CHANGES AND THEIR REGRESSION IN THE OSSEOUS SYSTEM IN RATS AFTER ADMINISTERING A CYTOSTATIC DRUG INHIBITING TUMOR CELL DIVISION IN THE PHASE OF DNA SYNTHESIS

Urszula Cegiela, Maria Pytlik, Waldemar Janiec

Department of Pharmacology, Silesian Medical University, Inglitównska 4, PL-41-200 Sosnowiec, Poland


Chemotherapeutic drugs may disturb the bone tissue metabolism and cause osteopenia, however, the pathomechanism of the damaging effect of cytostatics on this tissue has not been well recognized so far. The detrimental effect may result from a direct cytotoxic action of these drugs on cells remodeling the bone, or on osteogenic cells present in the bone and in the bone marrow, or may be the result of hormonal disorder caused by impaired function of gonads.

The aim of this study was to investigate the in vivo effect of 5-fluorouracil (5-FU), a cytostatic agent which inhibits tumor cell division in the phase of DNA synthesis, on the bone remodeling in rats and to examine whether the period of 4 weeks was sufficient for regression of changes elicited by administering 5-FU. Changes in the bone tissue following administration of 5-FU and their regression were evaluated by assessing macrometric and histomorphometric parameters as well as of mechanical properties of the femur.

The tests were carried out on male Wistar rats. 5-FU was administered at the doses: 30 mg/kg per os (po) daily for 5 days every 2 weeks; 15 mg/kg im daily for 5 days every 2 weeks; 65 mg/kg im once weekly. Changes in the osseous tissue were examined 4 weeks after the first dose of 5-FU administration. Regression of the changes was examined 8 weeks after the first dose of 5-FU administration (the 5-FU was not administered between 30th and 57th day after the first dose of 5-FU administration)

As a result of our research, it was established that 5-FU disturbed the bone remodeling processes in rats, mostly by impairing the process of new bone matrix synthesis, which leads to impaired mineralization process and decreased mechanical endurance of the femur. It was also established that the period of 4 weeks was not sufficient for regression of the changes in the osseous tissue caused by 5-FU administration.

Key words: 5-fluorouracil, macrometric parameters, histomorphometric parameters, bone mechanical properties, osteopenia, bones, rats