

ORAL ADMINISTRATION OF PROSULTIAMINE IMPROVED THE SYMPTOMS IN PATIENTS WITH OVERACTIVE BLADDER ASSOCIATED WITH HTLV-1-RELATED MYELOPATHY/TROPICAL SPASTIC PARAPARESIS, AND ALSO REDUCED URINARY BIOMARKERS.

Hypothesis / aims of study

We had previously reported the efficacy of oral prosultiamine in not only improving the motor function, but also improving the urination function, in patients with HTLV-1-related myelopathy/tropical spastic paraparesis (HAM/TSP) [1].

Here, we report our study of the changes of the overactive bladder symptom scores (OABSS) and urodynamic study parameters, as well as of the changes in the urinary biomarkers of overactive bladder (OAB), i.e., urinary nerve growth factor (NGF) and adenosine triphosphate (ATP), in patients with OAB associated with HAM/TSP following administration of prosultiamine.

Study design, materials and methods

The subjects were patients with OAB associated with HAM/TSP. OAB was defined as a total OABSS of 3 or more, and a score of 2 or more on Question 3 (Q3). Patients who provided informed consent for participation in the study received oral prosultiamine 300 mg once daily in the morning, and were examined for changes in the OABSS and changes in the urinary NGF and urinary ATP at 12 weeks (12 W) after the administration, as compared to the values measured prior to the administration (0 W). An urodynamic study was also conducted to evaluate the objective signs before and after the administration.

A total of 16 neurogenic OAB patients accompanying HAM/TSP were enrolled in this study (3 men and 13 women; 31 to-80 years (mean \pm SD; 60.2 \pm 11.5)). Concomitant therapies such as immunomodulators and drugs for the neurogenic bladder were continued on the condition that the dose was kept constant during the study period. Patients with history of malignancy, pelvic radiotherapy, neurologic disease except for HAM/TSP, active urinary tract infections, renal impairment (creatinine clearance, 70 ml/min) were excluded. Urinary NGF and ATP were corrected by the urinary creatinine (Cr). Measurements were conducted in pooled urine samples at the maximum volume, while the urinary NGF and ATP were measured by ELISA and chemiluminescence assay using a luciferase reagent, respectively.

Results

Of the 16 patients with HAM/TSP, the OABSS improved in 12 patients (75%) ($p = 0.0035$). Among the OABSS subscales, improvement was particularly observed in the nighttime frequency (Q2) and urgency (Q3). Although no significant difference was observed in the severity of urgency incontinence (Q4) after the treatment, the symptoms improved 12 weeks after the administration in 7 of the 12 patients (58.3%) who had urgency incontinence before the administration. Urgency incontinence disappeared in 3 of the patients (25%) (Table 1).

Urinary NGF/Cr and ATP/Cr significantly decreased after prosultiamine treatment as compared with the levels measured prior to the treatment (Figures 1, 2). In regard to the urodynamic study parameters, the maximum desire to void increased from 322.0 \pm 137.3 mL to 373.6 \pm 145.2 mL ($p = 0.034$). While detrusor overactivity was observed in 10 patients before the treatment, it was noted in only 4 patients after the treatment ($p = 0.077$). The maximum flow rate showed a recovering trend, improving from 7.7 \pm 6.7 mL/sec before treatment to 9.8 \pm 6.6 mL/sec after the treatment ($p = 0.064$).

Although one patient had mild gastrointestinal symptoms, no major adverse events occurred and the treatment was completed in all patients.

Table.1 Changes in the OABSS after treatment

OABSS	0W	12W	P value
Q1. Daytime frequency	0.7 \pm 0.5	0.4 \pm 0.5	0.0679
Q2. Nighttime frequency	2.4 \pm 1.3	1.6 \pm 1.0	0.0284
Q3. Urgency	3.1 \pm 0.9	1.6 \pm 1.5	0.0013
Q4. Urgency incontinence	1.8 \pm 1.4	1.4 \pm 1.4	0.2721
Total score	7.9 \pm 2.4	5.2 \pm 3.6	0.0035

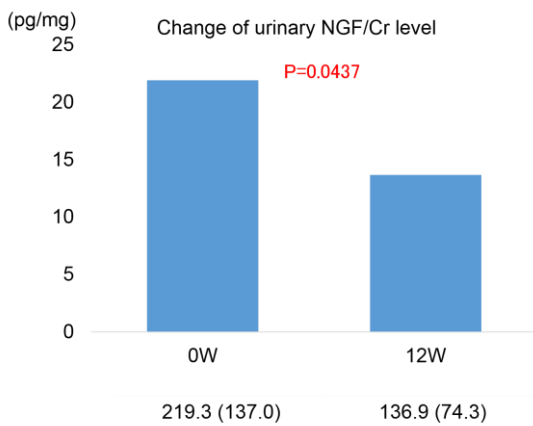


Fig.1 Changes in the urinary NGF/Cr after oral prosultiamine administration

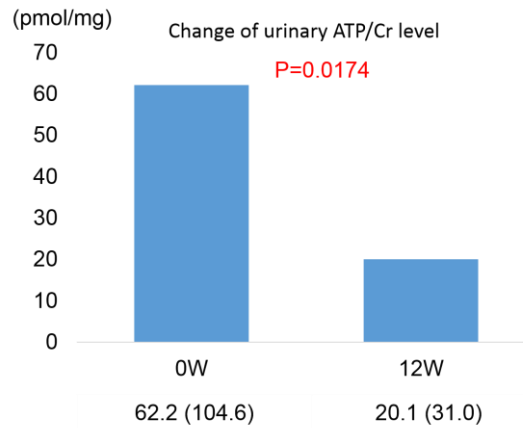


Fig. 2 Changes in the urinary ATP/Cr after oral prosultiamine administration

Interpretation of results

HAM/TSP is a chronic progressive spinal cord disease encountered in some patients with human T-cell leukemia virus infection. With regard to the urination function, urine collection disorder frequently occurs in the early stage after the onset of HAM/TSP, including nocturia in 81.4%, urinary incontinence in 76.9%, and urinary urgency in 74.4% of patients [2]. Previous studies have reported finding of inflammatory cell infiltration in the bladder interstitium, suggesting that the virus may infiltrate not only the spinal cord, but also the urinary bladder wall [3]. While the precise mechanism is still unknown, prosultiamine treatment is considered to be useful in patients with HAM/TSP for not only improving the motor function, but also improving the urination function. With the improvement of the OAB, and moreover, improvement of the urinary biomarkers such as NGF/Cr and ATP/Cr as well, prosultiamine presumably exerts efficacy not only against the spinal cord lesion, but also locally in the urinary bladder in patients with HAM/TSP. That is, the drug may be expected as a potentially useful therapeutic agent for not only OAB, but also for the interstitial cystitis/pelvic bladder syndrome associated with chronic cystitis symptoms.

Concluding message

Prosultiamine may be a useful therapeutic drug for pollakisuria, such as in patients with OAB.

References

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Disclosures

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