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Corticosteroid therapy in TSP/HAM patients: The results from a 10 years open cohort

Mariana Garcia Croda [a,1], Augusto César Penalva de Oliveira [a,1], Maria Paulina Posada Vergara [a], Francisco Bonasser [b], Jerusa Smid [a], Alberto José da Silva Duarte [c], Jorge Casseb [a,c,*]

[a] *HTLV Clinic, Institute of Infectious Diseases "Emílio Ribas", São Paulo, Brazil*
[b] *Institute of Infectious Diseases "Emílio Ribas", São Paulo, Brazil*
[c] *Laboratory of Allergy and Clinical Immunology at São Paulo University Medical School, São Paulo, Brazil*

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Abstract

Background: The use of corticosteroids for treating tropical spastic paraparesis/HTLV-1 associated myelopathy (TSP/HAM) has yielded controversial results. We report the use of corticosteroids for the treatment of TSP/HAM in an open cohort.
Methods: The clinical efficacy of long-term, high dose of corticosteroid therapy was studied in thirty-nine TSP/HAM patients. Disability and motor dysfunction was evaluated based on the Disability Status Scale (DSS), Osame's Motor Disability Scales (OMDS), and Incapacity Status Scale (ISS), before and after treatment. Treatment included use of methyl-prednisolone, 1 g/day for three days, every 3–4 months. The primary end-point was a change in the scores of the neurological scales from baseline until the fifth visit after therapy.
Results: After a mean follow-up of 2.2 years and an average of four pulses per patient, we noted a significant neurological improvement, reaching 24.5% according to the ISS score. No statistically significant differences in scores according to the OMDS and DSS scales were noted.
Conclusion: We observed neurological improvement with the use of corticosteroids, with physical therapy and antispastic-drugs as adjunctive treatment. However, randomized clinical trials should be done to assess the use of corticosteroids and other potentially useful immune-based therapies for TSP/HAM treatment.

Keywords: HTLV-1; TSP/HAM; Treatment; Brazil; Corticosteroid

1. Introduction

Tropical spastic paraparesis/HTLV-1 associated myelopathy (TSP/HAM), caused by human T lymphotropic virus type 1 (HTLV-1), has an incidence of 1 case per 100 HTLV-1 infected carriers in highly endemic populations [1]. The major histopathological characteristic of TSP/HAM is a chronic inflammation of the white and gray matter of the spinal cord followed by a degenerative process that preferentially affects the white matter in the lower spinal cord [2,3]. TSP/HAM is characterized by a chronic slowly progressive spastic paraparesis with bladder disturbances, absent or mild sensory loss and low back pain, with seropositivity for HTLV-1 antibodies, in the absence of spinal cord compression [4,5]. Despite the more usual presentation characterized by a slow progression, 21.5% of the patients may experience a rapid progression, with severe disability two years after the onset of symptoms [6]. This phenomenon is related to older

* Corresponding author. Medical School at São Paulo University, Av. Dr. Eneas de Carvalho Aguiar 500, Building II, Third floor, São Paulo, SP Brazil. Tel.:+55 11 3061 7194; fax: +55 11 3061 7190.
E-mail address: Jorge_casseb@yahoo.com.br (J. Casseb).
[1] Both authors contributed equally to this study.

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age of onset, parenteral HTLV-1 transmission route, high viral loads, and high antibody titers [7–9].

There is no established therapy for TSP/HAM. Most treatments have been directed at reducing inflammation in the affected tissues. Others such as interferon-α [10–13] have both antiviral and immunomodulatory capacity. Various alternative treatments such as oral prednisolone, intrathecal hydrocortisone [13–15], plasmapheresis [16], vitamin C [17]. and antiretroviral drugs [18–21] have been reported. There are also some reports about the transient benefits of immunotherapy, Pentoxyfiline, Danazol and more recently milk drinks containing *Lactobacillus casei* [22–25]. Even though corticosteroids are the most widely used therapy for TSP/HAM, few clinical trials with corticosteroids have been published recently.

In Brazil HTLV-1 infection is endemic in some areas [26]. We have been following an open HTLV cohort since 1997 to study some epidemiological, laboratory and clinical characteristics of this infection in the city of São Paulo [27,28]. Therefore, we tried to assess the clinical corticosteroid effects on TSP/HAM in a long-term follow-up. Herein, we describe the results of this treatment.

