

ASSESSMENT OF NANOPARTICULATED RESVERATROL AND LOSARTAN IN THE PROPHYLAXIS OF OSTEOPOROSIS

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ABSTRACT: *The study demonstrated that eight weeks after bilateral ovariectomy in female white Wistar rats, develops endothelial dysfunction of bone microvasculature and deterioration of regional blood flow in the bone, leading to the emergence of generalized osteoporosis. Nanoparticulated forms of Losartan and Nanoparticulated forms of Resveratrol, possessing endothelial protective action, effectively prevent the reduction of regional microcirculation in bone tissue, keeping it at the level of intact rats. It is allowed to maintain an adequate level of bone remodeling processes, which manifested by slowing the thinning of bone trabeculae.*

KEYWORDS -osteoporosis, dysfunction of endothelial, Bivalos, Nanoparticulated forms of Losartan, Nanoparticulated forms of Resveratrol.

I. INTRODUCTION

Blood flow plays an important role in the remodeling, reparative and regeneration of bone tissue. The deterioration of blood flow leads to the suppression of activity of osteoblasts and osteoclasts [7]. The cause of the circulatory disorders of bone may be due to vascular endothelial dysfunction, which means the deterioration of microcirculation which can lead to osteopenia, causing osteoporosis [6]. At the same time, modern pharmacological studies have shown positive effects of osteoprotective drugs, correcting endothelial dysfunction, which include Losartan and Resveratrol [1,3]. Currently, the actual problem of modern experiments and clinical pharmacology is to increase the efficiency and to reduce the side effects of the drug. This can be achieved by nanoparticulated drugs with their combination in a lowered dose.

II. OBJECTIVE

The aim of the present study is to investigate the Antiosteoporotic properties of Nanoparticulated-Resveratrol and Nanoparticulated- Losartan.

III. MATERIALS AND METHODS

In the experiment, we used 187 female Wistar rats weighing 200-300g. All studies were performed under general anesthesia. Osteoporosis was modeled by bilateral ovariectomy [5]. Osteoporosis development was assessed after eight weeks (on day 57) after bilateral ovariectomy. Animals were divided into 7 groups: I - Control, false-operated animals (№ - 42); II – after bilateral ovariectomy without administrations of drugs (№ - 30); III (№ - 35) – After bilateral ovariectomy, rats were treated for eight weeks with Losartan 6 mg / kg, which was administered intraperitoneally; IV (№ - 20) - Resveratrol was administered intraperitoneally in a dose of 2 mg / kg. In Group V (№ - 20), the drug used for comparison was administered - Bivalos dose 171 mg / kg; in Group VI (№ - 20) after bilateral ovariectomy, animals were treated with eight weeks Nanoparticulated form of Losartan 0,6 mg / kg. In Group VII (№ - 20), group of rats were treated with Nanoparticulated form of Resveratrol in a dose of 0,2 mg / kg. The animals with Nanoforms of Resveratrol and Nanoforms of Losartan were administered as the same pattern as that of the usual forms of these substances.

After 8 weeks, the level of microcirculation in the proximal metaphysis of femur was measured. Microcirculation parameters were recorded using a Laser Doppler Flowmeter Biopac system MP-100 and the sensor TSD-144. Recording and data processing was implemented by the program AcqKnowledge - 3.8.-4.2. Microcirculation values were expressed in perfusion units (PU). Development of endothelial dysfunction was assessed after intraosseous blood flow measurement. This experiment was performed on endothelium-dependent vasodilation (EDVD) in response to an intravenous bolus injection of Acetylcholine solution at a dose of 40 mg / kg [8] and endothelium-nondependent vasodilation (ENVD) in response to a bolus injection of Sodium Nitroprusside solution at a dose of 30 mg / kg [2]. For an assessment of endothelial dysfunction in osteoporosis, the coefficient of endothelial dysfunction (CED) was done on the basis of Laser Doppler Flowmetry that results in proximal metaphysis of femur [4,6].

IV. RESULTS AND DISCUSSION

The level of microcirculation in rats in the control group I was $100,5 \pm 4,4$ PU, animals of group II (model of osteoporosis) - $61,5 \pm 3,7$ PU. In group III (Losartan) - $100,0 \pm 2,3$ PU; in Group IV (Resveratrol) - $91,0 \pm 4,3$ PU; in group V (Bivalos) - $86,5 \pm 5,0$ PU; Group VI (Nanofoms- Losartan) - $95,2 \pm 2,0$ PU and Group VII (Nanofoms- Resveratrol) - $86,6 \pm 1,6$ PU. Thus, these results indicate that Losartan, Resveratrol, and their respective nanoparticulated forms, along with Bivalos, prevents the reduction of regional blood flow in the proximal metaphysis of femur. The values obtained were significantly higher than those groups of animals without osteoporosis.

It was ascertain that all the studied drugs, except Bivalos, resulted in proportion between the area of triangle above the curve of restoration of the level of microcirculation in bone, in response to Acetylcholine and Nitroprusside to those of false-operated animals. The studied drugs significantly reduces CED, demonstrating endothelial protective action to the following values: Losartan - $1,5 \pm 0,2$, Nanofoms- Losartan - $1,5 \pm 0,2$, Resveratrol - $1,3 \pm 0,2$, Nanofoms- Resveratrol - $1,3 \pm 0,1$. CED value in the group of animals treated with Bivalos- $2,1 \pm 0,2$, whereas the figure in rats without osteoporosis was equal to $1,3 \pm 0,2$, and in rats with osteoporosis, which have not been carried out - $2,4 \pm 0,2$.

Through microscopy and histomorphometric measurement of proximal metaphysis of femur, the average width of the bone trabeculae were found as follows: group I - $97,7 \pm 1,0$ mm; Group II - $61,7 \pm 1,2$ mm; in Group III - $84,8 \pm 0,6$ mm; in Group IV - $90,0 \pm 3,4$ mm; in Group V - $89,1 \pm 1,1$ mm; in Group VI - $81,2 \pm 0,6$ mm in Group VII - $84,2 \pm 0,7$ mm.

V. CONCLUSION

It can be concluded that Losartan, Resveratrol and nanoparticulated forms of these drugs, except Bivalos, have a pronounced endothelial protective effect on the model of bilateral ovariectomy, manifested by the reduction in the coefficient of endothelial dysfunction. All drugs studied effectively prevent the reduction in the microcirculation of the proximal metaphysis of femur, as well as preventing the decrease of bone trabeculae width, i.e. to have osteoprotective action.

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