Conclusions

Our results do not show overall significance. A plausible explanation for this result appears to be a power problem. Since $p_{overall} = 0.090$ is not significant we performed a sensitivity analysis (see Figure) and we inspected the specific differences between groups. Ensuing power analysis, in a design with only two arms (control vs. FES) showed that with 20 patients in each arm we might have reached statistical significance and that a strong treatment effect (standardized effect = 0.80, power=0.80) on bladder overactivity in group 2 (FES) would have been reached. This is the first study in which a homogeneous study population was established and efficacy was measured quantitatively, indicating a large effect of intravaginal FES in women with proven bladder overactivity.

Table 1: Comparison of Baseline Characteristics (T=0, *N=57*)

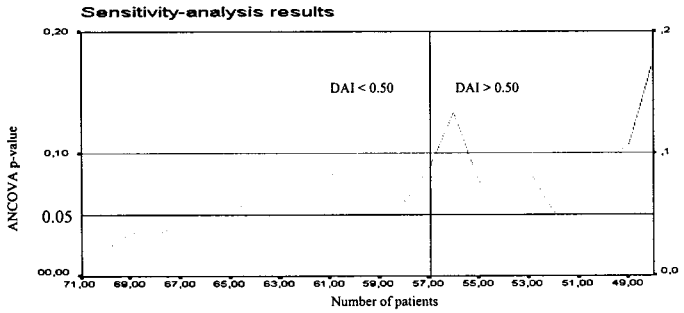
	Controls	LUTE	FES	Combination
Padtest MUDO in ml. mean (sd) *N*	65 (87) *14*	62 (93) *13*	120 (225) *14*	113 (170) *16*
Frequency voidings / hrs mean (sd) *N*	1.28 (0.52) *14*	1.33 (0.57) *13*	1.19 (0.56) *14*	1.06 (0.46) *16*
Volume / voiding (ml) mean (sd) *N*	144 (74) *14*	143 (59) *13*	131 (66) *14*	105 (52) *16*
Dai-1 mean (sd) *N*	0.853 (0.145) *14*	0.843 (0.164) *13*	0.841 (0.180) *14*	0.865 (0.165) *16*
IIQ-7 mean (sd) *N*	0.77 (0.74) *14*	0.99 (0.75) *13*	0.91 (0.69) *13*	0.61 (0.58) *14*

No significant differences between groups on baseline characteristics were found

Table 2: Statistical characteristics / results dai and difference of dai (N = 57/ dai pre ∃ 0,50)

Egroup	DAI pre-means	Sd	DAI post-means	Sd	diff.dai	sd
Control	0,853	0,145	0,795	0,255	0.058	0.188
LUTE	0,843	0,164	0,622	0,389	0.221	0.370
FES	0,841	0,180	0,567	0,370	0.274	0.354
Combination	0,865	0,165	0,830	0,292	0.035	0.261
Total:	0,851	0,160	0,709	0,339	0.142	0.310

Figure:



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ELECTROPHYSIOLOGICAL EVALUATION OF POTENTIAL ADVERSE EFFECTS OF TOLTERODINE, OXYBUTYNIN AND TROSPIUM CHLORIDE ON THE CENTRAL NERVOUS SYSTEM

Aims of Study: Tolterodine, oxybutynin and trospium chloride are antimuscarinic agents commonly used in the treatment of the overactive bladder. These agents differ in terms of their lipid solubility and, therefore, may cross the blood-brain barrier to different extent. However, comparative data regarding their influence on the central nervous system (CNS) are limited. The objective of this study was to evaluate the effects of these antimuscarinic agents on the CNS by using quantitative-topographical EEG (qEEG).

Methods: In a single-blind, placebo-controlled, parallel-group, multiple-dose study, 64 healthy male volunteers (aged 18–35 years) were randomised to receive tolterodine 2 mg twice daily, oxybutynin 5 mg three times daily (tid) or trospium chloride 15 mg tid. Changes from baseline in spectral EEG-power (μV^2) were evaluated in 6 frequency bands at 17 electrode positions (qEEG) during rest and under mental demand over a period of 14 hours. Safety assessments included monitoring of adverse events, vital signs and 12-lead ECG recordings.

Results: Oxybutynin caused statistically significant power reduction in theta, alpha1, alpha2 and beta1 EEG frequency bands, consistent with a probable direct CNS effect. Maximum effects were seen 1-2 hours after dosing. Cumulative effects from multiple dosing were noted. Tolterodine and trospium chloride induced only a marginal effect on the CNS, as shown by a slight theta power reduction. Such effects were assumed to be of secondary origin, reflecting the feedback control from the periphery to Barrington's nucleus (the pontine micturition centre). Oxybutynin differed significantly from tolterodine and trospium chloride in terms of effects on theta, alpha1, alpha2 and beta1 power. No significant difference was found between trospium chloride and tolterodine.

A total of 57 adverse events were reported (4 placebo; 14 tolterodine; 15 trospium chloride; and 24 by oxybutynin recipients), of which 36 were CNS-related. Only 19 of the CNS-related adverse events were classified as drug-related (3 tolterodine; 5 trospium chloride; and 11 oxybutynin).

Conclusions: Oxybutynin (a tertiary amine) has significant effects on the CNS as measured with qEEG, while tolterodine and trospium chloride show marginal effects. These differences are explained by the fact that tolterodine (a tertiary amine) and its active metabolite have a lipophilicity 30 and >350 times lower than oxybutynin, respectively, while trospium chloride is a quaternary amine that barely crosses the blood-brain barrier.

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Title (type in CAPITAL LETTERS, leave one blank line before the text): A COMPARATIVE STUDY OF MAGNETIC VERSUS ELECTRICAL STIMULATION ON INHIBITION OF DETRUSOR OVERACTIVITY