

HYPERCHOLESTEROLEMIC DIET INFLUENCES THE COLLAGEN REMODELING OF THE BLADDER WALL EXTRACELLULAR MATRIX IN RAT MODEL

Hypothesis / aims of study

Types I and III collagens are the most prevalent in bladder wall whereas type III collagen is the first synthesized in fibrosis process. Bladder outlet obstruction (BOO) promotes this process and hypercholesterolemia is also believed to create conditions for it, although no morphological association has already been demonstrated. This study was conducted to verify if a hypercholesterolemic diet (HCD) promotes structural bladder wall modifications regarding collagen composition.

Study design, materials and methods

Forty-five female 4-week-old Wistar rats were divided into three groups: 1) control group fed a normal diet (ND); 2) model of bladder outlet obstruction (BOO) group fed an ND; and 3) group fed an HCD (1.25% cholesterol). Total serum cholesterol, LDL cholesterol and body weight were assessed at baseline. Four weeks later, group 2 underwent a surgical procedure resulting in a partial BOO, while groups 1 and 3 underwent a similar surgical procedure that did not result in a BOO. Six weeks later, all animals had their bladders removed; serum cholesterol and LDL cholesterol levels and body weights were measured. Morphological analysis was performed by Picosirius-red staining and immunohistochemistry for types I and III collagen. Statistical analysis was completed, comparing groups by the one-way ANOVA method and Tukey multiple comparisons when appropriate. Significance was considered when $p < 0.05$.

Results

Rats fed an HCD exhibited a significant increase in LDL cholesterol levels ($p < 0.001$) and body weight ($p = 0.017$), when compared to the groups fed an ND during the ten-week study period. Moreover, the HCD induced significant morphological alterations of the bladder wall extracellular matrix, regarding immature collagen fibers and the amounts of type III collagen, when compared to the control group ($p = 0.002$, Δm 0.852 μm ; CI 95% 0.292 – 1.412 and $p = 0.016$, Δm 1.559 μm ; CI 95% 0.262 – 2.857, respectively), resembling the process promoted in the BOO model.

Fig. 1 Bladder section stained with Picosirius red under polarized light microscopy. The fragments show mature collagen fiber on an orange-reddish color and the immature collagen fibers on a green-yellowish color. A – Group 1; B – Group 2 and C – Group 3 (Original magnification x400)

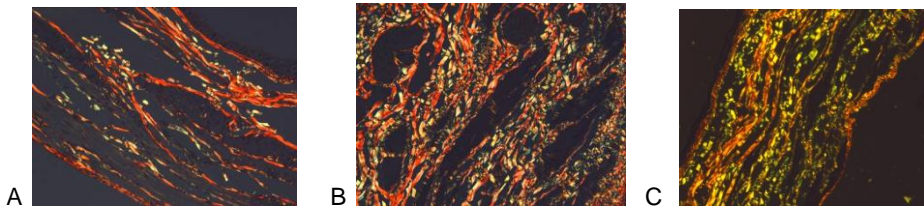


Fig. 2 Box-whisker plots of data of (A) immature collagen fibers stained with Picosirius red (μm) and of (B) immunofluorescence to type III collagen (μm) in control (1), BOO model (2) and HCD (3) groups (ANOVA One-Way and Tukey's method)

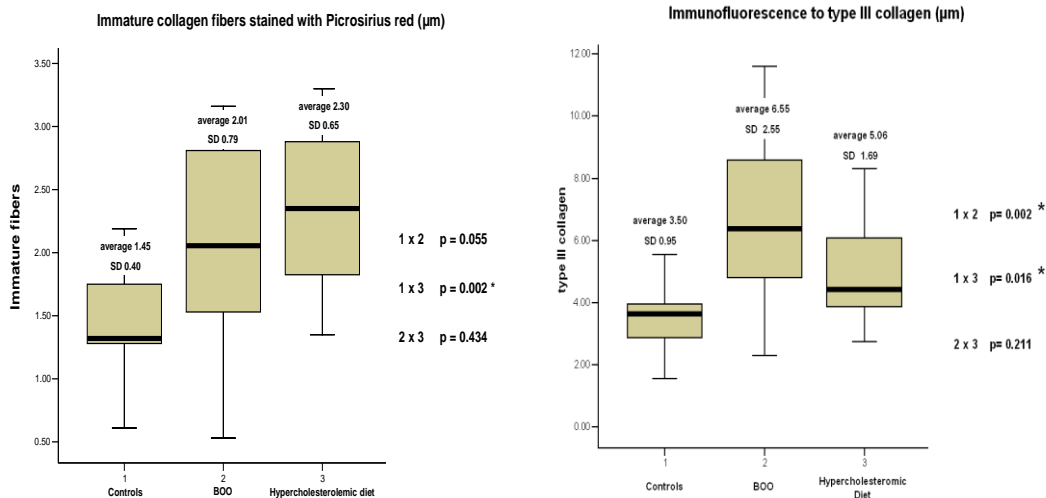
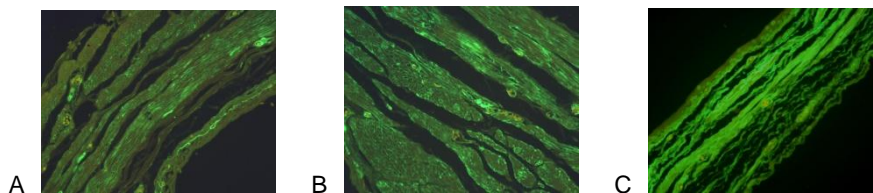


Fig. 3 Immunofluorescence to type III collagen in bladder wall section of control (A), BOO model (B) and HCD (C). There is an evident higher amount of type III collagen in B and C, relative to A (Original magnification x400)



Interpretation of results

Although likely, we cannot infer that a high LDL cholesterol level itself promotes an increase in bladder collagen type III, since weight gain was also observed in these rats; vascular components of the bladder were not studied, nor were the bladder function or micturition habits registered. However, the fact presented here that a hypercholesterolemic diet promotes changes in the collagen composition of the bladder wall extracellular matrix in rats, resembling that caused by a bladder outlet obstruction, justifies future research on this matter, such as dietary influences on the BOO model, bladder function studies and possible pharmacological prevention of hypercholesterolemia.

Concluding message

A hypercholesterolemic diet in Wistar rats promoted morphological changes of the bladder extracellular matrix in terms of collagen composition, as well as increases in body weight and LDL cholesterol.

<i>Specify source of funding or grant</i>	Fundação de Apoio à Pesquisa do Estado de São Paulo / Brasil
<i>Is this a clinical trial?</i>	No
<i>What were the subjects in the study?</i>	ANIMAL
<i>Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?</i>	Yes
<i>Name of ethics committee</i>	Comissão de Ética para Análise de Projetos de Pesquisa - University of Sao Paulo - Brasil