THE EFFECT OF NICOTINE ADMINISTRATION ON FEMORAL NECK RIGIDITY AND WORK TO FAILURE OF RAT OSTEOPOROTIC BONES

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Abstract: The aim of whole study is the determination, how the administration of Nicotine affects the mechanical properties of the rat osteoporotic bones. The study was divided into two parts. First part was founded on the bone test by the three-point bending test. In this part of the study is used bending test of the rat femoral neck. The experiment was performed on 24 male rats that were divided into three groups. Nicotine was administered in dose of 15 μg per day added to the water. We calculated several biomechanical parameters of bone that can be used to characterize the bone integrity, such as rigidity *S* and the work to failure *U* and compared the results of each group.

Introduction

Osteoporosis is a disease in which the density and quality of bone are reduced, leading to weakness of the skeleton and increased risk of fracture, particularly of the spine, wrist, hip, pelvis and upper arm.

The experimental osteoporotic models are used for testing anti-osteoporotic effects of various drugs. Rat oöphorectomy (OOX) is often used as an osteoporotic model. After oöphorectomy increases significantly the osteoclastic activity and develops the osteoporosis. It is possible to administrate the tested agents to this model.

There exist several methods determining bone properties (bone strength), e.g. ultrasound transmission velocity (UTV) and bone mineral density (BMD). These methods are widely used as possible predictors of the bending strength of osteoporotic long rat bones and may simulate a model for the human postmenopausal osteoporosis. Direct biomechanical testing of bone undoubtedly provides more information about mechanical integrity.

Bending can be applied to the bone using either three or four-point bending. Three-point bending is used more often for measuring the mechanical properties because of its simplicity, but it has the disadvantage of creating high shear stresses near the midsection of the bone. In the bending test the whole bone is loaded in bending until failure.

We have already tested several drugs, e.g. thyroxin, estrogens, fosamax. But now we wanted to know the effect of Nicotine on the mechanical properties of rat osteoporotic bones. Nicotine is in the cigarettes and lots of people smoke, so we decided to test this drug.

Whole work is divided into two parts. In the first part of the study we tested male rat osteoporotic femur by three-point bending test [1] and we calculated the parameters of the bone that they characterize the bone integrity and geometry, such as extrinsic stiffness *S*, work to failure *U*, cross-sectional area *A* of bone in the place of the loading, cross-sectional modulus W_{omin} of bone and the bending strength σ_{omax}. We developed the methodology for the determination of cross-sectional modulus of rat bone by the digital image of bone cross-section obtained by the flat scanner [2].

The aim of this part of study is the determination the administration of Nicotine effect on the bone mechanical properties as the rigidity and work to failure of rat femoral neck.

This work is founded on the co-operation of Czech Technical University in Prague, Faculty of Mechanical Engineering, Laboratory of Human Biomechanics and the First Faculty of Medicine, Charles University in Prague.

Materials and Methods

The experiment was performed on 24 male rats with an initial body weight of 180-200g that were divided into three groups: I – oöphorectomy (OOX) and placebo application s.c., II – Nicotine and III – OOX + Nicotine. Nicotine was administered in dose of 15 μg per day added to the water.

After four months, the rats were killed by decapitation. The left femur was removed and cleaned of the soft tissue and immediately frozen at the temperature of -20°C.

During 24 hours before testing the bones were hydrated in the distilled water at the room temperature. The proximal part of femur casted in the epoxy 510 (E15) (Figure 1) was mounted in the loading fixture (Figure 2). The head of femur was loading by upper part of jig with the displacement 2mm/min to the failure (Figure 3).

