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ANIMAL MODEL FOR CHRONIC STRESS URINARY INCONTINENCE

Hypothesis / aims of study

Stress urinary incontinence (SUI) is a common problem in women but its pathophysiology is still not completely understood. SUI is often associated with vaginal delivery. Pudendal neuropathy and muscular damage to the pelvic floor musculature are often-quoted causes of SUI after birth trauma. Developing an animal model for SUI is based on two lines of thought. Lue's research team induced SUI by simulating a birth trauma in rats by dilating the vagina (1). Brubaker's research team caused a direct pudendal nerve laesion, without dilating the vagina (2).
The impact of these manipulations were evaluated in different ways: histological studies, immunohistochemical staining, electron microscopy, functional modifications (leak point pressure measurement, cystometry). These evaluations have been performed only a short time after inducing incontinence. An animal model for chronic SUI is lacking so far. We present a modified animal model for SUI which allows the evaluation of chronic SUI on lower urinary tract function .

Study design, materials and methods

With permission of the local ethics committee female virgin wistar rats were used (n=8). A transurethral catheter (22G) was inserted to avoid bladder overdistension during the procedure. SUI was induced by simulating a birth trauma (1): intravaginal balloon inflation (5 ml) during 3 hours. The rats were anaesthetised by a mixture of intraperitoneal ketamine (100 mg/kg) and xylazine (15 mg/kg). They were given analgesia (tramadol 5 mg/kg po) one day postoperatively. The duration of SUI was evaluated under light anesthesia (ketamine 20 mg/kg xylazine 3 mg/kg) at weekly interval. SUI was objectivated by the sneeze test using a rat whisker inserted into the nostril to induce sneezing (3). The sneeze test was conducted twice and was considered positive if urinary leakage was observed from the external meatus during both tests. If the sneeze test was negative intravaginal balloon inflation was repeated. Total duration of the procedure was 8 weeks.
Urinary retention was evaluated daily by manually palpation of the rats' lower abdomen.
Urinary infection was evaluated on microscopy. After 8 weeks the rats were sacrified and a bladder strip was prepared for morphometric analysis: the paraffin embedded formalin fixed sections (PEFFS) were stained with H&E to evaluate neutrophyl granulocytes and lymfocytes. To detect mastcells PEFFS were stained with toluidin blue.
A control group (n=8) underwent the same procedure without intravaginal balloon inflation.

Results

During the total study period all rats had occasionally negative sneeze test without a clear pattern over the 8 weeks. They were all dilated again. If the sneeze test was positive and subsequently no vaginal distension was repeated at that time, the test was always negative 14 days after the previous distension. Repeated dilation made SUI to persist in all rats during the entire period. None of the rats in the control group showed urinary leakage during any of the sneeze tests.
Urinary retention did not occur during this study. No signs of urinary infection were found on microscopic analysis. Bladder histology was normal and no granulocyt, lymfocyt or mast cell infiltration was observed. No difference was found with analysis of the bladders in the control group.
Using this procedure all rats survived anaesthesia and surgical manipulation.

Interpretation of results

Simulation of birth trauma in an animal model studying influences of SUI on lower urinary tract function has previously been described. However only the short term influence of SUI was studied. By repeating birth trauma simulation, we were able to induce a prolonged period of SUI in rats, which was objectivated through repeated sneeze tests. This study shows that a 14 day interval between vaginal distensions is to long to induce SUI continuously. Our data suggest an optimal interval between 7 and 14 days.

Evaluating the presence of SUI at weekly intervals by the sneeze test under light anaesthesia and performing vaginal distension if the test is negative, enables to produce SUI for a prolonged period of at least 8 weeks without urinary retention or signs of urinary tract infection.

Concluding message

A prolonged period of SUI can be obtained in a rat model using only minor manipulations. Such an animal model can be used to evaluate the long term influence of SUI on lower urinary tract function, which may improve treatment strategies in women with SUI. Whether an 8 weeks period is sufficient to produce significant changes on lower urinary tract function is currently being evaluated.

References

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