DANAZOL

A NEW PERSPECTIVE IN THE TREATMENT OF HTLV-1 ASSOCIATED MYELOPATHY
(PRELIMINARY REPORT)

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SUMMARY — We investigated the efficacy of danazol treatment in eight patients with HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP). Treatment with danazol yielded clinical improvement of urinary control and gait disturbances in 7 out of the 8 patients. The improvement was noted within 15 days of danazol administration. Analysis of factors of relevance to the clinical improvement with danazol showed that the beneficial response was preferentially found in females.

KEY WORDS: tropical spastic paraparesis, HTLV-1, myelopathy, danazol, treatment of HAM.

Danazol: uma no?i perspectiva no tratamento da mielopatia associada a HTLV-1 (relato preliminar)

RESUMO — Investigamos a eficácia do danazol, um andrógeno sintético, no tratamento de 5 mulheres e 3 homens com mielopatia associada a HTDV-1. Dentro do período de 15 dias após o início da administração da droga houve melhora significativa do controle urinário e aumento da força muscular em membros inferiores. Os resultados clínicos obtidos foram mais pronunciados em mulheres que em homens.

PALAVRAS-CHAVE: paraparesia espástica tropical, HTLV-1, mielopatia, danazol, tratamento da HAM.

HTLV-1 associated myelopathy (HAM) has been found to be prevalent in Japan, the Caribbean Islands and Africa/2. In Brazil, antibodies to HTLV-1 were found in serum and cerebrospinal fluid (CSF) of patients with tropical spastic paraparesis by several authors 7,8,10. HAM has been treated empirically with corticosteroids 9, zidovudine 2, gammaglobulin 6 and alpha-interferon 5 with controversial results. Danazol, a synthetic androgen, has been used in patients with autoimmune hemolytic anemia as well as several autoimmune disorders i. A recent open basis preliminary study involving this drug reported good results and minimal side effects in seven patients presenting with HAM. So, we decided to give danazol to patients with HAM.

PATIENTS AND METHOD — Danazol (600 mg/day) was given orally three times daily (200 mg/dosis) to five women and three men with ages ranging from 38 to 56 years. All patients had progressive spastic paraparesis with a duration time between 6 and 36 months, neurogenic bladder, and reduction in libido or masculine sexual impotence. Five cases had sensitive syndromes characterized by paresthesia and dysesthesia in the lower limbs. Magnetic resonance image of thoracic region did not reveal compressive, expansive or traumatic lesions of the spinal cord. CSF and serum samples were collected from the patients and tested to HTLV-1 with a commercially available enzyme immunoassay (EIA); the specimens were repeatedly reactive in this screening test, and underwent confirmatory testing by Western blot assay.

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RESULTS — There was a significant improvement in the strength of lower extremities in seven patients (p=0.02, Wilcoxon signed rank test) after one month danazol treatment that persisted with the use of the drug. In one male any increase of strength in his legs was observed meanwhile he noticed better control of the bladder. The continence of bladder improved in all patients as has been observed with serially urodynamic analysis in three women and one man. Five patients had weight gain and two reported lethargy. Two women referred amenorrhea and serum transaminases arose in another. These side effects disappeared with lowering of the drug to 400 mg daily. Although the patients tested had approximately the same time of disease, the beneficial response was preferentially found in females than in males.

COMMENTS — There is some evidence that gonadal steroids influence both in vitro and in vivo the immune function. Amenorrhea, hirsutism, hepatic dysfunction as well as lethargy and weight gain have been described as some of the side effects of danazol i. These pharmacologic and side effects are dose dependent and are usually reversible on withdrawal of the drug as we have noted in our patients. Several factors such as the anabolic effect of danazol and the mood elevating property of steroids may play some role in the results described. However all of our patients had improvement of urinary control after two months of therapy which points to an action of the drug on the nervous system. Our results point to a new useful drug in the treatment of patients with HAM, although larger and controlled studies have to be done in order to clarify the real validity of danazol in the treatment of HAM.

REFERENCES