar a atividade osteoblástica e a atividade reparadora tecidual óssea, atuar de forma diferente do alendronato de sódio, que demonstrou atividade preponderantemente antirreabsortiva.

Introduction

Glucocorticoid-induced osteoporosis is a serious and common complication in prolonged treatments with these drugs. A decrease in bone formation and an increase in its resorption are commonly observed in these cases.[1]

This is a progressive disease that courses with the structural deterioration of bone tissue, leading to fragility and increased susceptibility to fractures caused by bone mass reduction and increased bone turnover.[2]

The treatment of glucocorticoid-induced osteoporosis aims at avoiding future fractures that decrease the quality of life. Bisphosphonates, among them alendronate sodium, act predominantly by inhibiting the resorption of bone tissue and are currently used in anti-osteoporosis drug therapies.[2,3]

According to Drake et al.,[4] alendronate sodium is approved for clinical use in the prevention and treatment of glucocorticoid-induced osteoporosis; its efficacy is higher when vitamin D and calcium levels are adequate.

Alendronate sodium has been reported to reduce bone loss in patients treated with moderate to high doses of prednisone for heterogeneous conditions.[3,5]

However, alendronate sodium, despite reducing the incidence of fractures, does not lead to bone formation gains. Moreover, its prolonged use has shown several side effects, such as subtrochanteric femoral fractures, mandible osteonecrosis, and esophageal irritation, among others, hindering patient adherence to treatment.[4,6]

In a dyslipidemia model with ovariectomized rats, Lin et al.[7] found that atorvastatin, clinically used in the treatment of dyslipidemias, not only decreased serum lipid levels but also promoted biomechanical bone improvement and increased collagen in the bone tissue.

Some recent studies have reported the role of statins in bone formation by stimulating the expression of bone morphogenetic protein (BMP)-2, which leads to osteoblastic differentiation and consequent bone formation. An increase in the transcription of the BMP-2 gene was observed, which is probably responsible for its effects.[8]

Based on these findings, it is believed that statins, if selectively directed to the bone, could have beneficial effects in the treatment of osteoporosis and fractures. These observations have aroused great interest in the scientific community; several studies have been conducted, demonstrating the role of statins in the improvement of bone density and in the reduction of the number of fractures.[9]

The present study is aimed at assessing, through biometric and bone histomorphometric evaluation, as well as biochemical markers, the effects of atorvastatin calcium in female rats with dexamethasone-induced osteoporosis.

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