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Title: Long-term catheterisation in the rat as an animal model for detrusorinstability

Aims of the study:

Studies to determine the effects of intravesically administered drugs are usually performed in short-term catheterisation models as described by Conte et al (1). In these rat studies cystometries were performed mainly within hours to 14 days after catheter implant. The aim of this study was to determine the background effect of catheter implant on cystometric parameters, in a rat model.

Methods:

Operation technique

8 female Whistar rats weighing 220-250 g were anesthetised with pentobarbital (1 ml/kg, Sanofi, Brussels) and amoxicilline LA SC (0,125 mg/kg) was administered pre-operatively. The abdomen and neck were shaved and disinfected with iodine alcohol. A 2 cm suprapubic midline incision was made and the bladder was exposed. A purse string was made at the bladder dome using a 4/0 polyester suture (Ethibond, Ethicon) incorporating a 16G In-syte catheter (Beckton-Dickinson) with the needle removed. Through the remaining sheet, a 22 cm long PE-50 polyethylene cathether (Clay-Adams) was inserted. Aseptic technique was used while implanting the catheter. The sheet was then removed and the purse string was tightened. The catheter was tunnelled subcutaneously towards the neck of the animals, where it was fixed using two 2/0 silk sutures. The abdomen was closed in separate layers using 4/0 Vicryl (Ethicon), and 4/0 Vicryl rapide for intracutaneous skin closure. Additional Ethilon 5/0 sutures were placed if needed. The animals were then housed in separate cages under standard laboratory conditions.

Cystometry

Cystometry was performed in conscious rats using a standard pressure transducer (Baxter) and a Dataq Instruments DI-730-USB analogue-digital convertingdevice. Recordings were made using the Windacq Pro+ data-acquisition software. Cystometries were recorded on days 7, 14 and 21 after implantation. Each rat was placed in a restraining cage during cystometry. Bladder was filled at a rate of 160 µl/min using a T-tube and a Harvard syringe pump 11. Sterile saline at room temperature was used as infusion fluid. Four reproducible voiding cycles were recorded and analysed from each rat.

For each parameter student's paired t-test was performed in order to test statistical significance with α=0,05 against baseline. Parameters used were maximal detrusor pressure, maximal pressure of unstable contractions, maximal voiding pressure, baseline pressure and the amplitude of the 'after contraction'.

Results:

After 14 days all bladders showed unstable contractions. By day 21, two rats had removed their catheter and thus were unable to be measured again. There was a significant difference in all parameters between

day 7 and day 14. Especially the maximal detrusor pressure (P=0.0004) and maximal voiding pressure (p= 0.0003) showed a significant increase. The amplitude of the maximal unstable contraction raised significantly (p= 0.02), as well as the baseline (p=0.01) and the amplitude of the 'after contraction' (p=0.02). Between day 14 and day 21 the maximal voiding pressure was the only parameter showing significant changes (p= 0.01).

Conclusion:

Significant changes appear in all urodynamic parameters between day 7 and day 14. Between day 14 and 21 only the maximal voiding pressure increases significantly. All effects were obtained spontaneously, just by means of the catheter implant. These data suggest that catheter implantation by itself generates detrusorinstability. The urodynamic traces seem to be very unreliable from day 1 to day 14. From day 14 on, their unreliability decreases and they reach a 'steady state'.

These findings imply that our long term catheterisation model allows reproducible cystometries from day 14 on, and that it can be used in medium long term studies for detrusorinstability.

Reference:

Conte,B., D'Aranno,V., Santicioli,P., Giuliani,S., Mancinelli,A., Furio,M., Maggi,C.A., Meli,A., New method for recording cystometrograms in conscious freely moving rats, J. Pharmacol. Methods, 19 (1988) 57-61.

Figs 1 and 2: Both examples of the Box-Whisker plots for two of our parameters.

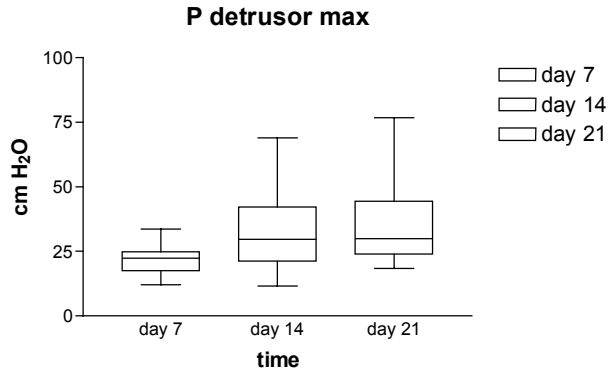

Fig 1

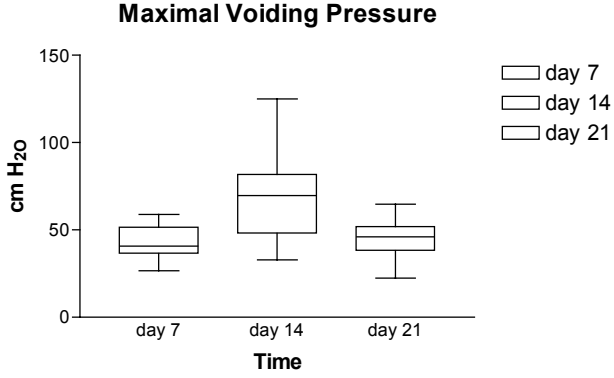

Fig 2

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