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NEW TREATMENT STRATEGY FOR NEUROGENIC BLADDER IN PATIENTS WITH HTLV-1-ASSOCIATED MYELOPATHY

Hypothesis / aims of study

The timing and morphology of neurogenic bladder occurring in patients with HTLV-1-associated myelopathy (HAM) vary. In general, symptomatic treatment is given, and some patients are not receiving sufficient treatment. There are patients with chronic disease who have no other alternative but to perform clean intermittent self-catheterization due to detrusor underactivity, which affects the quality of life (QOL) in many cases. Prosultiamine is expected to be a drug that can induce apoptosis of HTLV-1-infected cells [1]. In this study, we evaluated the clinical effect of prosultiamine in HAM patients with neurogenic bladder.

Study design, materials and methods

The participants in this study were 15 patients (5 men and 10 women) who had the urge to void and neurogenic bladder induced by HAM. Prosultiamine capsules (300 mg) were orally administered once daily before breakfast consecutively for 12 weeks. The test was performed without changing the drug during administration. Subjective symptoms were evaluated using the nocturia QOL questionnaire (N-QOL) and overactive bladder syndrome score (OABSS). Urodynamic study (UDS) was conducted to determine objective findings. Subjects were evaluated before the start of administration and after 12 weeks of administration. Although 3 subjects had mild digestive symptoms, no other adverse reactions were observed. Wilcoxon signed-rank test was used for statistical analysis; $P < 0.05$ was considered to indicate statistically significant differences.

Results

The mean age of the patients was 62.7 years (range, 44-80 years) and the mean duration of the disease was 21.9 years (range, 3-51 years). Eight patients could void spontaneously before the start of the study. The overall and subscale scores on N-QOL at baseline and after 12 weeks of administration are shown in Fig.1. The N-QOL score significantly improved in all questions, except Q6 (Fluid restriction) and Q8 (Disturbance of others). QOL also improved in the total score as well as subscale scores.

The results of the OABSS are shown in Fig.2. In the OABSS questionnaire, the scores of Q1, Q2, and Q3 significantly improved.

The results of the UDS are shown in Table 2. The bladder capacity and detrusor pressure improved after treatment. The urinary stream significantly increased in patients who could void spontaneously. Seven patients had detrusor-sphincter dyssynergia (DSD) before treatment, which disappeared in 3 patients (42.9%) after 12 weeks of treatment. Detrusor overactivity (DO) was present in 9 subjects, and had disappeared in all at the end of treatment. One subject had spontaneous voiding.

Interpretation of results

Prosultiamine treatment increased the bladder capacity as well as detrusor pressure. The UDS confirmed that this treatment resulted in a significant increase in the maximum urinary flow rate. Furthermore, improvements were observed in DSD and DO, the most characteristic bladder dysfunctions in HAM patients. This fact corresponds to the improvements in the N-QOL score and OABSS obtained as subjective data. To the best of our knowledge, this is the first report with such detailed analysis on the determination of treatment effects on bladder functions.

Prosultiamine was originally developed to improve tissue or cell migration of vitamin B1. However, prosultiamine migration to spinal cord tissues or bladder tissues may exert effects at the tissue level. Further analyses in this regard are necessary in the future.

Concluding message

It is considered that oral prosultiamine could be a promising novel therapeutic drug for patients with neurogenic bladder due to HAM.

References

1. Disulfide-mediated apoptosis of human T-lymphotrophc virus type-I (HTLV-I)-infected cells in patients with HTLV-I-associated myelopathy/tropical spastic paraparesis. Antivir Ther. 2009;14(4):533-42.

Disclosures

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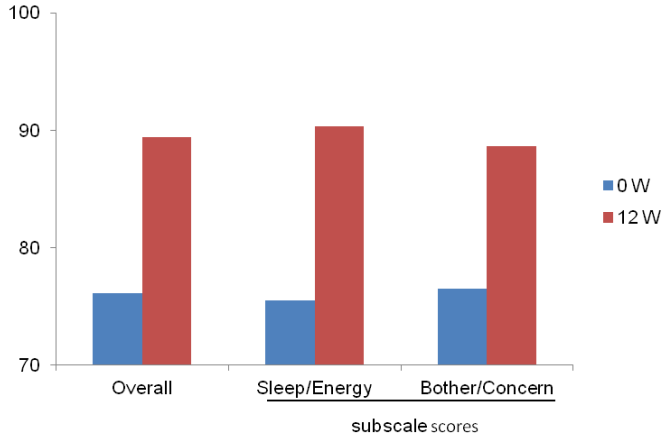
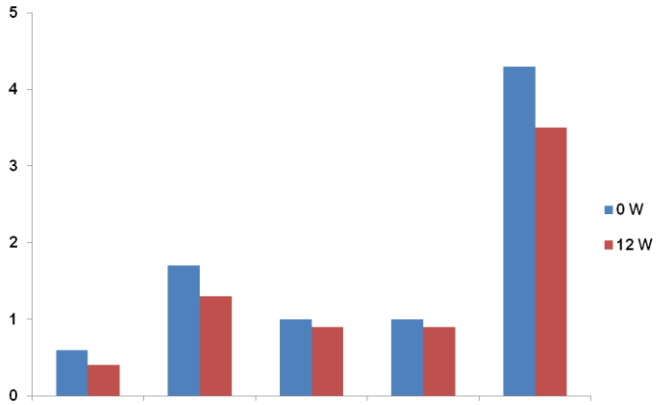
Fig.1 Comparison of the N-QOL score before and after administration



0 W	76.1 (21.0)	75.6 (21.9)	76.5 (24.0)
12 W	89.4 (10.0)	90.3 (12.6)	88.6 (10.6)
P value	0.011	0.004	0.035

Fig.2 Comparison of OABSS before and after administration



0 W	0.6 (0.5)	1.7 (1.1)	1.0 (1.5)	1.0 (1.5)	4.3 (3.8)
12 W	0.4 (0.5)	1.3 (1.0)	0.9 (1.1)	0.9 (1.2)	3.5 (2.9)
P value	0.016	0.004	0.014	0.11	0.095

Table 1 UDS findings

	0 W	12 W	*P* value
Maximum flow rate (mL/sec)*	8.5 ± 6.2	12.0 ± 6.5	0.038
Maximum bladder capacity (mL)	362.9 ± 113.7	440.1 ± 88.3	0.0029
Detrusor pressure (cmH_2O)	13.7 ± 10.9	22.1 ± 12.0	0.042
Voided volume (mL)	200 ± 194.4	175.9 ± 145.9	0.813
Residual urine volume rate (%)	55.6 ± 33.3	58.1 ± 28.63	0.477

*N = 8: Patients who could void spontaneously before the start of the study