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THE EFFECTS OF ANTI-CHOLINERGIC DRUGS FOR OVERACTIVE BLADDER ON COGNITIVE IMPAIRMENT, MENTAL DYSFUNCTION AND MOTOR DYSFUNCTION IN PATIENTS WITH NEUROLOGICAL DISEASE.

Hypothesis / aims of study

Anti-cholinergic drugs are generally used for the treatment of overactive bladder. In Japan, propiverine hydrochloride (propiverine) and oxybutynin chloride (oxybutynin) were usually used. There were some cases of cognitive dysfunction in association with oxybutynin treatment and a few cases of propiverine-induced parkinsonism. There, however, were few reports to estimate the detail centrally-acting effects of propiverine in patients with neurological disease, especially aged patients with dementia/mild cognitive impairment and/or motor dysfunction such as parkinsonism. We, therefore, investigate the effects of propiverine on cognitive impairment, mental function and motor dysfunction in patients with neurological disease.

Study design, materials and methods

The subjects were 18 aged patients with overactive bladder and neurological disease in our hospital, especially dementia/mild cognitive impairment and/or parkinsonism (male: female 13:5, average age 71 ± 8.2 years). These neurological diseases contained multiple cerebral infarction (n=8), multiple cerebral infarction + Parkinson disease (n=6), Parkinson disease (n=3), and multiple cerebral infarction + Alzheimer disease (n=1). Clinical Dementia Rating CDR was used in the staging of cognitive impairment in these patients: Normal (CDR 0) in 2, Border zone (CDR 0.5) in 8 Mild dementia (CDR 1) in 5, Moderate dementia (CDR 2) in 3. Propiverine (10-30mg) was administered in all these patients. Various neurological functions and another symptoms associated with side-effect were evaluated before taking propiverine, one-month after taking propiverine, another one-month after up-dosing of propiverine, and/or one-month after washout of propiverine. The tests of neurological functions were the questionnaire of lower urinary tract symptom, the measurement of post void residual (PVR), the scales of higher brain function, the questionnaire based on Clinician's Interview-Based Impression of Change (CIVIC), the analysis of cerebral blood flow by ^{99m}Tc-ECD single photon-emission computed tomography (SPECT), and the scale of motor function. CIVIC included disability assessment for dementia (DAD), Behavioral Pathology in Alzheimer's Disease (Behave-AD), Mental Function Impairment Scale (MENFIS). The scales of higher brain function included Mini-mental State Examination (MMSE), Alzheimer's Disease Assessment Scale (ADAS-J), Wechsler Adult Intelligence Scale (WAIS-R), Wisconsin Card Sourting Test (WCST), Hamamatsu Higher Brain Function Scale (HHBFS). The scales of motor function included Unified Parkinson's Disease Rating Scale (UPDRS) and the measurement of motor speed.

Furthermore, in another 14 patients (male: female 5:9, average age 82 ± 4.5 years)with severe dementia (CDR 3) including Alzheimer disease (n=7), 1 frontotemporal dementia (n=1), mixed dementia (n=4) and un-differential dementia (n=2), similar study were done in the nursing home. Propiverine (20mg) was administered in all these patients. Some tests were evaluated before taking propiverine and one-month after taking propiverine. The tests were the bladder diary, the measurement of PVR, the scales of higher brain function, the observation based on CIVIC, and the scales of motor function. The scales of higher brain function included MMSE, digit span/ digit span backwards, digit learning, word fluency test and similarity test.

Results

In our hospital.

In comparison with the results before taking propiverine, after taking propiverine, lower urinary tract symptoms such as urinary frequency and urinary urgency were improved dose-dependently, but neither of the PVR, the scales of higher brain function, the questionnaire based on CIVIC, the analysis of cerebral blood flow nor the scales of motor function were changed significantly. About symptoms associated with side-effect, three patients had dry

mouth after taking 20mg propiverine, one patients had constipation after taking 20mg propiverine.

In the nursing home.

In comparison with the results before taking 20mg propiverine, after taking 20mg propiverine, urinary frequency and incontinence were improved expect one patient having increase in PVR (from 0 ml to 150 ml), but neither of the scales of higher brain function, the change based on CIVIC, nor the scales of motor function were changed significantly. About symptoms associated with side-effect, two patients had dry mouth after taking 20mg propiverine, three patients had constipation after taking 20mg propiverine.

Interpretation of results

These results suggest that propiverine has no significant effect on cognitive impairment, mental function and motor dysfunction in patients with neurological disease, even in aged patients with dementia and motor dysfunction such as parkinsonism.

Concluding message

Therefore, propiverine, which is an anti-cholinergic drug for overactive bladder, could be used safely in patients with neurological disease.