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LOW TESTOSTERONE LEVELS LEAD TO THE DEVELOPMENT OF OXIDATIVE STRESS AND COLLAGEN DEPOSITION IN THE MALE RAT URETHRAL SPHINCTER

Hypothesis / aims of study

Urinary incontinence in the elderly can be caused by or associated with a range of medical conditions. Prostatic disease, stroke, neurological and musculoskeletal conditions contribute in men. The physiopathology of urinary incontinence is frequently described in terms of damage that occurs at tissue or cell level[1]. Thus, this study had the aims of contributing towards understanding the manifestations of the urethral sphincter in the presence of low levels of sexual hormones (using a model for induced aging) and also evaluating the beneficial action of alpha-tocopherol (antioxidant) for avoiding states of oxidative stress.

Study design, materials and methods

The project was approved by the University Ethical Committee.

Forty male rats of Wistar breed weighing 250-300g were used, divided into four groups: **group I –** subjected to a sham procedure; **group II –** subjected to bilateral orchiectomy and sacrificed eight weeks after the procedure; **group III –** subjected to bilateral orchiectomy with alpha-tocopherol supplementation for four weeks preceding the procedure; and **group IV –** subjected to bilateral orchiectomy with alpha-tocopherol supplementation for four weeks preceding the procedure and for eight weeks afterwards. At the end of the experiment, the urethral sphincter was dissected and analyzed stereologically using a M-42 grading test, with evaluation of the volumetric density of the collagen as well as muscular fibers. The presence of oxidative stress was determined by means of assaying the tissue level of 8-isoprostane. Variance analysis was used for the statistical analysis.

Results

The volumetric concentrations of collagen were 11,70%, 34,21%, 21,12% and 12,23%, in groups I, II, III and IV, respectively. The statistical analysis demonstrated that the fiber concentration was statistically greater in group II than in the other groups (p=0.012). Group I presented significantly lower collagen levels. Thus, the greatest fibrosis occurred in the castrated group without alpha-tocopherol replacement (figure 1). Vitamin supplementation for eight weeks presented the highest protection against the damage caused by castration. Regarding the muscle concentration, the volumetric density was 88,30%; 65,79%; 73,88% and 68,77% in groups I, II, III and IV, respectively (figure 1). Analysis of 8-isoprostane levels showed high concentrations of oxygen-reactive species in group II, in relation to the other groups (p=0.02) (figure 2).

Figure 1: The ratio smooth muscle\collagen fibers in the urethral sphincter in different groups. (* p < 0.05 groups I and IV compared to groups II and III).

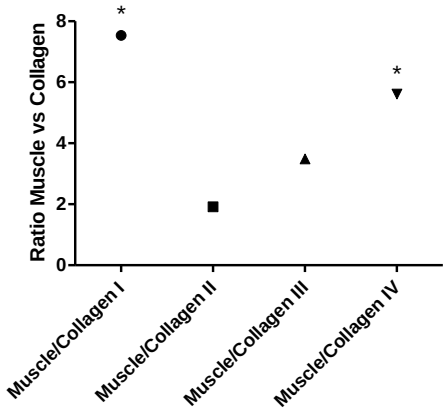


Figure 2. Conjunctive proliferation (red). a) urethral sphincter from group I (sham); b) urethral sphincter from group II (orchiectomized).

Figure 2_a

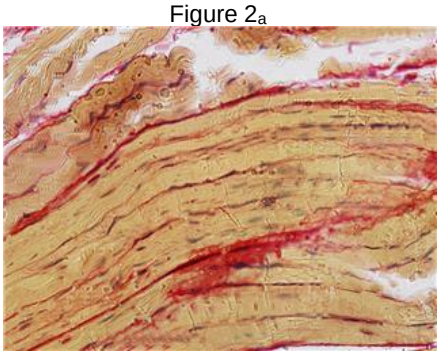
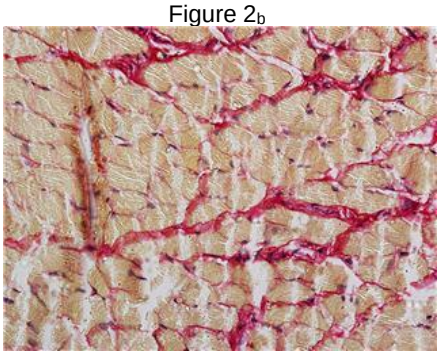


Figure 2_b



Interpretation of results

Castration of male rats caused oxidative stress in the male urethral sphincter complex, thus demonstrating that low testosterone levels lead to the development of oxidative stress and with consequently increased collagen deposition and decrease in the volumetric density of the smooth muscle. Alpha-tocopherol supplementation avoided the generation of free radicals and the fibrosis that they cause in muscle tissue.

Concluding message

From a broader perspective, it is suggested that low testosterone levels are associated with the induction of free radical formation in male rat urethral sphincter. It is further suggested that the use of antioxidants has a protective role in situations of male hypogonadism, thereby avoiding or minimizing the effects of sphincter dysfunctions coming from muscle damage.

References

[1]J Urology (2008) Mar 14; Epub ahead of print.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**ETHICAL COMMITTEE OF FEDERAL UNIVERSITY OF SÃO PAULO**