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Effects of raloxifene on development of the methotrexate-induced changes in bone mechanical properties of male rats

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Abstract:
Methotrexate, a cytostatic and immunosuppressive drug, has been reported to deteriorate the osseous system. Raloxifene, a selective estrogen receptor modulator, is used in the prevention and treatment of postmenopausal osteoporosis. There is a lack of data on possible ways of preventing the unwanted skeletal effects of prolonged immunosuppressive therapy. The aim of the present study was to investigate the effects of raloxifene on mechanical properties of the femur in male rats administered methotrexate.
The experiments were carried out on mature male Wistar rats, which were divided into 6 groups: controls, rats administered raloxifene hydrochloride (5 mg/kg *po*), rats administered methotrexate (0.5 mg/kg *po* or *im*), and rats administered raloxifene hydrochloride (5 mg/kg *po*) plus methotrexate (0.5 mg/kg *po* or *im*). Raloxifene was administered for 28 days and methothrexate was administered for the first 10 days of the experiment. After 28 days of drug administration, mechanical parameters of the whole femur were determined: the extrinsic stiffness, the ultimate load and the breaking load, deformation caused by the ultimate and breaking loads, and the load causing fracture of the femoral neck. Additionally, the mass of isolated femurs and their mineral and calcium content were determined.
Intragastrically or intramuscularly administered methotrexate impaired the endurance of the tested bones. Administration of raloxifene alone had no significant effects on the mechanical parameters of the femur. Administration of raloxifene resulted in a reduction of the adverse changes in the osseous system induced by methotrexate.
Concluding, the experiments demonstrated a protective action of raloxifene against the effects of methotrexate on the osseous system in male rats.

Key words:
femur, male rats, methotrexate, raloxifene