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GERIATRIC OAB: PROPIVERINE (A PERIPHERAL ANTICHOLINERGIC AGENT) CAN BE ADDED ON TO DONEPEZIL (A CENTRAL CHOLINERGIC AGENT) WITHOUT COGNITIVE ALTERATION

Hypothesis / aims of study

Geriatric population often have cognitive decline and overactive bladder (OAB) together; both of which significantly affect the quality of life (QOL) in the individuals. However, previously, no reports have been available to see mutual cognitive interaction between propiverine (a peripheral anitcholinergic agent) and donepezil (a central cholinergic agent; a central acetylcholinesterase inhibitor).

Study design, materials and methods

Patients – Nineteen patients were prospectively enrolled in the study. All of them fulfilled the following inclusion criteria: 1) patients who are already taking 5 mg/day donepezil because of their cognitive problems, 2) patients who also have significant QOL problems because of their OAB, 3) patients, together with their families, who provided informed consent before participating in the study. They were 5 men and 14 women; mean age, 77 years old (62-88 years); comorbid gait disorder, 12; underlying diseases, Alzheimer's disease (AD), 6, multiple cerebral infarction (MCI), 5, AD and MCI, 5, dementia with Lewy bodies, 2, fronto-temporal dementia, 1, the diagnoses made by neurological examination, MRI, SPECT and MIBG cardiac scintigraphy. Methods – In order to ameliorate OAB, we added on 20 mg/day propiverine to donepezil for 3 months. Bladder questionnaire including urinary urgency, urinary frequency and incontinence, and cognitive assessment scales (mini-mental state wxamination [MMSE, 0-30, decrease as impairment], Alzheimer's Disease Assessment Scale cognitive subscale [ADAS-cog, 0-70, increase as impairment) were made before and 3 months after addition of propiverine. Statistical analysis was made using Student's paired *t*-test.

Results

All patients were well tolerated with propiverine treatment and none was dropped out from the study. The first assessment (before propiverine) showed moderate cognitive decline in the patients as a mean MMSE score of 19.8 (range 10-29, including mild cognitive impairment) (0-30, decrease as impairment; normal > 24) and a mean ADAS-cog score of 19.9 (range 7-35) (0-70, increase as impairment; normal < 15). All patients had OAB including urinary urgency incontinence in 5. The second assessment (3 months after propiverine) showed that OAB were mildly ameliorated and urinary urgency incontinence was noted in 4. Bladder QOL was improved in the patients. No significant change of cognitive parameters was noted as a mean MMSE score of 19.2 (range 8-29) **(Figure 1)** and a mean ADAS-cog score of 20.2 (range 4-38) **(Figure 2)**. None of the patients developed nighttime confusion or other adverse cognitive problems after propiverine treatment.

Interpretation of results

Since natural decline of ADAScog score in AD patients is estimated as 2.4 points per a year (in other dementing diseases annual cognitive decline is not well known), and 58% of our patients had AD, the above changes in MMSE and ADAScog scale seemed to be minimum. None of our patients developed nighttime confusion or other adverse cognitive problems after propiverine treatment. This is the first report to show that propiverine did not affect donepezil's central cognitive enhancing action. This is presumably brought about by different action of the drugs between inside (donepezil, a centrally-acting acetylcholinesterase inhibitor) and outside (propiverine, a mainly peripherally-acting, competitive nonselective muscarinic receptor antagonist) the blood-brain barrier.

Concluding message

Propiverine (a peripheral anticholinergic agent) can be added on to donepezil (a central cholinergic agent) without marked cognitive alteration. This combination therapy seems to be a choice in order to ameliorate geriatric bladder QOL.

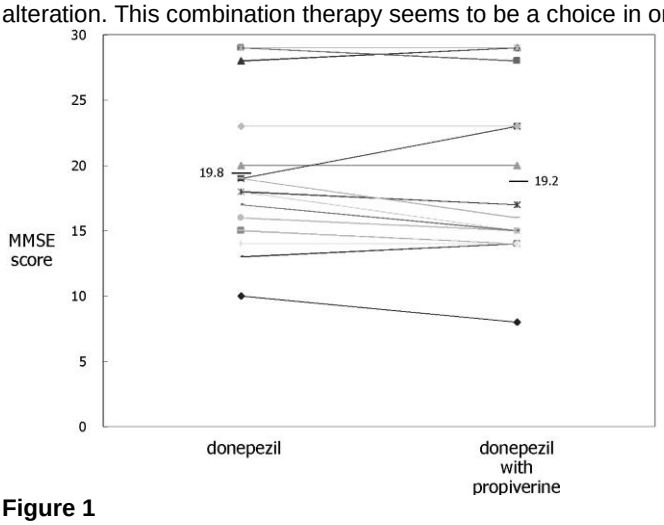

Figure 1

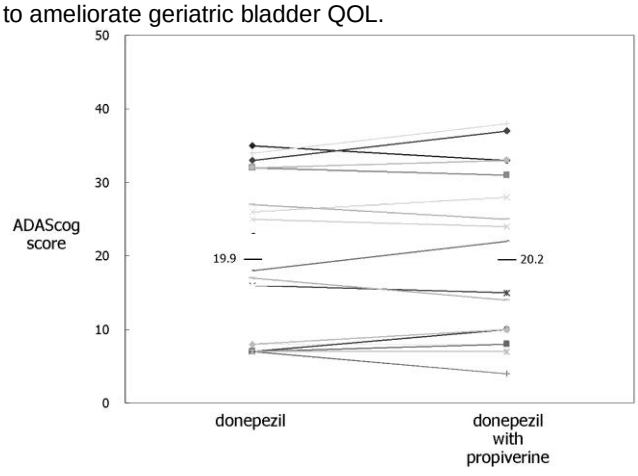

Figure 2

Specify source of funding or grant	**no funding or grant**
Is this a clinical trial?	**No**

What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Toho University Sakura Medical Center, Ethics Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**