

EFFECTS OF SIMVASTATIN ON THE DEVELOPMENT OF OSTEOPENIA CAUSED BY OVARIECTOMY IN RATS

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Simvastatin is a competitive inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-determining enzyme for cholesterol synthesis which is used in the treatment of hypercholesterolemias, particularly in type IIa and IIb hyperlipoproteinemias, frequently in postmenopausal women. Inhibition of cholesterol synthesis by simvastatin may cause disorders of bone remodelling.

The aim of the present study was to investigate the effects of simvastatin (3 mg and 6 mg/kg/day *per os*) administered for 4 weeks on the development of ovariectomy-induced osteopenia in 3-month-old female Wistar rats. The experiments were carried out on six groups of animals: I (C) – sham operated rats, II (S-3) – sham operated rats + simvastatin 3 mg/kg/day *po*, III (S-6) – sham operated rats + simvastatin 6 mg/kg/day *po*, IV (OVX) – ovariectomized rats, V (OVX + S-3) – ovariectomized rats + simvastatin 3 mg/kg/day *po*, VI (OVX + S-6) – ovariectomized rats + simvastatin 6 mg/kg/day *po*. In all the groups, we examined body weight gain, and macrometrical, histomorphometrical and mechanical parameters.

Bilateral ovariectomy induced osteopenic skeletal changes in mature female rats. In cortical bone, ovariectomy intensified resorption processes at the marrow cavity, as indicated by a decrease in endosteal transverse growth and an increase in transverse cross-section surface area of the marrow cavity in the tibia. Intensification of resorption processes was observed in cancellous bone (a statistically significant decrease in the width of trabeculae in the epiphysis and metaphysis of the femur). Structural changes in the long bones resulting from bilateral ovariectomy were manifested by deterioration of mechanical properties of the shaft and neck of the femur. The force needed to fracture the neck and shaft of the femur was significantly smaller than that in sham operated rats. Simvastatin (3 and 6 mg/kg/day *po*) slightly influenced bone remodelling in sham operated rats. Simvastatin (3 and 6 mg/kg *po* daily) administered to ovariectomized rats intensified bone formation processes and decreased bone resorption processes induced by bilateral ovariectomy, showing stronger activity at 6 mg/kg.

Key words: *simvastatin, bone, ovariectomy, rats, osteopenia*

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