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CONSCIOUS RATS WITH BLADDER OUTLET OBSTRUCTION OR INTRAVESICAL PGE2 ADMINISTRATION AS EXPERIMENTAL DETRUSOR OVERACTIVITY MODELS

Hypothesis / aims of study

Because the physiology of the rat and human bladders have many similarities, many rat models of experimental detrusor overactivity (DO) have been used to study the pathophysiology of DO. However, no single animal model can be expected to reproduce all the various pathophysiologies causing DO in humans, and several animal models may be required to study relevant mechanisms involved in DO. DO models in awake rats can be evaluated using pressure/ volume–parameters. However, DO has not been well quantified objectively, because of lack of recording of abdominal pressure. In this study, we studied DO during the filling phase objectively by measuring intra-abdominal and intravesical pressures simultaneously in two model of DO 1) rats with partial bladder outlet obstruction and 2) animals receiving intravesical PGE2.

Study design, materials and methods

Sprague Dawley rats (n=24) were used. Twelve female rats were subjected to sham or partial bladder outlet obstruction for 2 weeks. Six female and 6 male rats were given PGE_2 intravesically to induce DO. Intravesical pressure (IVP) was recorded via an open catheter in the bladder and intraabdominal pressure (IAP) via an intraabdominal balloon catheter.[1] Continuous cystometry was performed three days after the catheters were inserted. Conventional urodynamic parameters of pressure and volume were investigated. IVP rises (IVPRs) during the filling phase were defined as increments that exceeded 2 cmH_2O from baseline. IVPRs were counted, and it was determined which were caused by abdominal straining or DO according to the presence of simultaneous changes in IAP. Detrusor pressure (DP) was defined as the IVP corrected for IAP. All statistical calculations were based on the number of individual animals and significant differences were considered at $p<0.05$.

Results

Rats receiving intravesical PGE2 showed increased pressure parameters and decreased volume parameters comparing to baseline state (normal rats before PGE2 instillation). Obstructed rats showed no change in pressure parameters, but had increased volume parameters comparing to sham, excepting the micturition volume (Table 1). Obstructed rats and rats receiving intravesical PGE2 showed greater frequency of IVPRS, compared to their controls. DO represented up to 90% of the IVPRs in obstructed rats, and 33 % (female) and 38 % (male) in rats receiving PGE2, with the remainder caused by abdominal straining (Table 2).

Interpretation of results

Rats receiving intravesical PGE2 show similar characteristics to overactive bladder of human in pressure and volume parameters, but part of what is recorded as DO may be misunderstood as abdominal straining. The obstructed rat is a suitable model of experimental DO, but shows no changes in pressure and volume parameters.

Concluding message

More than one model may be necessary for the study of the pathophysiology of DO and for evaluation of drugs aimed for the treatment of DO.

References

1. NUU (2007) 27; 88-95.

TABLE I. Pressure & volume Parameters (cmH_2O) in Rats During Conscious Cystometry Before and After Intravesical Infusion of PGE2 (50 μM) and in Rats Subjected to Sham-Operation or Partial Bladder Outlet Obstruction (BOO).

		BP cmH2O	MP cmH2O	BC mL	MV mL	RV mL	MI min^{-1}
MALE							
Baseline (n=6)	IVP	10.2±1.2	62.2±5.6	1.22± 0.08	1.20± 0.09	0.02± 0.01	7.75± 0.63
	DP	7.9±1.0**	59.7± 5.8**				
PGE2 (n=6)	IVP	15.1±2.6†	121.9± 10.6††	0.74± 0.09††	0.74± 0.09††	0	4.97± 0.55††
	DP	13.2±2.7*†	119.0± 10.6**††				
FEMALE							
Baseline (n=6)	IVP	10.0± 0.9	54.5± 3.8	1.18± 0.10	1.16± 0.10	0.02± 0.01	7.01± 0.57
	DP	8.1± 0.8**	51.5± 3.8**				
PGE2 (n=6)	IVP	13.2± 1.2†	106.9± 9.8††	0.83± 0.10††	0.81± 0.09††	0.01± 0.01	5.12± 0.55††
	DP	11.8± 1.3*†	103.8± 9.8**††				

SHAM (n=6)	IVP	11.7± 0.6	67.8± 7.1				
	DP	8.8± 1.1**	63.9± 7.2**	2.04± 0.30	1.97± 0.31	0.06± 0.03	5.78± 0.64
BOO (n=6)	IVP	13.2± 1.0	68.8±7.7				
	DP	11.2± 1.1**	64.7± 8.1**	2.52± 0.26‡	1.23± 0.27	1.29± 0.43‡	7.54± 0.66‡

IVP, intravesical pressure; DP, detrusor pressure (IVP -IAP); BP, basal pressure; MP, micturition pressure. BC, bladder capacity; MV, micturition volume; RV, residual urine; MI, micturition interval. Results are expressed as mean and SEM. *P < 0.05. **P < 0.01. (paired Student's t-test) versus IVP. †P < 0.05. ††P < 0.01. (paired Student's t-test) versus baseline. ‡P < 0.05. (unpaired Student's t-test) versus sham.

TABLE 2. Characteristics of IVPRs during filling phase in Rats During Conscious Cystometry Before and After Intravesical Infusion of PGE2 (50 μM) and in Rats Subjected to Sham-Operation or Partial Bladder Outlet Obstruction (BOO).

	Time of Filling Phase. min	Freq. of IVPRs. min^{-1}	Freq. of AS. min^{-1}	Freq. of DO. min^{-1}	Percentage of AS. and DO in total IVPRs (%)
MALE					
Baseline (n=6)	7.7± 0.6	0.7± 0.1	0.7± 0.1	0	100 : 0
PGE2 (n=6)	5.0± 0.6**	1.8± 0.2**	1.1± 0.2	0.7± 0.2*	62: 38
FEMALE					
Baseline (n=6)	7± 0.6	0.8± 0.1	0.8± 0.1	0	100 : 0
PGE2 (n=6)	5.1± 0.5**	1.5± 0.3*	1.0± 0.2	0.5± 0.2*	67 :33
SHAM (n=6)	5.8± 0.6	0.9± 0.1	0.9± 0.1	0	100 : 0
BOO (n=6)	9.8± 1.8	1.9± 0.3†	0.2± 0††	1.7± 0.3††	10 : 90

IVPR: intra-vesical pressure rise, IVP: Intra-vesical pressure, DP: Detrusor pressure,AS: Abdominal straining. Results are expressed as mean ± standard error of the mean. *P < 0.05. **P < 0.01. (paired Student's t-test) versus baseline. †P < 0.05. ††P < 0.01. (unpaired Student's t-test) versus sham.

Specify source of funding or grant	**The Korea Science and Engineering Foundation(KOSEF) grant funded by the Korea government (MOST) (No. R01-2006-000-10850-0)**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Inha University Animal Ethic Committee**