Clinical efficacy of an anticolinergic agent in HAM/TPS patients with neurogenic bladder

Resposta a agente anticolinérgico na bexiga neurogênica por HTLV-I

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ABSTRACT

Objective: To describe the efficacy of the propantheline bromide in neurogenic bladder in HTLV-I infected patients. Methods: From January/2001 to February/2004, twenty-one HTLV-I-carriers (7 men and 14 women) were selected for treatment with propantheline bromide 15 mg, PO, 2 to 3 times a day for 3 months, not discontinuing in the follow-up. At the end of the treatment period, patients were reevaluated through specific questionnaires for urinary symptoms (UDI) and quality of life (Ditrovie). Results: From the 21 patients enrolled, 15 (71.4%) presented important clinical improvement, referring decrease of urinary frequency, urgency and loss, nocturia, and even total control of the dysfunction. Conclusion: We observed an efficient response to the anticholinergic agent propantheline bromide in urinary dysfunction caused by the HTLV-I.

Keywords: Human T-lymphotropic virus 1; Paraparesis, tropical spastic; Cholinergic antagonists; Bladder, neurogenic

INTRODUCTION

Human T-lymphotropic virus 1 (HTLV-I) is a retrovirus considered to be the etiological agent of a chronic myelopathy known as HTLV-I associated myelopathy (HAM) or tropical spastic paraparesis (TSP)⁷,⁸. HTLV-I infection is transmitted through blood transfusions, sexual intercourse, contaminated needles and breastfeeding.

Moreira et al. (1993) observed in the city of Salvador a prevalence of 1.8% of HTLV-I infection among healthy subjects and 18.4% in patients hospitalized in an infectious disease service.⁹ In a recent study (1997), Galvão-Castro et al.¹⁰ observed a prevalence of 1.35% among blood donors in Salvador.

Neurological manifestations have an insidious onset, followed by a variable period of latency. The first complaints are generally related to motricity, asymmetrical functional limitation of crural muscles, associated with weakness, rigidity and loss of sensitivity of lower limbs, in addition to low back pain. These manifestations indicate functional peripheral involvement.
There may also be urinary and intestinal disorders, as well as erectile dysfunction\(^5-7\). In Brazil, HAM/TSP is clinically characterized by the presence of paraparesis with increased deep tendon reflexes, bilateral Babinski’s sign, altered deep sensitivity and severe vesical dysfunction\(^9\).

Urological manifestations are present in up to 90% of HAM/TSP patients. They have an insidious onset and they may rarely present as early manifestations of myelopathy\(^9-10\). Patients initially present increased urinary frequency, slow progression to urgency and urgency incontinence\(^11-13\). To have a more conclusive assessment of symptoms, it is important to order biochemical renal function tests, uroanalysis, uroculture, as well as urodynamic study and urinary system ultrasound\(^14\). Urodynamic study is a method widely used to classify and neurogenic bladder, and to guide management of the disorder. The main urodynamic alteration in patients with HAM/TSP and urinary symptoms is vesical hyperreflexia\(^15-17\). Vesical hyperreflexia can explain increased frequency, urgency and urgency incontinence.

Anticholinergic acting drugs are widely used to treat neurogenic bladder with hyperreflexive detrusor for relaxing the muscle, thus increasing bladder capacity, reducing urinary frequency and leading to complete or partial improvement of urinary leaks. This is the first study, to our knowledge, that used anticholinergic agents to treat neurogenic bladder caused by HTLV-I.

**OBJECTIVE**

The purpose of the present study was to describe the efficacy of propantheline bromide in treating neurogenic bladder in HTLV-I patients.

**METHODS**

From January 2001 to February 2004, 318 patients who had positive serology for HTLV-I were seen in the Multidisciplinary Outpatients Clinic for HTLV-I, at the Hospital Universitário Professor Edgard Santos, Universidade Federal da Bahia, in Brazil. In all cases, the diagnosis of HTLV-I infection was defined by Elisa test (Cambridge Biotech Corp., Worcester, MA, USA), and confirmed by Western blot (HTLV blot 2.4, Genelab, Singapore).

