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DISCONTINUOUS (12 HR) CYSTOMETRY IN CONSCIOUS FREELY-MOVING RATS: EFFECT OF INDOMETHACIN AND OXYBUTYNIN.

Aims of Study

Cystometry is a widely used in vivo method for quantitative studies on physiopharmacology of micturition in several animal species, as well as to evaluate changes in urodynamic parameters associated with urinary incontinence in humans. During cystometry in animals, continuous filling of bladder is obtained in constrained rats by an intravesical catheter connected to a delivery system which pumps saline into the bladder at constant rate. In our experience continuous cystometry in conscious rats performed for long periods revealed detrimental effects on basal values of urodynamic parameters, particularly a decrease in peak micturition pressure (MP). This finding represents a problem in evaluating the effect of orally administered compound with long duration of action. To overcome these problems, a cystometrographic method in freely-moving rats with bladder discontinuously infused with saline, was developed. By this method, the effects of an oral dose of indomethacin and oxybutynin were evaluated.

Methods

Cystometry in conscious male rats was performed one day after catheter (Portex, ID 0.58 mm, OD 0.96 mm) implantation in the bladder dome. The catheter was exteriorized through a subcutaneous tunnel in the retroscapular area, where it was connected to a swivel at the top of the cage, thus allowing free movement to animals in a 20-25 cm size cage. On the day of the experiment, the free tip of the cannula was connected by a T-shape tube to a pressure transducer and to a peristaltic pump for infusion of warm saline solution (37^{o} C) into the urinary bladder at a constant rate of 0.1 ml/min. Two urodynamic parameters from the cystometrogram were recorded on a polygraph and were evaluated: bladder volume capacity (BVC) and micturition pressure (MP). Basal BVC and MP were evaluated as mean values from the cystometrograms recorded 90-120 minutes prior to treatment. Then the bladder infusion was stopped, the animals were treated orally with the test compound or vehicle. The bladder infusion was restarted 1 hour after drug or vehicle administration, using a 1 hr on/off cycle and changes in BVC and MP were evaluated for 10 hr.

Results

The percent changes of BVC and MP induced by oral administration of indomethacin (1 mg/kg) and oxybutinin (3 mg/kg) in comparison with changes observed in their matched control groups are shown in Fig. 1 and 2.

In rats treated with vehicle, BVC values recorded up to 10 hr after treatment did not significantly change in comparison with basal values. Similarly, MP was practically unchanged, and the decrease observed was no more than 10%.

Oxybutinin induced a slight increase of BVC that was significantly different than control group only at 4 h after administration. Indomethacin induced a sustained and long lasting increase of BVC significantly different from controls from 4 h to 8 h after administration.

Both compounds induced a marked decrease of MP from 2h to 10 h after administration. The decrease was significantly different either from basal values and vehicle treated groups.

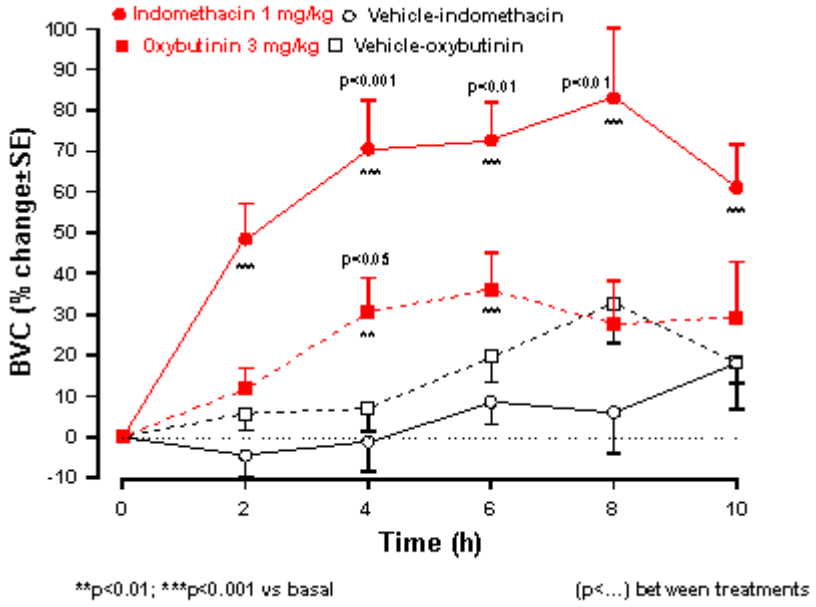

Fig. 1

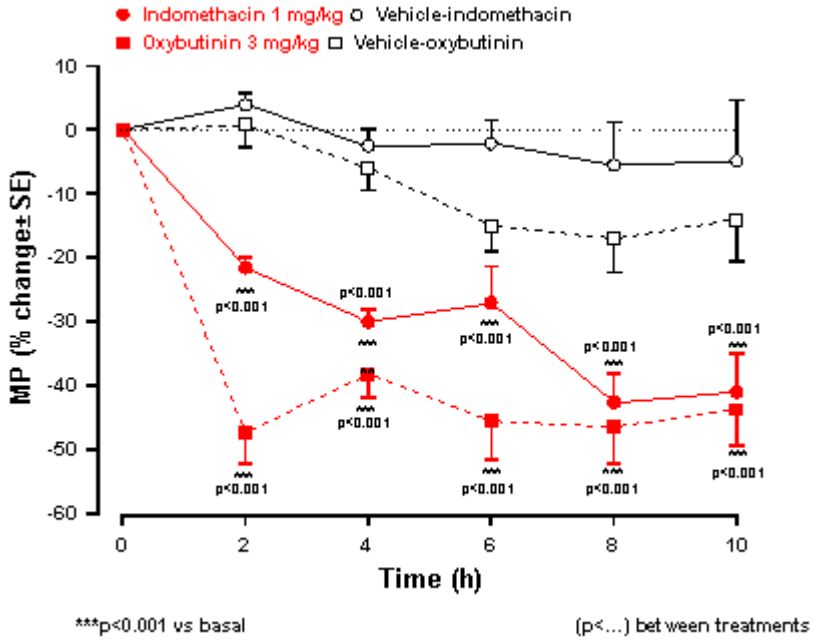

Fig. 2

Conclusions

Discontinuous cystometry (1 hr on and 1 hr off) in conscious freely-moving rats appears a suitable model to evaluate the effects of long-lasting compounds on the micturition reflex. Cystometrographic parameters in control animals, in particular MP, did not substantially change in the 11-12 hr period of observation, in contrast to our previous experience utilizing continuous infusion of the bladder.