

DESENSITIZATION OF C-FIBERS BY MEANS OF INTRAVESICAL RESINIFERATOXIN INSTILLATION TREATS PAINFUL BLADDER, INTERSTITIAL CYSTITIS AND OVERACTIVE BLADDER

Aims of Study

Frequency, urgency, incontinence and sometimes pain are common symptoms for overactive bladder (OAB), interstitial cystitis (IC) and painful bladder (PB). Although no etiopathogenesis based treatment has been proposed for these conditions till now, it is tempting to assume that they may in fact represent different manifestations of so-called "neurogenic inflammation of the bladder", an illness in which the previously silent afferent c-fibers may be engaged. Unmyelinated afferent nociceptive terminals (c-fibers) are this group of spinal sensory fibers that could be activated by either inflammation or decentralization. After this activation a reorganization of bladder reflexes occurs, leading to the development of aforementioned symptoms common for PB, OAB, IC.

As an increase in the number of CGRP- and SP-containing nerve fibers was demonstrated in all of the aforementioned clinical conditions, it appears possible that a selective neurotoxin affecting C-fibers (like resiniferatoxin; RTX) could be used for treatment of PB, IC and OAB. Therefore, we decided to evaluate the effectiveness of RTX in the treatment of the abovementioned diseases.

Methods

Thirty one patients were included in the study. The pre-treatment evaluation included urodynamic examination, urine cytology and culture. In all patients previous treatment modalities have failed.

The diagnosis was established using the following principles:

1. Patient was considered as having OAB when detrussor instability, reduced first desire to void volume and reduced maximum cystometric capacity were demonstrated during the urodynamic together with frequency and urgency. In this group of patients the urine cytology was normal (no signs of inflammation) as well as they were not reporting with pain syndromes during or after voiding;
2. IC was diagnosed when all or some of the aforementioned symptoms existed together with positive cytology (inflammation) and pain;
3. PB when patients demonstrated pain, frequency, urgency, reduced cystometric capacity, however without inflammatory changes in urine cytology.

RTX administration:

Before treatment with RTX, the bladder was anaesthetized with an instillation of 20 ml of 2% lidocaine solution. Afterwards, RTX was administered in a form of intravesical instillation in a concentration of 100 nmol-500 nmol in 30% ethanol solution. The volume of instilled drug was 20 ml. RTX was left in the bladder for 30 min. During the treatment the intravesical pressure was constantly monitored.

The efficacy of the treatment was evaluated after 3 and 6 months as well as after 1 year.

Results

OAB was found in 15 patients (3 women, 12 men; mean age 57.3),

IC was diagnosed in 8 patients (2 men, 6 women, mean age 61.2),

and PB in 8 women (mean age 57.3) .

Detailed data at baseline are shown in Table 1.

No increase in the intravesical pressure was observed in patients responding well to the therapy. However, in 30% of patients resistant to the RTX instillation a spontaneous contraction of the bladder (up to 50 cm H₂O) was observed.

Neither haematuria nor urinary retention was observed after the RTX treatment. In the case of OAB patients RTX instillation was successful in 46.6% of them, while 20% reported a symptomatic improvement, 66.6% of PB patients were cured and 16.6% improved. Within the group of IC patients cure rate was 50% and improvement was observed in 16.6% of them. A significant increase in the volume at the first desire to void, as well as in the cystometric capacity, paralleled by a significant decrease in the voiding frequency were observed in the OAB and IC groups. Therapeutic effect of RTX lasted for 1-12 months, being the shortest in IC and PB patients (2.3 and 3.6 months, respectively), while in patients with OAB this effect lasted up to 7.1 months in the average. Data before and 3 months after the treatment are shown in Table 1.

Table 1

Disease	Baseline					3 months after the treatment				
	D	N	FD	CC	DI	D	N	FD	CC	DI
PB	7.7	2.0	132	276,5		6.2	0.75	209	446,75	
IC	15.3	6.0	63,3	138		11.3	2.66	96,6	293,3	
OAB	11.2	4.2	81,85	151,28	76,42	5.2	1.4	189,28	300,57	48,2

Legend: D-daytime frequency (n), N-nighttime frequency (n), FD-first desire to void (ml), CC-cystometric capacity (ml), DI-maximum pressure of unstable detrusor contraction (cm H₂O), data represent mean values

Conclusions

The overall therapeutic efficacy of RTX in the treatment of OAB, PB and IC is at the level of 50%, which may be indicative for an important involvement of c-fibers in the etiopathogenesis of, at least some, of these disorders.