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The biomechanical study of bone of adult rats after application of cisplatine and α-aescin

Bone is a special form of connective tissue made up of microscopic crystals of phosphates of calcium, particularly hydroxyapatites, within a matrix of collagen. The collagen in turn is organized in a complex 3-dimensional way. Because of its high calcium and phosphate content, bone plays an important role in calcium homeostasis. It protects vital organs, and the rigidity it provides permits for locomotion and the support of loads against gravity. Resistance properties of bone tissue are connected with the correct course of processes regulating mineral metabolism, particularly calcium-phosphorus metabolism. Cisplatine (cis-Diamminedichloro-platinum), being one of the cytostatics, is widely applied in the treatment of neoplasms. It is especially efficient in the treatment of cancer of ovary, testicles and others. It is an alkyling drug and its mechanism consists in joining the alkyl active radicles. During this process many functions of the cells get disturbed. The citostatics, besides having therapeutic properties, may be toxic for the normal tissues and change protein synthesis. A-aescin is a biologically active 3-terpene saponin obtained from chestnut tree. It stimulates glikorticogenesis and the function of hialuronidase and elastase enzymes.

The aim of the study was to test the selected resistance parameters of bone after application of cisplatine and after application of α-aescin as well as cisplatine coadministered with α-aescin.

MATERIAL AND METHODS

The study was carried out upon 40 albino adult male Wistar rats of body weight 290–310 g, which were divided into four experimental groups. Group I animals received intrapretitoneally cisplatine dissolved in physiological saline in doses of 0.1ml/m^2 of the body surface. Group II animals received α-aescin dissoved in physiological saline in dose 0.5ml per each 100g of body weight. Group III animals received cisplatine and α-aescin at the same time. Every day the control group animals (IV group) received physiological saline in doses of 0.25 ml per each 100 g of body weight. The experiment was carried out in three stages, each of them lasting five days. There was a 48-hour break in drug administration between the individual stages. After 56 days of experiment the animals were anaesthetised with chloroform and decapitated. Prepared femoral bones were exposed to resistance tests with the use of Instron 4302 apparatus equipped with breaking head adjusted to operation range 0•1kN as well as X-t recorder to register force-deformation interrelationship with the help of the following parameters: loading speed – 2.5mm/min, velocity of recorder tape–100mm/min. The bone

preparations positioned crosswise on two support points at most stable position were influenced by definite force once until reaching the breaking point. The values of the force needed for breaking were read on the register and they denoted the resistance of the tested bone. The results were analyzed statistically. Each measurement result was characterized by M–arithmetic mean, SD – standard deviation, SE – mean error of arithmetic mean and V – variability coefficient.

RESULTS

The studies carried out on adult male rats allowed us to evaluate mechanical resistance of femoral bone base under static loads after application of such preparations as cisplatine and α-aescin. The experiment proved that in the studied group of animals treated with cisplatine there was noticed a considerable decrease of bone resistance manifested by smaller force needed to cause the fracture as compared to the control group. In the group of animals receiving cisplatine the values of breaking force were within the range of 190.3–191.2 N and this means the decrease of resistance as compared to control group by 8.2%, and in the group receiving cisplatine and α-aescin at the same time given the values were within 193.1–194.3N – the decrease of resistance as compared to control group was smaller by 6.5%. In the control group and in the group of animals receiving α-aescin the values were approximately 205.2–209.1 N and 206.1–209.5 N (Fig.1). The differences in resistance in group I and control group are statistically significant, in group II and the control group they are not. No substantial differences in types of fractures in individually tested groups were noticed. Totally in 40 cases of fracture, 24 fractures were oblique fractures, 12 – transverse and multiple.

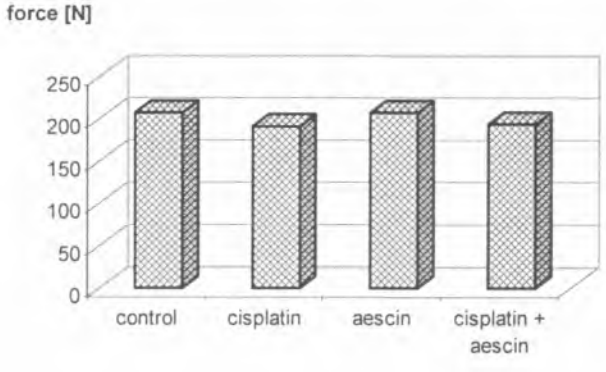

Fig. 1. Average breaking force in experimental groups

DISCUSSION

Biomechanical changes in bone resistance play an important role in many pathological conditions. All of the factors influencing directly or indirectly the metabolism of osseous tissue change significantly its biochemical parameters, including resistance to fracture under the influence of variable breaking force (2,4), and module of elasticity (1,7). Many authors

(5,9,10) emphasise the relationship between the bone microscopic structure and its mechanical strength. Chronic therapy with antineoplastic drugs changes biomechanical properties of bones (3,8). Wie et al. described the effect of cyclophosphamide upon the endurance of a healthy bone and found the decrease of its resistance to flexion of metaphysial part of femoral bone diaphysis(11). Pelker at al. analyzed the effect of methotrexate and adriamycin on bones of rats. Due to a frequent use of cisplatine in bone neoplasms or in others tumors, it seems advisible to investigate the influence of this medication upon biomechanical properties as well as upon macroscopic and microscopic structure of bones. There are references concerning a beneficial effect of solcoseryl on bone tissue while applying vincristin (6).

CONCLUSIONS

The bone is a tissue undergoing continuous changes during which bone-losing reactions are balanced with bone-formation processes. Cytostatics, like cisplatine, cause disorder of this balance leading to weakening of mechanical resistance of bones. The results of our studies on application of cisplatine indicate a negative influence of the applied preparation on the mechanical strength of femur bones in rats. On the basis of the present investigation, it may be claimed that harmful effect of cisplatine as an essential cytostatic used in chemoterapy of bone neoplasms or other tumors may not be reduced by a concomitant administration of a-aescin. Other drugs protecting bone tissue against unfavourable effect of cytostatics should be searched for.

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SUMMARY

The experiment proved that cisplatine reduces the mechanical strength of bone by 8.2% as compared to the control group. No significant difference in the increase of bone strength were observed in the group of animals which received α-aescin as compared to a control group. Such an increase of bone strength was not confirmed in the case of administration of both cisplatine and α-aescin.

Biomechaniczne badanie kości u dorosłych szczurów po podaniu cisplatyny i α-aescinu

W pracy badano wpływ cisplatyny oraz cisplatyny i α-aescinu podanego łącznie na wytrzymałość mechaniczną kości u dorosłych szczurów. Cisplatynę i α-aescin podawano dootrzewnowo. Z przeprowadzonych doświadczeń wynika, że w grupie zwierząt, którym podawano cisplatynę, wytrzymałość spadła o 8,2% w porównaniu z grupą kontrolną. Nie zauważono istotnych różnic statystycznych w wytrzymałości po podaniu α-aescinu w porównaniu z grupą kontrolną oraz po podaniu cisplatyny i α-aescinu łącznie w porównaniu z grupą zwierząt, którym podawano wyłącznie cisplatynę.