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

Aims of study: Functional pelvic floor electrical stimulation (FES) has been utilized as a treatment for urinary incontinence due to overactive bladder. Functional magnetic stimulation (FMS) has been applied by clinical neurophysiologists as a safe and noninvasive method for stimulation of nervous tissues(1). Recently, a continuous magnetic stimulator assuring long-time stimulation has been developed, and the effects on urethral closure and inhibition of detrusor contraction have been reported(2,3). The aims of our study was to perform a randomized study for investigating the urodynamic effects of FMS and FES on inhibition of detrusor overactivity.
Methods: Thirty-two patients with urinary incontinence due to detrusor instability (15 males, 17 females; aged 62.3 ± 16.6 years) were randomly assigned to two treatment groups (15 patients in the FMS group and 17 in the FES group). Stimulation was applied continuously at 10 Hz in both groups. For FMS the magnetic stimulator unit was set on an arm-chair type seat and had a built-in coil-cooling system and a concave-shaped coil, so that the patients could sit undressed during stimulation. For FES, a vaginal electrode was used in females and an surface electrode to the foreskin of the penis in males. Cystometry was performed before and during the stimulation.
Results: The two treatment groups were well matched with each other in terms of number of patients, age, sex, body weight and pre-treatment urodynamic parameters. Bladder capacity at first desire to void and and maximum cystometric capacity increased significantly during stimulation compared with prestimulation levels in both groups (p= 0.0054 and 0.0015, respectively, in the FMS group, and p= 0.0045 and 0.0229, respectively, in the FES group). However, the increase in maximum cystometric capacity was significantly (p=0.0135) greater in the FMS group (114.2±124.1 cmH2O, or 105.5±130.4% increase compared with pretreatment level) than that in the FES group (32.3±56.6 cmH2O, or 16.3±33.9% increase). Detrusor overactivity was abolished in 3 patients of the FMS group, but not in any patient of the FES group. No adverse effects were noted in any of the patients of both groups during the stimulation.
Conclusions: Although both treatments were effective, inhibition of detrusor overactivity appeared greater in the FMS group than in the FES group.
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EVENT DRIVEN ELECTRICAL STIMULATION OF THE DORSAL PENILE/CLITORAL NERVE REDUCES BLADDER CONTRACTION PRESSURE AND INCREASES BLADDER COMPLIANCE IN SCI PATIENTS

Background

The hyperreflexive and low compliant detrusor muscle in spinalised