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DEVELOPMENT OF RABBITS STRESS URINARY INCONTINENCE ANIMAL MODEL WITH ANATOMICAL-FUNCTIONAL EVALUATION OF URETHRAL SPHINCTER DEFICIENCY.

Hypothesis / aims of study To develop a rabbit urinary incontinence animal model with anatomical-functional evaluation of the urethral sphincter deficiency.

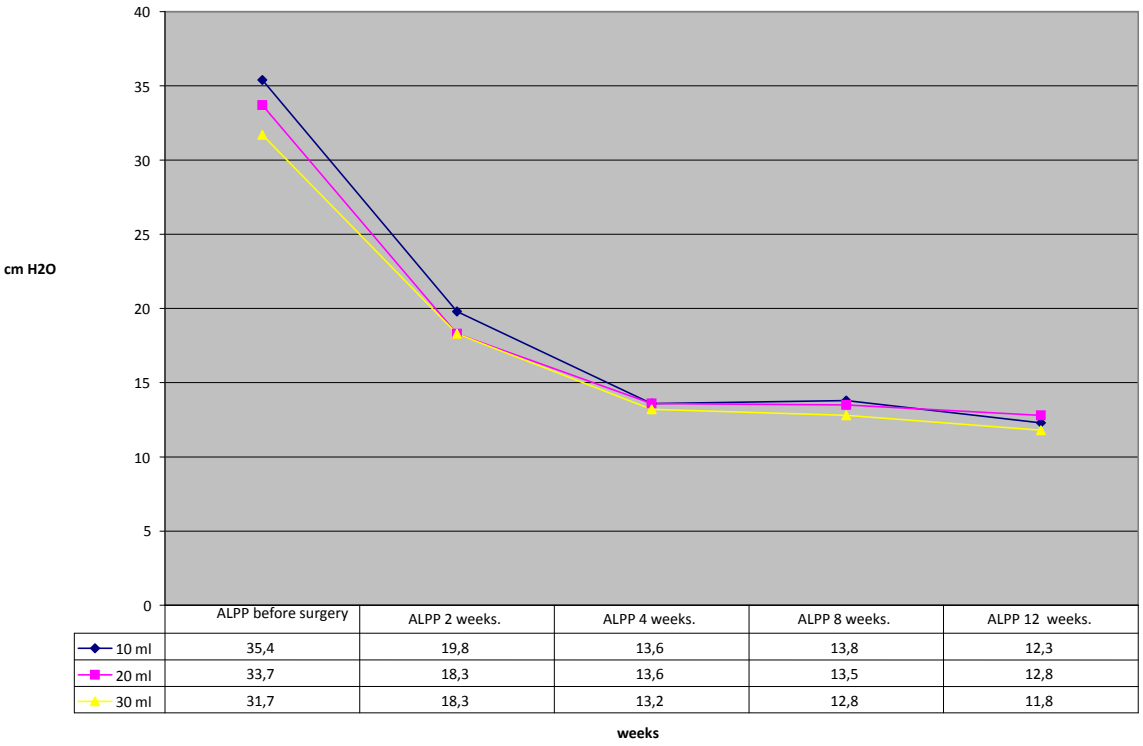
Study design, materials and methods Sixteen male New Zealand rabbits were undergone to urethrolysis and 4 rabbits were the sham group. We performed cistometric evaluation and we determine the abdominal leak point pressure (ALPP) at 10, 20, 30 ml of bladder filling before urethrolysis and with 2, 4, 8 and 12 weeks after urethrolysis. Four animals were sacrificed in each timepoint, just after determine the ALPP, to harvest the bladder and urethra. The samples were stained by Trichrome of Masson technique to determine the collagen and sooth muscle density.

Results After the urethrolysis, we observed a significant decrease in the ALPP ($p < 0,01$), in all timepoints, independent of the intravesical volume. In the first 4 weeks there was a progressive decrease on the ALPP, which stabilize afterward. The ALPP decrease was maintained for 12 weeks (Figure 1). After twelve weeks, it was observed a significant decrease in smooth muscle density ($p=0,01$), as well as, an increase in collagen density, vases and elastin ($p=0,01$) (Figure 2).

Interpretation of results The majority of urethral sphincter deficiency animal models were developed in rats. Those models have several limitations, including the urethral wall thickness, small bladder capacity, need for neurological damage, and reproducibility. In this study, we demonstrate that it is feasible to generate a urethral sphincter deficiency in rabbits by means of urethrolysis. We found a ALPP decrease associated with significant alterations in the smooth muscle fibers and collagen density in the urethra wall. The main objective in developing this animal model is to allow cell therapy studies. We believe that the present animal model will allow researches to better understand the effect of cell therapy on urethral function. Besides, it will allow studies with autologous cells transplantation, without the rats animal models limitations.

