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## **DISRUPTION OF COLLAGEN AND GLYCOSAMINOGLYCANS STATUS IN THE URETHRAL TISSUE OF PREGNANT RATS WITH STREPTOZOTOCIN INDUCED SEVERE DIABETES**

### Hypothesis / aims of study

A positive relationship between gestational diabetes and urinary incontinence was established by our group. The aim of this study was to analyze the distribution and quantification of the key structural extracellular matrix components, including total collagen, collagen I and III, collagen I/III ratio and sulfated glycosaminoglycans, in urethra of severe STZ-induced diabetic pregnant rats

### Study design, materials and methods

One hundred and twenty female Wistar rats were distributed in four experimental groups: virgin, pregnant, diabetic and diabetic pregnant. In adult life, diabetes was induced in rats by *streptozotocin* injection administered intravenously at 40 mg/kg to produce a permanent and severe diabetic state (blood glucose level >300 mg/dL). At day 21 of the experiment, the rats were lethally anesthetized and the urethra and vagina were extracted as a unit. Urethral and vaginal sections were cut and analyzed by a) histochemical staining for extracellular matrix and muscle structural components and morphometric analysis, b) immunohistochemistry to identify collagen I and III and Keratan sulfate, and c) Protein extraction and western blotting analysis for Collagen I, Collagen III and Keratan sulfate.

### Results

The total striated muscle is not only decreased but also this striated muscle is involved by more connective tissue characterized by an increase in the relative ratio of the collagen I/III and a decrease in total GAGs and Keratan sulfate.

### Interpretation of results

Our results highlighted the difference between ECM from urinary incontinence related to parturition and those induced by diabetes and pregnancy in rats. ECM related to parturition leads a decrease in collagen I/III ratio indicating a soft tissue (13), although our results demonstrated that ECM related to STZ-induced diabetes leads an increase of collagen I/III ratio, suggests a more rigid structure, supportive collagen around the urethra in favor of a stiffer urethral tissue. This can impair the biomechanical properties of the tissue making the closure of the urethra more difficult.

### Concluding message

The importance of this study is that it provides the first line of experimental evidence in support of a metabolic relationship between the elevated glycemic levels and urethral dysfunction in diabetic pregnant rats.

### Disclosures

**Funding:** FAPESP/Brazil (Process Number 2010/11703-4 e 2010/10740-3) **Clinical Trial:** No **Subjects:** ANIMAL **Species:** rat **Ethics Committee:** All of the experimental protocols were approved by UNESP Institutional Animal Care and Use Committee (process number 828-2010)