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A CANINE URINARY FREQUENCY MODEL ASSOSIATION WITH BLADDER HYPERACTIVITY

Aims of Study

Although symptoms of lower urinary tract dysfunction, including urinary incontinence, are common in our aging population, no selective drug therapy, or even a satisfactory animal model, has been established yet. Intravesical instillation of acetic acid as a chemical irritant of the bladder is known to facilitate micturition reflex in the rat. Accordingly, we developed a urinary frequency model by intravesical infusion of acetic acid, and performed cystometrography in conscious canines. Further, we evaluated the role of C- fiber afferents in this type of bladder hyperactivity, and investigated the effects of anticholinergic agents. The aim of this study was to evaluate the validity of the canine urinary frequency model, and to evaluate the efficacy of anticholinergic agents in this model.

Methods

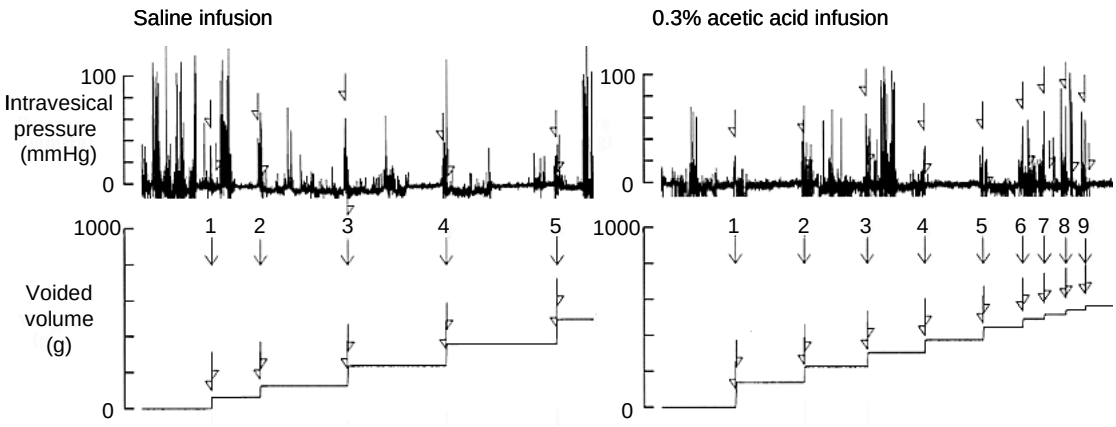
Nineteen male beagle dogs were used for the experiment. Under intravenous pentobarbital anesthesia, a polyurethane catheter was inserted into the bladder dome for cystometry. More than 2 weeks after the operation, the urodynamic parameters were measured telemetrically for 3 hr in the conscious animals. The following cystometric parameters were measured: intravesical pressure, urinary frequency, voided volume and micturition interval. Saline maintained at room temperature was infused into the bladder continuously at the rate of 180 mL/hr. After a preset period, acetic acid at concentrations of 0.1, 0.2 and 0.3 % in saline was infused into the bladder for period of 3 hr. In addition, the urodynamic parameters were compared between canine models of acetic acid-induced urinary frequency with and without hypogastric denervation. The anticholinergic drugs puropiverine and tolterodine were administered orally after a preset period. The effects of the drugs were assessed by comparing the cystometric parameters measured just before, and 30 minutes after the drug administration.

Results

Acetic acid infusion increased the urinary frequency and intravesical pressure, and decreased the micturition interval and voided volume in a concentration-dependent manner, in both canine models with and without hypogastric denervation. Following the infusion of saline, the measured urinary frequency, micturition interval, voided volume and intravesical pressure in the animals were 2.7, 70.1 min, 147.1 g and 54.2 mm Hg, respectively. In contrast, following intravesical infusion of 0.3% acetic acid, the urinary frequency, micturition interval, voided volume and intravesical pressure at micturition were 5.0, 36.8 min, 105.1 g, 79.4 mm Hg, respectively. In these canine models of bladder hyperactivity, puropiverine administration (1mg/kg, p.o.) was found to significantly increase the micturition interval and the voided volume.

Conclusions

The present study revealed that acetic acid intravesical infusion increased the urinary frequency in the conscious dogs and an anticholinergic drug effectively symptoms of lower urinary tract dysfunction. It was confirmed that the bladder hyperactivity model established by intravesical infusion of acetic acid showed increased micturition frequency due to the firing of C-fiber bladder afferents. It is thus expected to serve as a useful model for the evaluation of drugs for the treatment of urinary frequency. In this model, puropiverine, an anticholinergic drug, was shown to effect a decrease in the urinary frequency.


Saline infusion
0.3% acetic acid infusion
100
Intravesical pressure (mmHg)
0
1000
Voided volume (g)
0
1
2
3
4
5
6
7
8
9