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EFFECTS OF INTRATHECAL AND PERIPHERAL INJECTIONS OF A-1 ADRENERGIC RECEPTOR SUBTYPE SELECTIVE AND NON-SELECTIVE ANTAGONISTS, ON BLADDER ACTIVITY IN RAT MODELS WITH PARTIAL URETHRAL OBSTRUCTION

Hypothesis / aims of study
Up-regulations of α-1 AR and changes of subtype expression may occur in bladder overactivity induced by bladder outlet obstruction (BOO) and therefore, α-1 AR antagonists can also increase functional bladder capacity (FBC) and alleviated irritative symptoms. To search for the evidences of up-regulations and changes in subtype expression of α-1 AR, the effects of intrathecal (i.t.) or intraarterial (i.a.) injections of tamsulosin (α-1A subtype selective), naftopidil (α-1D subtype selective) and doxazosin (non-selective) on bladder activity were investigated. FBC, maximal vesical pressure (Pmax) and involuntary contraction were assessed in rat model with normal and partial bladder outlet obstruction (BOO).

Study design, materials and methods
Female Sprague-Dawley rats were used to investigate the action of α1 receptor antagonist on the bladder. Experimental rats were divided into normal (n=42) and partial BOO (n=48) groups. Partial obstruction of the bladder neck was surgically created. Cystometric studies were performed 6 weeks after surgery. Both groups were anesthetized with urethane, and continuous cystometry was performed. The a1-adrenoceptor antagonists (tamsulosin, naftopidil, doxazosin) were injected into the femoral artery (i.a.) and subarachnoid space (i.t.) at the level of L6-S1 spinal cord segment. Cystometric parameters, such as FBC, Pmax, frequency, frequency of involuntary contractions (FIC), were analyzed before and after the drug injection.

Results
Table 1. Change in the cystometric parameters before and after administration of the α1ARs antagonists in normal and partial BOO rats.

	Normal	BOO	p-value
Δ Frequency (/min)	-0.14±0.27	-0.22±0.39	>0.05
Δ FIC (/min)	-	-0.11±0.33	<0.05
Δ FBC (cc)	0.10±0.18	0.34±0.70	<0.05
Δ Pmax (mmHg)	-2.71±2.11	-2.98±2.95	<0.05

Δ Frequency: changes of frequency after administration of the α1ARs antagonists Δ FIC: change of frequency of involuntary contraction (FIC) after administration of the α1ARs antagonists, Δ FBC: change of functional bladder capacity (FBC) after administration of the α1ARs antagonists, Δ Pmax: change of maximal intravesical pressure after administration of the α1ARs antagonists,

Table 2. Change in the parameters before and after intraarterial (i.a.) and intrathecal (i.t.) injection of α1ARs antagonists in normal and BOO rats.

	Normal		BOO	
	i.a.	i.t.	i.a.	i.t.
Δ Frequency (/min)	-0.16±0.25	-0.13±0.28	-0.28±0.47	-0.13±0.23
Δ FIC (/min)			0.18±0.43	0.00±0.13
Δ FBC (cc)	0.18±0.22	0.00±0.01	0.46±0.92*†	0.19±0.16
Δ Pmax (mmHg)	-3.11±2.15	-2.38±2.08	-8.52±2.41†	-3.55±3.50

Δ Frequency: changes of frequency after administration of the α1ARs antagonists Δ FIC: change of frequency of involuntary contraction (FIC) after administration of the α1ARs antagonists, Δ FBC: change of functional bladder capacity (FBC) after administration of the α1ARs antagonists, Δ Pmax: change of maximal intravesical pressure after administration of the α1ARs antagonists,

*: p<0.05: normal vs. BOO
†: p<0.05; intraarterial vs. intrathecal

Interpretation of results

Increase in functional bladder capacity (FBC) and decrease in maximal intravesical pressure (Pmax) were observed after administrations of all three drugs (both i.t. and i.a.) in both normal and BOO rat models ($p<0.05$). Significant decrease in the frequency of involuntary contraction was observed in BOO rat models ($p<0.05$). Increase in FBC after administrations of α-1 AR antagonists (both i.t. and i.a.) was significantly greater in the BOO than in normal rats ($p<0.05$). In the BOO rat models, increase in FBC and decrease in Pmax were greater after intraarterial than after intrathecal injection ($p<0.05$). There were no significant differences in the degrees of the changes of cystometric parameters among three different α-1 AR antagonists.

Concluding message

In this experiment, evidence of the up-regulations of α-1 AR in BOO was shown by the greater increases of the functional bladder capacity in rats with BOO than in controls after α-1 AR antagonist injections. However, there were no subtype differences in the effects on the bladder activity. In addition to the antagonistic action of these agents on the α-1 AR receptors of detrusor, these agents may also act on the lumbosacral cord, but with less degree than on the detrusor in rats with BOO.

References

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