These patients answered a specific questionnaire about urinary symptoms (Urinary Distress Inventory – UDI)\(^18\) and a questionnaire about quality of life (Ditrovie)\(^19\). Patients that presented urinary symptoms of urgency incontinence or increased urinary frequency were asked to undergo urodynamic analysis. Seventy-four patients were submitted to urodynamic study and 47 (63.51%) presented vesical hyperactivity. Among them, 25 patients were treated with propantheline bromide and 22 are still using it. Four out of 25 patients treated with propantheline were lost to clinical follow-up. Finally, 21 patients (7 men and 14 women) aged between 28 and 70 years (mean age of 47.24 ± 9.99) participated in the study. They used propantheline bromide 15 mg PO, 2 to 3 times a day, for three months without interruptions. At the end of treatment period, patients were reassessed using the same questionnaires.

The present study was submitted to and approved by the Ethics Committee of the Hospital Universitário Edgard Santos, Universidade Federal da Bahia. The inclusion criteria were: increased urinary frequency symptoms (more than 8 times a day), nocturia (wake up at night to empty the bladder more than twice), urgency (sudden and mandatory need to urinate), urgency incontinence and detrusor hyperactivity in the urodynamic study.

We did not include patients who had neurological diseases, renal failure, liver failure, constipation, glaucoma, psychiatric disorders, urinary infection, pregnant women, patients that had used medication that acted on the central nervous system or interfered in the normal urinary function, and those who did not sign the informed consent term or did not follow the protocol.

Data were analyzed using the software SPSS, version 11.5. We used Wilcoxon test to check statistically significant differences between symptoms before and after treatment. Statistical significance was considered as a p value < 0.05.

**RESULTS**

Out of 21 patients followed-up, 15 (71.42%) presented significant clinical improvement detected by the questionnaires, reducing urinary frequency and urgency, nocturia, urinary loss and leading to total control of urinary dysfunction (Figures 1-4). There was expressive improvement in quality of life of these patients. The other six (21.1%) patients studied reported slight improvement of symptoms, maintained urinary loss complaints or reported increased urinary frequency.

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**Figure 1.** Urinary frequency before and after treatment
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Other muscarinic receptors outside the bladder. Some anticholinergic side effects are: constipation, blurred vision, gastritis and, in special, dry mouth, which is the main cause of non-compliance to treatment. In the present study, the drug of choice was propantheline bromide because it is an affordable drug and the population studied had low income. Moreover, the drug has marked anticholinergic action. As to tolerability, we observed incredibly high compliance to treatment. Patients were informed about the possible undesirable effects, especially dry mouth and the need to increase fluid intake and to use lozenges. Some patients had to resort to artificial saliva (Salivan®).

Treatment proved to be very effective and reduced the symptoms of detrusor hyperactivity: urgency, incontinence and increased urinary frequency. The present study showed significant improvement of urinary symptoms of the population studied; moreover, the results had a positive impact on the quality of life of these patients.

Patients who had partial or absent response to treatment were in advanced stages of myelopathy. The literature shows that the individuals with severe disability already have significant damage to the thoracic spinal region, and they tend to be refractory to therapies that aim to improve motor or vesical function.

CONCLUSION

HTLV-I infection causes chronic myelopathy and neurogenic bladder with significant urinary complaints. The exact characterization of the dysfunction and of therapy must be customized based on the urodynamic assessment. In the present study we observed a very efficient response of the anticholinergic agent propantheline bromide to the urinary disorder caused by HTLV-I.

This study suggests the benefits obtained with the use of this drug can be even greater than those previously described for the treatment of vesical hyperactivity from other causes.

REFERENCES


DISCUSSION

Drugs with anticholinergic action are the treatment of choice for neurogenic bladder with detrusor hyperactivity. When using these drugs, we should bear in mind the adverse events caused by the action on


