Conclusions: The new OD formulation of tolterodine is highly effective, safe and well tolerated in the treatment of overactive bladder. The effect on urgency and other patient perceptions is interesting and merits further study.

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

EFFECT ON SALIVARY OUTPUT FOLLOWING CONTROLLED-RELEASE OXYBUTYNIN AND TOLTERODINE.

Aims of Study. Both tolterodine (TOL) and controlled-release oxybutynin (OXY-XL) have been separately shown to be effective in the treatment of overactive bladder. Both OXY-XL and TOL have been shown to be associated with less dry mouth than conventional immediate-release oxybutynin (IR-OXY); however, these treatments have not been directly compared in a controlled study. Saliva output studies following all three treatments have been separately reported but differences in study methodology prevent comparison across studies. This is the first study that objectively evaluates dry mouth as measured by saliva output following the three medications and placebo.
Methods. This was a randomized, double-blind, four-treatment, four-period, crossover study. The four treatments were single doses of OXY-XL (10 mg), IR-OXY (5 mg), TOL (2 mg), and placebo, with a 5-7 day washout period between treatments. Saliva output (stimulated by chewing parafilm) was collected in a beaker over a 2-minute period at 1 to 2 hour intervals for 12 hours after dosing. Saliva output integrated as area under the curve (AUC) and the lowest saliva value production (TROUGH) over the 12-h period was estimated.
Results. All three medications resulted in significantly lower saliva AUC compared to placebo. OXY-XL and TOL were similar with respect to saliva AUC but significantly higher than IR-OXY (Table 1 & 2). All three medications also resulted in significantly lower saliva TROUGH compared to placebo. The lowest TROUGH value was observed with TOL followed by IR-OXY, OXY-XL and placebo (Table 1).

Table 1: Mean (SD) Saliva Production Parameters

Saliva Parameter	OXY-XL	TOL	IR-OXY	Placebo
AUC (g.h)	30 (15)	29 (17)	27 (15)	33 (17)
TROUGH (g/2min)	1.7 (1.0)	1.4 (0.9)	1.5 (0.9)	2.0 (1.1)

Table 2: Statistical Comparison (p-values)

Saliva Parameter	Active vs. Placebo	OXY-XL vs. IR-OXY	TOL vs. IR-OXY	OXY-XL vs. TOL
AUC (g.h)	<0.01	0.01	0.005	0.80
TROUGH (g/2min)	<0.001	0.05	0.96	0.06

Conclusion. This study showed that 10 mg controlled-release oxybutynin and 2 mg tolterodine appear to be similar with respect to dry mouth as measured by salivary output and associated with less dry mouth than 5 mg immediate-release oxybutynin.
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Title (type in CAPITAL LETTERS, leave one blank line before the text): RESIDUAL URINE AND URINARY RETENTION DUE TO ANTICHOLINERGIC THERAPY ? - RESULTS WITH PROPIVERINE

Aims of study One of the most troublesome adverse events under anticholinergic treatment is residual urine, in cases of urinary retention even requiring immediate medical intervention. Studies focussing on urge incontinence with limited patient numbers suggest that no increase of residual urine occurs under propiverine (prop.) [1]. Therefore, this presentation aims at an analysis of residual urine in an extended patient population suffering from urge incontinence, mixed urge/stress incontinence or urgency.

Material and methods In a post marketing drug surveillance (PMS) in 1476 patients suffering from urge incontinence, mixed urge/stress incontinence or urgency, residual urine was determined either by ultrasound or by catheter prior to (V0) and after 12 weeks of (V12) treatment with prop. The mean age was 58.5 ± 14.4 years. The distribution of sex ratio to the different subgroups corresponds with the epidemiologically estimated ratio. Furthermore, frequency/volume charts, mean dosage and tolerability were documented.

Results On average, a decrease of residual urine was documented. No relevant differences resulted for the three diagnostic subgroups, however the subgroup urgency with an over representation of males demonstrated a less pronounced decrease. Dependencies of prop. dosage (15 mg prop. b.i.d. or t.i.d.; mean daily dosage compare table) and residual urine could not be pointed out. An increase of residual urine resulted in 176 cases (11.9 %), 85 of them had already residual urine at V0. In three pat. urinary retention occured, one case documenting a urothel carcinoma of the bladder and the two others a history of benign prostate hyperplasia.

		urge incontinence n=609	urge/stress incontinence n=519	Urgency n=348
patients male [n/%]		107 / 17.6	41 / 7.9	114 / 32.9
female [n/%]		500 / 82.4	478 / 92.1	233 / 67.1
residual urine [ml]				
male	V0	30.9 ± 37.3	28.9 ± 35.9	23.6 ± 27.6
	V12	21.0 ± 24.6	17.6 ± 25.9	19.3 ± 21.8
	change	- 10.9	- 11.3	- 4.3
female	V0	21.9 ± 31.9	21.1 ± 30.1	13.8 ± 22.1
	V12	11.6 ± 18.1	13.4 ± 19.6	9.1 ± 15.6
	change	- 10.3	- 7.7	- 4.7
change [%] male / female		35.3 / 47.3	39.1 / 36.5	18.2 / 29.0
mean prop. dosage				
V0 [mg/d]		37.5 ± 9.4	37.6 ± 9.0	35.4 ± 9.2
V12 [mg/d]		32.3 ± 10.4	32.5 ± 10.8	29.6 ± 10.6