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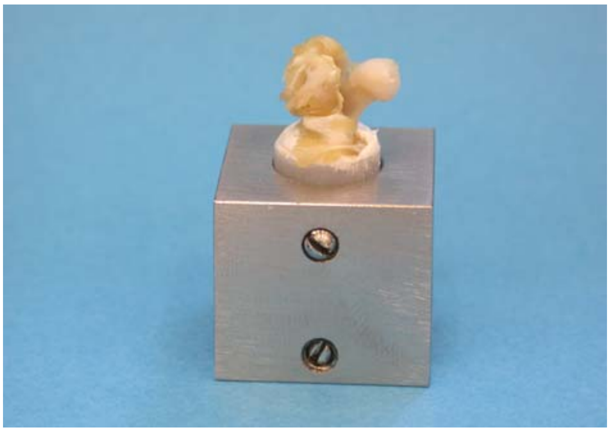

Figure 1: The bone casted in the epoxy

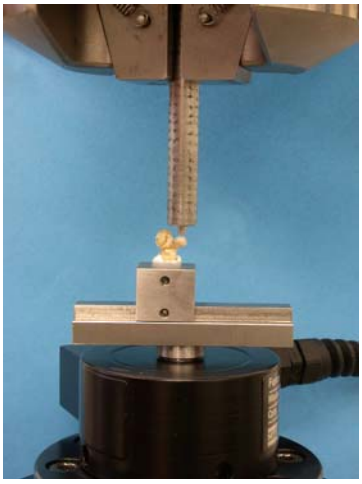

Figure 2: The loading fixture with the mounted bone

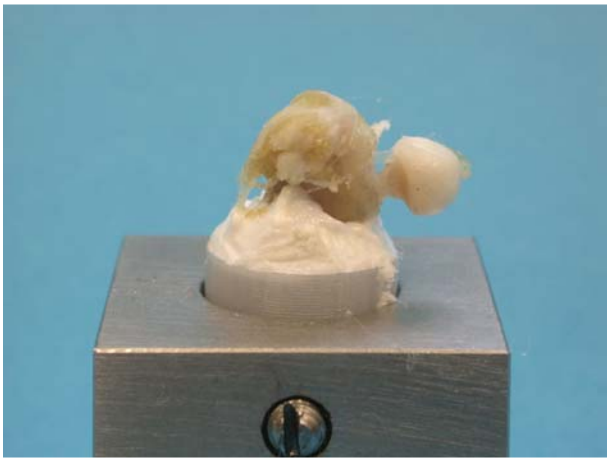

Figure 3: The fracture of femoral neck

Biomechanical testing system MTS Mini Bionix was used for experiment. The program controls crosshead speed and measures important quantities such as load, displacement and time.

We calculated several biomechanical parameters of bone that can be used to characterize the bone integrity, such as rigidity S and the work to failure U [3].

The rigidity or the extrinsic stiffness S is calculated from the equal (1).

$$S = F/d \qquad (1)$$

The work to failure U is amount of energy necessary to break the bone and it is calculated as the area under the load-displacement curve (Figure 4).

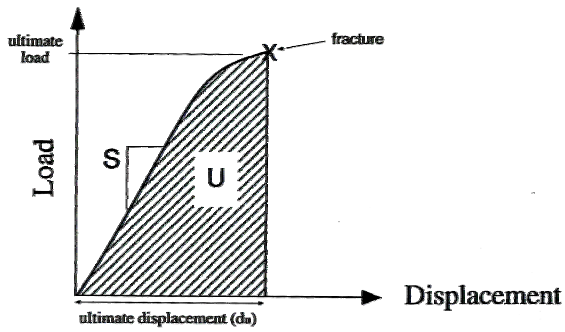

Figure 4: Load – Displacement curve

Results

The rigidity and work to failure values were computed by the algorithm that has been implemented in the computer program written in MATLAB. Table 1 shows outputs of this program and Figure 5 illustrates load – displacement curves of the selected specimens from each group.