2. Material and methods

This observational study of TSP/HAM patients was conducted at Institute of Infectious Diseases "Emilio Ribas" from June 1997 through June 2006; the Institute is a 250 bed public hospital in São Paulo, Brazil.

The TSP/HAM diagnosis was done according to the WHO TSP/HAM classification [29]. Inclusion criteria for the current study were: patients who had received intravenous methyl-prednisolone 1 g/day for three days (pulse therapy), absence of HIV infection, and at least two neurological scales entered (before and after pulse therapy) in their clinical records. The exclusion criteria were simultaneous use of other specific TSP/HAM therapy or diagnosis of diabetes mellitus. All participants signed an informed consent that was approved by the local Ethical Board at the Institute of Infectious Diseases.

The HTLV unit is composed of a multidisciplinary team including infectious diseases specialists, neurologists, a physical therapist and dentists. All study participants were examined both before and at least 40 days after pulse therapy. All patients had a previous urine examination to rule out a current urinary tract infection, and a stool examination for *Strongyloides stercoralis*, but regardless of the result they received empirical treatment with ivermectin. In some cases the pulse intervals were not regular, since several patients came from outside the city of São Paulo, making a regular follow-up not always possible.

All patients were clinically evaluated before and after pulse therapy. The following neurological scales were applied by neurologists in each patient visit: Disability Status Scale (DSS) proposed by Kurtzke in 1955 and the Incapacity Status Scale [30], both for Multiple Sclerosis [31,32], and the Osame's Motor Disability Score (OMDS), specific for TSP/HAM. The Incapacity Status Scale was devised to grade also disability. It consists of 16 items, namely: stair climbing, ambulation, toilet/chair/bed transfer, bowel function, bladder function, bathing/dressing, grooming, feeding, vision, speech and hearing, medical problems, mood and thought disturbances, met-nation, fatigability and sexual function. Each item is graded on 0–4 scale with 0 being normal function and 4 being loss of function. Motor dysfunction was evaluated on the basis of the Osame's Motor Disability Score, in which motor dysfunction is graded on a scale from 0 (normal walking and running) to 13 (completely bedridden).

The primary end-point was a change in the scores of the neurological scales from baseline until the fifth visit after pulse therapy. Student's *t*-test (paired) was used to assess the differences in the neurological scale scores. Statistical analyses were performed using SAS 9.1 (Cary, NC, EUA).

3. Results

During the period from June 1997 to June 2006, 66 patients were enrolled in our cohort with TSP/HAM. A total of 27 patients were excluded, either because of the absence of neurological examinations in their records before pulse

Table 1
Characteristics of the TSP/HAM patients by gender

Variables	Female (%)	Male (%)	Total (%)
	n=26	*n*=13	*n*=39
Age (range)	46 (23–74)	48 (24–72)	47 (23–74)
Clinical symptoms at admission			
Bladder disturbance	21 (81%)	11 (85%)	32 (82%)
Weakness in lower limbs	22 (85%)	9 (69%)	31 (79%)
Spasticity in lower limbs	21 (81%)	9 (69%)	30 (77%)
Impotence	–	8 (62%)	8 (62%)
Low lumbar pain	13 (50%)	6 (46%)	19 (49%)
Constipation	10 (38%)	7 (54%)	17 (44%)
Use of others medications			
Yes	20 (77%)	11 (84%)	31 (79%)
No	6 (13%)	2 (16%)	8 (21%)
Baclofen	18 (75%)	8 (62%)	26 (83%)
Tricyclic antidepressants	6 (26%)	2 (16%)	8 (27%)
Vitamin B	2 (10%)	1 (2%)	3 (10%)
Oxibutinine	1 (5%)	2 (16%)	3 (10%)
Physical therapy			
Yes	13 (50%)	3 (23%)	16 (41%)
No	13 (50%)	11 (77%)	23 (52%)
Risk factors for HTLV-1 infection			
IDU	–	1 (8%)	1 (3%)
Blood transfusion before 1993	2 (8%)	1 (8%)	3 (8%)
Sexual partner HTLV-1 infected	3 (12%)	–	3 (8%)
Sexual partner IDU	3 (12%)	–	3 (8%)
Mother HTLV-1 infected	3 (12%)	1 (8%)	4 (10%)
Unknown*	8 (31%)	8 (60%)	25 (63%)

*Unknown: Patients from endemic areas, with possible but not proven maternal transmission.