Conclusions An general increase of residual urine attributable to anticholinergics is not documented by PMS data of prop. A clinical study comprising urge incontinence supports, that no residual urine developed [1]. In a clinical study on pat. suffering from BPH, pollakisuria and urinary incontinence, an increase of residual urine occured only in a minor percentage (6/75 pat.), a retention of urine manifested in rare cases (2/75 pat.) [2]. Pharmacologic experiments demonstrate increased maximal bladder capacity under prop. without an increase of residual urine [4]. A clinical study focussing on reflex incontinence resulted in an increase of residual urine (37 ml) after two weeks of prop. treatment, significantly more than under placebo (p=0.01) [3]. However due to small pat. numbers, pat. suffering from reflex incontinence or infravesical obstruction were not evaluated in the PMS data. Neglecting contraindications was responsible for the cases of urinary retention under prop. In these elderly pat. reduced body weight and concomitant medication were additional triggering factors for this adverse

event. This concept that prop. only induces an increase of residual urine in infravesical obstruction, e.g. in BPH or reflex incontinence associated with DSD, or in reduced detrusor contractility must be investigated further.

[1] Madersbacher et al. BJU 1999; 84: 646-651
[2] Saito et al. Jap J Urol Surg 1999; 12: 525-536
[3] Stöhrer et al. Spinal Cord 1999; 37: 196-200
[4] Tsuchida et al. Acta urol jap 1990; 36: 915-919

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

EFFICACY OF EXTRAMURAL PHYSICAL THERAPY MODALITIES IN WOMEN WITH PROVEN BLADDER OVERACTIVITY: A RANDOMIZED CLINICAL TRIAL

Aims of Study

The symptoms of bladder overactivity consist of urgency, frequency, nocturia and/or urge incontinence. The underlying etiology is still only partially understood. In this study bladder overactivity is perceived as a dysfunction of the bladder in which a subject has no or decreased control over sudden contractions of the detrusor muscle, so that this leads to premature passage of urine [1]. To guarantee homogeneity of the study population a tool was found in the application of ambulatory urodynamics. The Detrusor Activity Index (DAI), based on ambulatory urodynamics, uses results of extramural ambulatory cystometry to quantify detrusor activity during several consecutive filling phases [2]. The aim of this study is to assess the efficacy of lower urinary tract exercises (LUTE) and functional electrostimulation (FES) in women with proven bladder overactivity (DAI $\geq$ 0.5).

Methods

In a single blind randomized clinical trial with four arms we studied the efficacy of three treatment modalities, i.e. LUTE (group 1), office and home based FES (group 2) and office based FES and LUTE (group 3) versus a no-treatment group (group 4). During a 2-week qualification period inclusion and exclusion criteria were checked, medical history was taken, a micturition diary combined with pad test was obtained and, finally, ambulatory urodynamics according to ICS standards [3] were performed. The data at the end of this period established baseline values. After the qualification period each patient of groups 1-3 received 9 treatment sessions, once a week. LUTE consisted of patient information, bladder training, specific pelvic floor muscle exercises (PFME) and toilet behavior. FES was applied vaginally with a stochastic electrical current between 4 and 10 Hz, at maximal tolerable level. A portable microprocessor controlled system, the ProUrge system (Innocept Medizintechnik Inc, Gladbeck, Germany) was used. In this study the DAI was the principal effect parameter. The ambulatory urodynamics were taken before randomization and at the end of the study period (within 14 days). Subjective outcome was measured by the Incontinence Impact Questionnaire (IIQ-7) [4]. This was done twice identically, after the first ambulatory investigation and at the end of the study period (within 14 days).

Results

Out of a total of 83 patients with symptoms of urgency and frequency, indicative for an overactive bladder, 71 patients had pre and post-treatment DAI values; from these, a subgroup of 57 randomized patients, mean age 55.2 (sd. 13.5) with DAI $\geq$ 0.5, were considered as having *proven* bladder overactivity and were evaluated. Baseline characteristics (see Table 1), based on standardized medical history and baseline values of outcome parameters showed no statistical differences between groups. In repeated measures ANCOVA of DAI-score differences between pre- and post-treatment conditions overall differences over therapy groups were not statistically significant ($F=2.28$ by 3 and 52 df; **$p=0.090$**) (see Table 2). ANOVA of IIQ-7-score differences between pre- and post treatment conditions showed no statistical overall differences over therapy groups ($F=1.10$ by 3 and 48 df; $p=0.358$)