

A NEW ANIMAL MODEL TO EVALUATE THE COMBINED EFFECTS OF DIABETES AND BIRTH TRAUMA ON URINARY INCONTINENCE

Hypothesis / aims of study

Diabetes mellitus (DM) causes debilitating and devastating complications, including lower urinary tract (LUT) complications, such as urinary incontinence {1}. Women with DM have a higher prevalence of LUT complications, contributing to the high prevalence of urinary incontinence (30-60%) among adult women in the US {2}. However, the mechanistic relationship of increased risk for urinary incontinence among diabetic women is poorly understood. To date, there is no animal model to study effects of birth trauma AND diabetes on urinary incontinence.

We hypothesized that the response of diabetes to birth trauma involves:

1. Increased severity of incontinence
2. Increased duration and delayed recovery of injuries resulting from vaginal delivery.

The study aim was to examine the effects of vaginal distension as a surrogate for vaginal birth trauma on urinary incontinence and bladder function, as measured by leak point pressure (LPP) and **awake** cystometrogram (CMG) in diabetic female rats.

Study design, materials and methods

Six to eight weeks after establishment of DM in virgin female Sprague Dawley rats by intraperitoneal injection of streptozocin (60 mg/kg), a suprapubic tube (SPT) was implanted in 16 diabetic and 16 age, sex, and weight matched control rats. Three days later, the LPP was measured by instilling the bladder with normal saline at 6 mL/hr via the SPT which was connected to both a syringe pump and a pressure transducer. Bladder capacity was measured at the first sign of visible leakage. Bladder was then refilled at ½ capacity, at which point Crede maneuver was simulated by applying gentle pressure to abdomen. When leakage was noticed, pressure was immediately released, and the peak pressure was recorded as LPP. The LPP was tested 3-5 times on each rat to insure consistent results. Diabetic and control animals were then randomized to undergo vaginal distension (VD) or sham vaginal distension (SVD), creating four groups: 1) diabetes with vaginal distension (DM+VD), 2) diabetes with sham vaginal distension (DM + SVD), 3) controls with vaginal distension (Ct+VD) or 4) controls with sham vaginal distension (Ct+SVD). VD was performed as modified from previous work {3}. After adequate anesthesia, the vagina was first accommodated to a larger capacity by subsequently inserting and removing increasing sizes of urethral dilators to avoid rupture. Then a modified 10F catheter was inserted and distended with 3 ml of water for 3 hours. Animals in the sham distension groups were anesthetized and had the vagina accommodated using the urethral dilators. Catheter was inserted but not inflated. Four and ten days after the procedures all the animals underwent repeat measurements of LPP and **awake** CMG. *Polyview* software was used to analyze all data. Wilcoxon Signed Rank tests were performed to evaluate the changes between time points within each group. To compare differences between groups in the change of variables over time, Kruskal-Wallis tests were performed. This study protocol was approved by our institution's IACUC for animal safety.

Results

A total of 32 (n=8 in each group) were used for this study. LPP at the baseline was equal among all four groups. LPP at the baseline was equal among all four groups (Figure 1). The change in LPP from baseline to 4 days was significantly different between the VD groups and the sham groups ($p \leq 0.001$). (Figure 2) By 10 days after VD, the Ct+VD group showed significant increase in LPP from 4 days ($p \leq 0.003$), whereas the DM+VD group had little change in LPP ($p = 0.001$). (Figure 3) Moreover, looking at the change from baseline LPP to 10 days, DM+VD group is significantly different from that of both control groups ($p < 0.03$). CMG showed significant increase in bladder capacity and mean interval of both DM groups 4 days after the procedures.

Fig 1: Baseline LPP

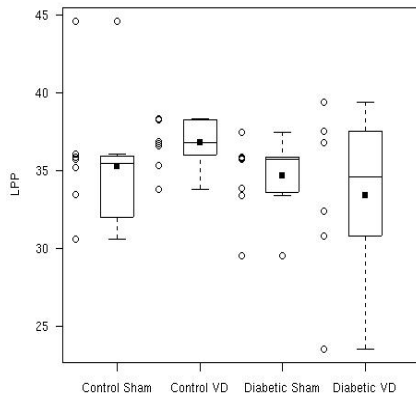


Fig 2: LPP at 4 days

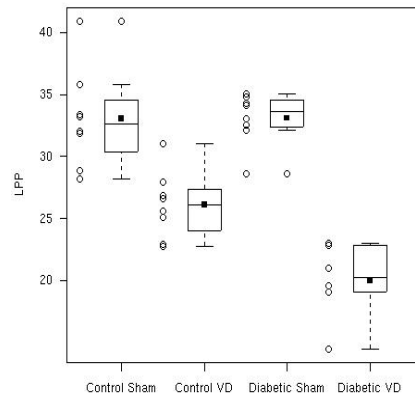
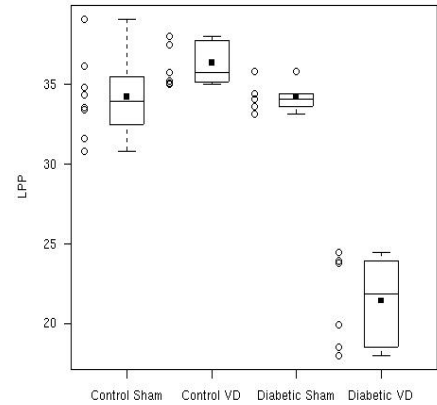


Fig 3: LPP at 10 days



Interpretation of results

As we hypothesized, vaginal distention caused stress urinary incontinence in both diabetic and control female rats, as evidenced by significant decrease in LPP compared to the baseline as well as compared to the sham groups. By 10 days, however, the control rats were able to recover back to their baseline LPP levels, whereas the diabetic rats continued to have decreased LPP. The combined effects of diabetes and vaginal distention may be responsible for the prolonged and more severe urinary incontinence in this group.

Concluding message

Vaginal distension in diabetic female rat results in increased severity of urinary incontinence as measured by LPP. Diabetes causes delayed recovery from effects of vaginal distension on urinary incontinence despite a larger bladder capacity. This model can be used in studying the mechanistic explanation for a higher incidence of urinary incontinence among parous diabetic women.

References

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