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Title: INTRAVESICAL RESINIFERATOXIN VERSUS CAPSAICIN IN THE TREATMENT OF DETRUSOR

HYPEREFLEXIA IN SPINAL CORD INJURED PATIENTS.

Aims of Study

Current strategies for treating detrusor hyperreflexia (DH) due to neurogenic bladder disorders relies on partially blocking the efferent parasympathetic innervation to the bladder by means of anticholinergics, which frequently cause intolerable adverse effects so that doses are insufficient to restore continence. Resiniferatoxin (RTX), an agent with ultra-potent capsaicin-like activity but with minimal initial excitatory effects, should be more efficacious in achieving improvement. We compared the clinical and urodynamic effects of intravesical instillation of capsaicin and of RTX in a group of spinal cord injured (SCI) patients with refractary DH.

Methods

Twenty four patients with DH due to chronic spinal cord injury, not responsive to anticholinergic drugs, were prospectively randomized to receive intravesical capsaicin (Group 1) or RTX (Group 2). Patients assigned to Group 1 underwent intravesical instillation of 100 ml saline solution containing 2mM capsaicin dissolved in 30% alcohol (Group 1), and those assigned to Group 2 received 30 ml saline solution containing 10⁻⁷ M RTX (Group 2). Both solutions were retained in the bladder over 45 minutes with accompanying urodynamic monitoring. All patients underwent repeated urodynamics at 30 and 60 days. The following data were analysed: uninhibited detrusor contractions threshold and amplitude, and bladder capacity. The occurrence of local or systemic adverse effects was noted.

Results

Urodynamic results are showed in Tab. 1.

Tab. 1		threshold (ml)			amplitude (cm H ₂ 0)				capacity (ml)	
Grou	baselin	30 days	60 days	basel	30 days	60	baselin	30 days	60 days	
ps	е			ine		days	е			
No.										
1	145±47	199.3±57.	185±44	72.3±	70.3±2	68.6±	172±41	219±94	215±73.8	
	.4	6	.3	35	1	27	.2	.4		
									(P=0.087)	
		(p=0.081)	(p=0.07		(p=0.09	(p=0.		(p=0.09		
			6)		5)	08)		2)		
2	176±54	249.6±10	275±97	57.2±	61.5±3	61.8±	239.3±	365±12	357±121	
	.3	7	.9	28	6	26	77	3		
									(p=0.036)	
		(p=0.025)	(p=0.01		(P=0.07	(P=0.		(p=0.00		
)		8)	08)		1)		

In baseline examination there was no significant difference between urodynamic data of the two groups. During capsaicin instillation autonomic dysreflexia was detected in 5 patients and, early after treatment, we observed, haematuria in 5 patients, severe suprapubic discomfort in 9 and incresed spasticity and spasms legs in all cases. Four patients in Group 1 reported subjectively improvement at 30 days. During and after RTX instillation we did not observe any local or systemic side effects. Clinical improvement after RTX instillation was reported by most of patients at 30 and 60 days.

Conclusions

Little information is available on clinical effects and long-term follow-up of C fiber afferent desensitizing agents in the treatment of DH due to spinal cord injury and no consistent data comparing clinical and urodynamic results of capsaicin and RTX instillation has been reported. Our results indicate that intravesical therapy which blocks the afferent arm of the reflex causing detrusor contraction is effective in patients with resistant DH. Our study shows that RTX is more effective than capsaicin in increasing uninhibited detrusor contractions threshold and bladder capacity, without causing any adverse effect. As it is approximately 1,000 times more potent than capsaicin but with minimal initial excitatory effects, it can be used in concentrations so low that noxious effects are not eliciteAlthough dose and treatment schedules are to be well established, intravesical RTX may represent a new approach in the treatment of neurogenic DH.