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INCREASED TIME TO RECOVERY DUE TO INCREASED DURATION OF VAGINAL DISTENSION IN A RAT MODEL

Hypothesis / aims of study

Vaginal delivery of children causes traumatic injury to tissues of the pelvic floor and is correlated with stress urinary incontinence (SUI). In addition, increased duration of 2nd stage of labor is correlated with increased incidence of SUI. However, the mechanisms of organ and tissue injury leading to incontinence are unknown. We tested the hypothesis that increased duration of vaginal distension results in decreased urethral resistance and increased time to recovery in a rat model of simulated childbirth injuries. The aims of this study were to determine the effects of increased duration of vaginal distension on 1) voiding cystometry; 2) leak point pressure (LPP); and 3) histopathology of the urethra.

Study design, materials and methods

Sixty nine virgin female rats underwent vaginal distension using a 10fr Foley catheter inflated with 3ml water for either 1 hour or 4 hours. Thirty three age-matched rats underwent a sham-distension with catheter placement but not balloon inflation. Conscious cystometry and anesthetized LPP were measured via a suprapubic bladder catheter 4 days, 10 days, or 6 weeks after vaginal distension. The bladder was filled with saline via the catheter at 5ml/hr for conscious cystometry while bladder pressure and voided volume were continuously recorded. Three voids were recorded and the mean was calculated for each animal.

After cystometry the rats were anesthetized with urethrane i.p. for LPP measurement. The bladder was palpated to empty and filled to approximately half capacity. While bladder pressure was continuously recorded, a gentle Crede maneuver was applied to slowly increase abdominal pressure. At the first indication of saline leakage through the urethra, the externally applied abdominal pressure was rapidly removed. Peak pressure in the absence of a detrusor contraction was taken as LPP. The increase in external abdominal pressure (P_{abd}) and LPP were recorded 3 times and the mean was calculated for each rat. Data is presented as mean +/- standard error. A two way ANOVA followed by a Student-Newman-Keuls posthoc test was performed with $p<0.05$ indicating a significant difference. Immediately after LPP measurement, the rats were euthanized and the urethra and vagina were dissected, fixed, and embedded for histopathology, which was analyzed qualitatively.

Results

Urinary volume during cystometry was significantly increased 6 weeks after a sham distension compared to the other time points (Figure 1a), indicative of normal animal and bladder growth in the intervening time. Both vaginal distension groups failed to demonstrate this age-dependent change (Figure 1b). Peak voiding pressure increased significantly 4 days after either a 1 hour or a 4 hour vaginal distension, a difference attributable to changes in baseline bladder pressure since the increase in pressure during voiding were not significant (Figure 1c). There were no significant differences in voiding pressures compared to the sham group either 10 days or 6 weeks after either vaginal distension.

P_{abd} during a LPP test was significantly reduced 4 days after either a 1 hour or a 4 hour vaginal distension, indicative of decreased urethral resistance (Figure 2a). Ten days after a 4 hour distension, P_{abd} remained significantly low. Six weeks after distension, there were no significant differences between the three groups. Four days after either a 1 hour or a 4 hour vaginal distension, LPP was significantly reduced compared to the sham group (Figure 2b). LPP was significantly reduced at 4 and 10 days after either a 1 hour or a 4 hour distension compared to 6 weeks after distension. Light microscopy, particularly at the 10 day time point, demonstrated signs of injury suggestive of increased urethral injury after 4 hours of distension. Focal inflammatory infiltrates were observed in the submucosa of the vagina and extravasated red blood cells were found in the border between the vagina and urethra of some animals.