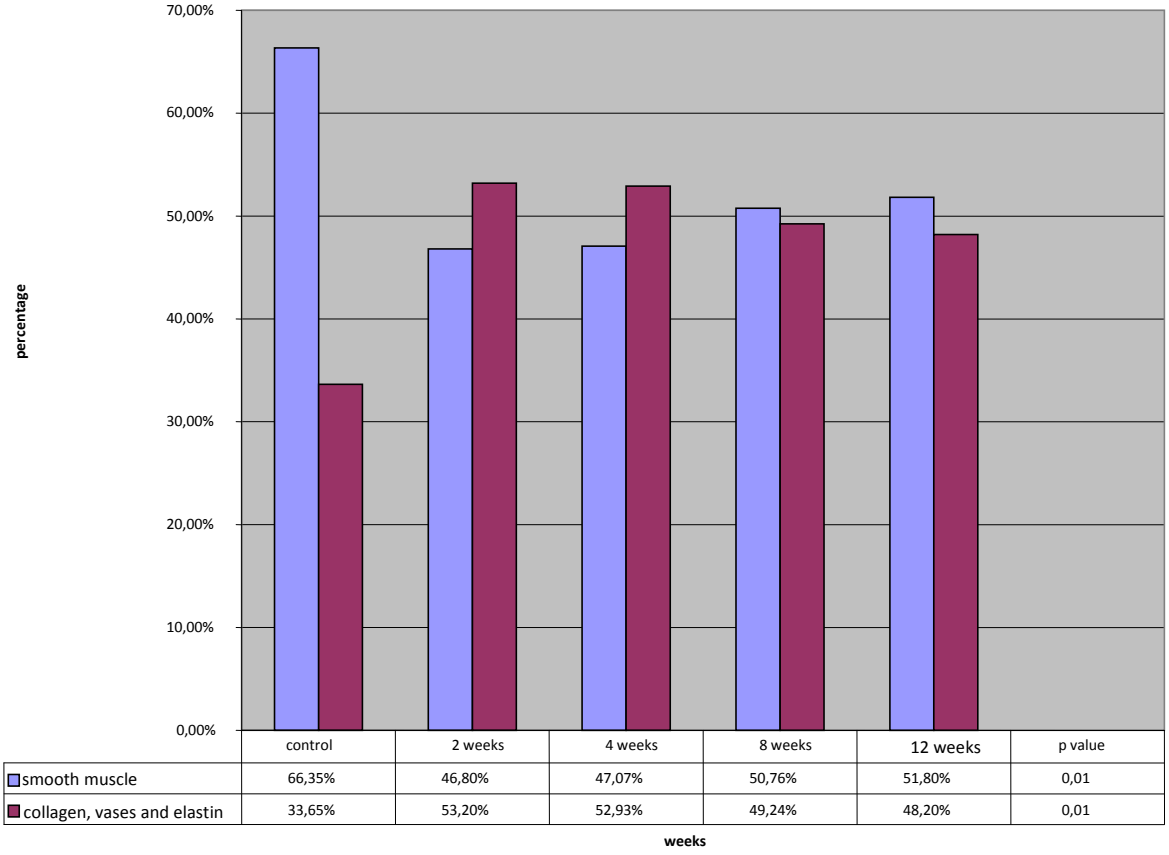
Concluding message This study demonstrate that by means of Urethrolysis it is possible to generate a sphincteric urethral damage with significant and sustainable decrease in ALPP and urethral smooth muscle density. This animal model may be helpful to test new therapies, specially the new cell therapies, such as stem cells injection for stress urinary incontinence treatment.

Figure 1: Significant decrease in the ALPP ($p < 0,01$), in all timepoints, independent of the intravesical volume.



	ALPP before surgery	ALPP 2 weeks.	ALPP 4 weeks.	ALPP 8 weeks.	ALPP 12 weeks.
10 ml	35,4	19,8	13,6	13,8	12,3
20 ml	33,7	18,3	13,6	13,5	12,8
30 ml	31,7	18,3	13,2	12,8	11,8

Figure 2: Histological analysis evidenced decrease in the density of smooth muscle as well as, the increase in the density of collagen, vases and elastin (p=0,01).



	control	2 weeks	4 weeks	8 weeks	12 weeks	p value
smooth muscle	66,35%	46,80%	47,07%	50,76%	51,80%	0,01
collagen, vases and elastin	33,65%	53,20%	52,93%	49,24%	48,20%	0,01

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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	**CEP 0078/07 by Federal University of São Paulo - Brazil**