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Table 1: The resulting values of the extrinsic stiffness *S* and the work to failure *U*

Sample no.	Group	extrinsic stiffness *S* [N/mm]	Mean [N/mm]	SE [N/mm]	work to failure *U* [mJ]	Mean [mJ]	SE [mJ]
1	I	124,594	158,42	± 8,94	17,978	38,97	± 4,43
2		130,456			34,832		
3		186,391			44,486		
4		170,429			52,367		
5		167,061			30,455		
6		137,403			51,281		
7		159,410			50,290		
8		191,604			30,105		
9	II	153,845	165,44	± 15,70	40,729	35,93	± 6,39
10		127,257			39,832		
11		131,004			71,348		
12		175,054			19,810		
13		108,803			21,544		
14		222,085			29,531		
15		173,291			17,163		
16		232,212			47,455		
17	III	224,485	181,95	± 18,99	42,395	36,35	± 1,66
18		121,852			35,269		
19		111,155			40,115		
20		194,548			26,668		
21		234,825			35,465		
22		123,811			34,753		
23		230,997			38,286		
24		213,950			37,816		

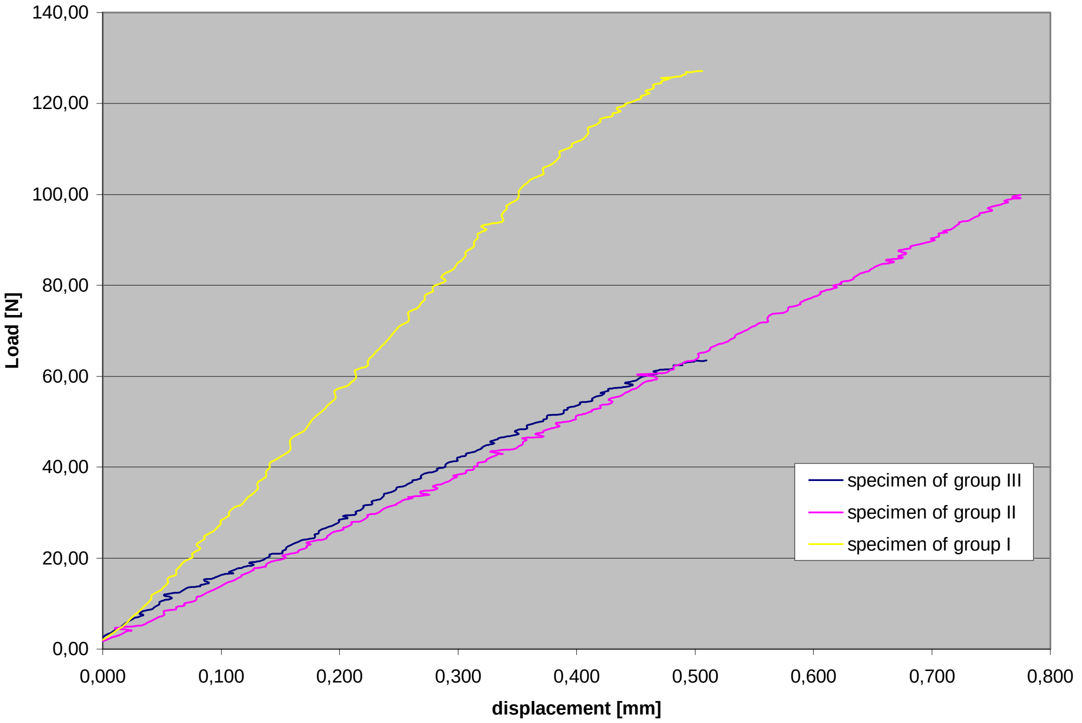

Figure 5: Load – displacement curves of selected specimens from each group

Discussion

The effect of Nicotine administration on the mechanical properties of rat femoral neck is evident from Tab.1. The differences between groups are not statistic significant though the tendency of rigidity decrease is apparent.

The results of the first part of this study (three-point bending test of rat femur) were similar.

Conclusions

From this type of the experiment we obtain more authoritative values then by three-point bending test because the fracture of femoral neck is the most frequent condition within osteoporosis.

The methodology of femoral neck testing was used in this study firstly. We want to use more specimens and determinate the geometric characteristics of femoral neck for more precise results in other studies.

Acknowledgements

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