contractility subjects on placebo achieved UI goal rate (20% v 41%, p=0.22) and cure (19% v 10%, p=0.5). Percent improvement did not differ significantly in subjects older and younger than 65 on both OXY (78% v 70%, p=0.97) and placebo (40% v 6%, p=0.92). UI was subjectively cured or much better in 81% of OXY and 37% of placebo subjects (p=0.001). Treatment satisfaction rates were high (OXY 96%, placebo 56%, p=0.01).

Predictors of improvement on OXY, controlling for other continence mechanisms, were higher uninhibitable contraction (UC) velocity (r=.54, p=0.0005), lower UC volume (r=-.46, p=0.004) and positive response to bulbocavernosus reflex or voluntary muscle contraction at the bladder neck (r=.55, p=0.004). Lower baseline PVR predicted cure (p=0.04). All men and 55% of women on OXY were cured (p=0.02). On placebo, a lower UC detrusor pressure in subjects with good proprioception (r=-.58, p=0.03) predicted improvement. Age and bladder capacity did not predict improvement on OXY or placebo.

Conclusions

1. Oxybutynin is more effective for urge UI in the elderly than previously reported when started in small doses and individually titrated to symptoms and PVR.
2. Subjects with DHIC improve as often as those with normal contractility, but are less likely to achieve cure.
3. Success with this approach does not diminish with age.
4. Brisk uninhibited contractions at low volumes, as well as functional extension of striated muscle to the bladder neck, predict improvement on oxybutynin.

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CENTRAL MUSCARINIC MECHANISM OF BLADDER OVERACTIVITY ASSOCIATED WITH ALZHEIMER TYPE SENILE DEMENTIA

Aim of study

To investigate the mechanisms of neurogenic bladder overactivity in Alzheimer type senile dementia in a conscious rat model.

Methods

Male Wistar rats were placed in a stereotaxic apparatus, and subjected to bilateral lesion of the basal forebrain by means of ibotenic acid (IA) injection (7.5 mg/rat on each side)(BF rats). Phosphate buffered saline (PBS) was injected to control rats (sham operated rats; SO rats). Cystometrograms (CMG) were obtained 7 to 10 days after IA/PBS injection. After CMG recording, choline-acetyltransferase (CAT) activities in the frontal cortices were assayed to assess the damage to cholinergic neuronal projections from basal forebrain to frontal cortices. The influences of intracerebroventricular administration of Oxotremorine M, muscarinic receptor agonist, or pirenzepine, M1 muscarinic receptor antagonist were investigated in conscious BF or SO rats. Antagonized effects of pirenzepine were also examined in BF rats. The effects of oxotremorine M or pirensepine directly injected into the PMC (pontine micturition center) were examined under urethane anesthesia.

Results: Bladder capacity become significantly smaller than before IA injection. Seven to 10 days after IA injection, bladder capacity was approximately 43% of SO rats. CAT activity in the frontal cortices was reduced in BF rats. Oxotremorine M increased bladder capacity in BF rats, while decreased in SO rats. Pirensepine significantly increased bladder capacity both in BF and SO rats, and antagonised the effect of oxotremorine M. Direct injection of oxotremorine M into the PMC decreased bladder capacity in BF and SO rats, while injection of pirensepine had no effects on CMG.

Conclusions

These results indicate that M1 muscarinic system in the cerebral cortex has inhibitory influence to micturition reflex pathway. Down-regulation of this inhibitory mechanism plays an important role on overactive bladder in Alzheimer type dementia. M2 muscarinic system in the brainstem is likely to have excitatory influence on micturition reflex pathway.

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

AN EFECT OF L-DOPA ON MICTURITION DISTURBANCE IN PATIENTS WITH PARKINSON'S DISEASE; A COMPARISON OF 'ON' AND 'OFF' PERIODS

Background Recently dopaminergic drugs are the main therapy for patients with Parkinson's disease (PD). However, exact effects of L-dopa on micturition are not ascertained. Animal experiments showed the fact that selective D2 receptor agonist quinpirole reduced bladder volume threshold for the micturition reflex in MPTP lesioned parkinsonian monkeys. We evaluated that an effect of L-dopa (D1/D2 receptor agonist) on micturition disturbance in patients with PD by using urodynamic studies.

Methods We recruited 10 patients with PD (including 5 men, 5 women), mean age 64 years. All patients have been taking dopaminergic drugs including only L-dopa / carbidopa in 3 and L-dopa / carbidopa with other antiparkinsonian drugs in 7. All patients showed marked 'on' (alleviation) and 'off' (worsening of motor performance) phenomenon in a day depending on the time of L-dopa medication. We performed detailed questionnaire of urinary symptoms and urodynamic assessments before ('off' period) and one hour after taking 100 mg of L-dopa / carbidopa ('on' period). No patient had apparent prostate hypertrophy on rectal examination and ultrasonography.

Results Comparing the 'on' period to the 'off' period, three complained exacerbation in urinary urgency in filling phase, however seven noticed improvement of voiding difficulty. Urodynamic study in the 'off' period showed that seven had detrusor hyperreflexia (DH) and none had detrusor sphincter dyssynergia (DSD). In the 'on' period, DH did not disappeared in any patients, but bladder capacity was decreased in 9 (-15 %) and increased in 1 patient. Bladder capacity of all three patients without DH was also decreased. Maximum value of watts factor (WFmax) was increased in all patients (+8.4 %). Residual urine volume (RV) was decreased in 5 (-85 %), unchanged in 4 and increased in 1 patient. All cases with unchanged RV had originally little residual urine volume (0-20 ml). DSD did not appeared in any patients, however maximum flow rate (Qmax) was decreased in 6, unchanged in 3 and increased in 1 patient and AG number (Pdet at Qmax – 2Qmax) was increased in 7, unchanged in 1 and decreased in 2 patients. Maximum urethral closure pressure (UPmax) was measured in 2 patients, and both patients showed UPmax was increased.

Conclusion Comparing urinary function in the 'on' and 'off' periods of L-dopa treatment, the results showed that L-dopa decreased bladder capacity in most of our patients, even without DH. In the voiding phase, L-dopa augmented detrusor contractility but also L-dopa increased urethra obstruction, and overall lessened post-micturition residuals in most patients. These findings may reflect central and peripheral dopaminergic action of L-dopa or its metabolite.