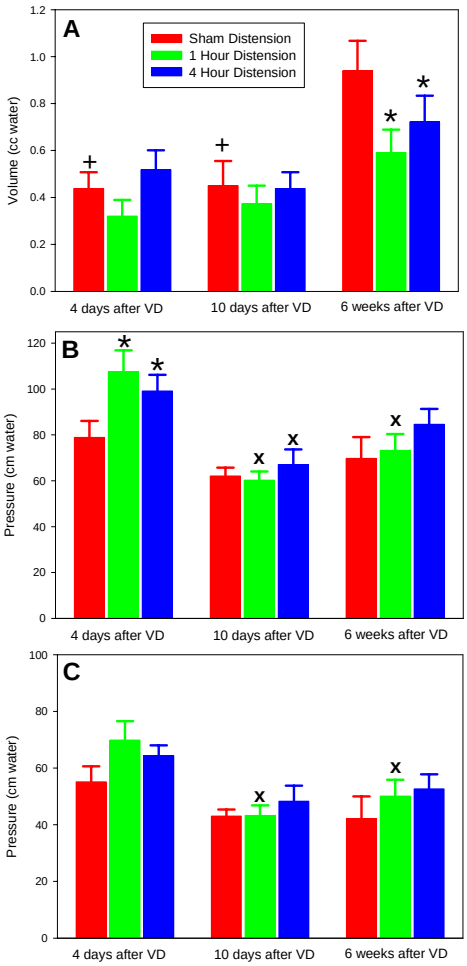

Figure 1. Conscious cystometry results. **A.** Urinary volume. **B.** Peak voiding pressure **C.** Increase in pressure during voiding. * indicates a significant difference compared to sham group. X indicates a significant difference compared to 4 day post-distension group.

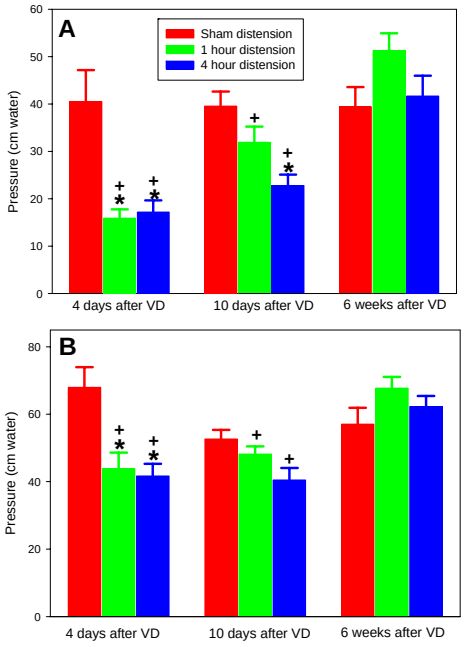

Figure 2. Leak Point Pressure testing results. **A.** Leak point pressure (LPP) **B.** Increase in abdominal pressure to leak (P_{abd}) * indicates a significant difference compared to sham group. + indicates a significant difference compared to 6 week post-distension group.

<u>Interpretation of results</u>

Increased cystometric baseline pressure is a short-term response to vaginal distension, possibly due to ischemic injury to the bladder, and resolves within 10 days. Both LPP and P_{abd} were significantly decreased in both distension groups 4 days after distension, indicative of short-term decreased urethral resistance and urethral dysfunction. Ten days after distension, P_{abd} was significantly decreased only in the 4 hour distension group, indicating that a longer recovery time is needed following a longer distension duration. Six weeks after vaginal distension, both LPP and P_{abd} were not significantly different from sham values, indicating a return to normal function. In contrast, 6 weeks after either a 1 hour or a 4 hour distension, the rats had not undergone the same increase in cystometric voided volume as the sham group, suggesting that some effects of vaginal distension do not resolve within 6 weeks. Haemorrhage and inflammation in histopathology of the distension groups are indicative both of acute injuries which may not completely recover within 6 weeks.

<u>Concluding message</u>

Increased duration of vaginal distension results in increased time to recovery but not increased extent of dysfunction. This suggests a longer lasting injury can be created with a longer duration distension. Pelvic floor damage incurred during vaginal distension likely occurs by multiple mechanisms, including ischemic and/or reperfusion injury in addition to

direct trauma to tissues and organs of the pelvic floor. Further experiments will investigate the mechanism of this injury as well as targeted treatments to facilitate recovery.

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