41

de Sèze M.[1], Wiart L.[2], de Sèze M.[3], Dosque J.[4], Hazane C.[4], Saubion J.[4], Moore N.[5], Barat M.[3], Joseph P. [3]

1. Neurologic rehabilitation unit. University Hospital Pellegrin., 2. Rehabilitation center Tour de Gassies 33523 Bruges, 3. Rehabilitation unit. University hospital Pellegrin, 4. Pharmacology department, University hospital Pellegrin, 5. Toxicology department, University hospital Pellegrin

EFFICACY AND TOLERANCE OF INTRAVESICAL INSTILLATION OF CAPSAICIN AND RESINIFERATOXIN FOR TREATMENT OF DETRUSOR HYPERREFLEXIA IN SPINAL CORD INJURED PATIENTS.
A DOUBLE-BLIND CONTROLLED STUDY: PRELIMINARY RESULTS.

Aims of Study

To compare the efficacy and the tolerance of intravesical instillation of capsaicin (CPS) versus resiniferatoxin (RTX), two specific neurotoxic agents to C-fiber afferents, in spinal cord injured patients suffering from severe urinary incontinence due to detrusor hyperreflexia.

Methods

This prospective double-blind randomised controlled study was approved by the ethics committee of our university hospital and patients gave written consents.

The inclusion criteria were adults spinal cord injured patients, suffering from symptoms of detrusor hyperreflexia (urinary incontinence, frequency, urgency) resistant to oral anticholinergic drugs. Exclusion criteria were vesicoureteral reflux, intravesical lesion, urinary tract, pregnancy, breast-feeding and hemocoagulation disorders.

On day zero (D0), patients were randomised to receive one intravesical instillation of 100ml RTX 50 nmol/l diluted in 10% ethanol (RTX group) or 100ml of CPS 1mmol/l diluted in glucidic solvent (CPS group). In the both group, the instillation lasted 30 minutes and were preceded by an anaesthetic intravesical instillation of 40 ml 2% lidocain during 20 minutes, accordingly with the referential protocol [1].

The evaluation were performed before instillation (D0), than one month (D30) and 3 months (D90) after. Efficacy was evaluated by voiding chart (number of daily voiding/catheterisation, leakage, urgency), urodynamic data (Maximum Cystometric Capacity, MCC; Maximal Detrusor Pressure, PD) recorded during saline cystometry (50ml/mn). General tolerance was judged by side effect record. Statistical analysis was carried out using the t-test and chi-2 test to compare the quantitative and qualitative data respectively. Values of $p<0.05$ were considered to be significant.

Results

On the forty first adults patients (24 F, 16M; 18 SCI, 22 MS, 45.0 years) prospectively included, 21 patients were randomised in RTX group and 19 patients in CPS group. Before instillation, the patients were comparable in the two groups, concerning the demographic and micturitional status (table 1-2).

Table 1	**RTX**	**CPS**	**p**
Population	21	19	NS
Sex (F/M)	10/11	13/6	NS
Disease (MS/SCI)	10/11	12/7	NS
Duration *(years)*	8.6	17.7	NS

Table 2	**Group**	**D0**	**D30**	***p 0/30***	**D90**	***p 0/90***
Voiding	RTX	9.5	8.2	*NS*	9.4	*NS*
	CPS	11.1	6.7	*0.01*	6.4	*0.05*
Leakages	RTX	6.9	2.2	*0.02*	4.3	*NS*
	CPS	6.0	3.0	*0.03*	2.6	*0.04*
Security delay (m)	RTX	9.1	18.4	*NS*	10.8	NS
	CPS	2.1	13.3	*0.01*	12.7	*0.04*
MCC	RTX	195.9	250.8	*NS*	320.1	*0.005*
	CPS	174.5	291.0	*0.01*	299.6	*0.01*
PD	RTX	75.4	70.5	*NS*	71.5	*0NS*
	CPS	74.8	73.4	*NS*	74.9	*NS*

The efficacy on day 30 was valuable for the first 33 patients, respectively 18 patients on CPS group and 15 patients on RTX group. There were an improvement in the 2 groups as regard as continence, frequency, urgency, MCC and QOL parameters. The benefits concerned 77.7% of the CPS group versus 66.6% of in the RTX. The improvement was better in the CPS group with difference who attempt a statistical

significance in all of the clinical parameters whereas it was restricted to the continence for the RTX group. A significant rise of MCC was showed only in the CPS group.

On day 90, the efficacy was possible for 25 patients, respectively 16 patients on CPS group and 9 patients on RTX group. The continence was still remained in 66.6% of the patients in the CPS group versus 55.5% in the RTX group. The benefit on day 90 remained significantly better in the CPS group than the RTX group excepted for MCC. The main duration of efficacy was 91.1 +/-96 days in RTX group and 66.8 +/-52 days in CPS group CG ($p<0.1$).

The immediate tolerance in the whole group of 40 patients appeared better in the RTX group than in the CPS group, with side effects occurrence in 35.7% and 52.6% respectively. Nevertheless, the side effect were short lasting and well tolerated in the both group. It never occur general complication.

Table 3	**Pubic pain**	**Uretral pain**	**Hematuria**	**ADR**	**Flush**	**Worsening**	**% of patients**
RTX	5	2	0	0	3	3	35.7%
CPS	9	3	1	0	5	4	52.6%
p	*0.03*	*NS*	*NS*	*NS*	*0.01*	*NS*	

Conclusions

This first controlled randomised trial comparing efficacy and tolerance of glucidic CPS and alcoholic RTX in patients presenting urinary incontinence due to neurogenic hyperreflectic bladder demonstrate that both drugs are efficient for improving clinical and urodynamical status. The glucidic CPS appeared efficiency, arguing for the relevance of the glucidic solvent. The benefit of CPS appeared better than RTX in the short/middle term, possibly due to their differential pharmacokinetics properties [2]. Early adverse effects are mild in the both treatments in regard of previous study using CAPS in alcoholic vehicle [1,2,3], corroborating the major role of ethanol in the tolerability of vanilloid instillation. The better tolerance of RTX than CAPS in glucidic solvent has to be confirmed in a larger group of patients.

References .[1] Fowler CJ *et al.* J NNP 1994; 57: 169-73.
[2] de Ridder D *et al.* BJU Int 2000; 86: 172-80. [3] de Sèze M *et al.* Neurourol Urodyn 199817:513-23.