Conclusions:

The study results confirm that the efficacy of trospium chloride in patients with different types of urge-syndrome is clinically relevant and statistically significant different to placebo. Furthermore, it has been demonstrated that trospium chloride is at least as effective and safe as tolterodine.

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Author(s): S.M. Di Stasi, A. Giannantoni, P. Navarra, G. Capelli, R. Massoud, and R.L. Stephen.

Institution, city, country:
"Tor Vergata" University of Rome, "Santa Lucia" Rehabilitation Hospital I.R.C.C.S. Rome, Catholic University of Rome, and Physion Labs. Medolla (MO); Italy.

Title (type in CAPITAL LETTERS, leave one blank line before the text):
ORAL AND INTRAVESICAL OXYBUTYNIN IN SPINAL CORD INJURY PATIENTS WITH DETRUSOR HYPERREFLEXIA: CLINICAL, URODYNAMIC AND PHARMACOKINETIC STUDIES.

Aims of Study

Oral oxybutynin, a valuable detrusor spasmolytic, is bedevilled by unpleasant side effects. Several reports indicate that intravesical oxybutynin is efficacious and lacks side effects in adults but no consistent urodynamic and pharmacokinetic patterns are evident. In this report, the urodynamic effects and pharmacokinetics of oxybutynin are described for ten spinal cord injury patients with detrusor hyperreflexia who received oral, intravesical passive diffusion (PD) and intravesical electromotive drug administration (EMDA) single doses of drug. Both sets of measurements are correlated to the methods of administration, therapeutic efficacy and anticholinergic side effects.

Methods

The study plan included six, 8 hour urodynamic sessions at weekly intervals in order to monitor the following situations applied randomly: *(a)* no treatment, *(b)* oral oxybutynin 5 mg, *(c)* intravesical 100 ml NaCl 0.9% x 60 min, *(d)* intravesical oxybutynin 5 mg in 100 ml NaCl 0.45% x 60 min, *(e)* intravesical 100 ml NaCl 0.9% with 5 mA x 30 min, *(f)* intravesical 5 mg oxybutynin in 100 ml NaCl 0.45% with 5 mA x 30 min. Each treatment was associated with periodic blood and bladder content sampling. During the study period patients were free from urinary infection and not receiving any drug that influenced detrusor and striated sphincter behavior. The occurence of local or systemic adverse effects was noted. Differences among group means were analyzed by ANOVA.

Results

The following data were analysed: number, maximum amplitude and duration of uninhibited detrusor contractions and urine volume residual (Table 1). There was subjective but no significant objective improvement over baseline with oral and intravesical PD oxybutynin. Conversely there was significant improvement in all objective urodynamic measurements with intravesical EMDA oxybutynin. Plasma profiles were a single peak and decay following oral oxybutynin and two distinct peaks with both intravesical PD and EMDA oxybutynin. AUC/8 h: intravesical PD 709 ng vs oral 1485 ng ($p < 0.005$) vs intravesical EMDA 2781 ng ($p < 0.001$). Bladder content samples confirmed oxybutynin absorption. Oral oxybutynin caused anticholinergic side effects in 6/10 patients. There were no side effects with intravesical PD or EMDA administrations.

Table 1. Urodynamic outcomes. Data are the means ± SEM of 10 observations per group.

	Uninhibited Detrusor Contractions			Urine Volume Residual	
UDM	Number	Amplitude cm H_2O	Duration sec	4 h ml	8 h ml
(a)	33.6 ± 7.2	64.1 ± 9.0	689.4 ± 406.7	36.2 ± 19.2	48.7 ± 31.2
(b)	25.1 ± 6.2	60.5 ± 10.2	559.3 ± 283.2	41.0 ± 31.4	43.0 ± 21.3
(c)	27.4 ± 6.2	65.4 ± 9.2	671.9 ± 508.4	42.8 ± 23.1	36.2 ± 23.6
(d)	21.9 ± 7.8	58.2 ± 8.8	574.2 ± 345.4	43.5 ± 25.1	47.8 ± 21.9
(e)	35.6 ± 9.0	57.0 ± 7.3	664.7 ± 567.1	44.3 ± 22.8	45.7 ± 12.2
(f)	9.2 ± 3.7	35.7 ± 10.5	265.1 ± 131.0	235.2 ± 110.7	237.5 ± 129.5
P value	0.0006	0.0049	0.0521	0.011	0.015

Conclusions

. Intravesical oxybutynin is a valid route of delivery and, although accelerated intravesical administration (EMDA) leads to significantly higher plasma levels, the side effects seen with oral oxybutynin do not occur.