Clinical improvement in chronic fatigue syndrome is associated with enhanced natural killer cell-mediated cytotoxicity: the results of a pilot study with Isoprinosine®

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Abstract. Chronic fatigue syndrome is associated with systemic and cognitive symptoms and with several immune abnormalities. The clinical impact of Isoprinosine® was evaluated in sixteen CFS patients, followed for 28 weeks in a single-blind, placebo controlled trial. Patients were also monitored for various immune parameters. Improvement based on clinical staging was observed in six of ten treated patients (60%). Clinically improved patients showed significantly enhanced natural killer (NK) cell activity, which correlated with the duration of Isoprinosine® treatment (p < 0.03). Treatment with Isoprinosine® resulted in significantly increased numbers of CD4+ T helper cells (p < 0.03). Treatment with Isoprinosine® for 12 weeks did not appreciably influence the in vitro production of IFN-γ, IL-1α, IL-10 or IL-12. However, IL-12 was significantly increased at week 28 (p <0.02) in patients who improved after treatment with Isoprinosine®. These results suggest that taking Isoprinosine® may benefit a subgroup of patients with CFS, and this clinical improvement is associated with enhanced NK cell function and IL-12 levels. Further trials to evaluate the use of Isoprinosine® in the treatment of CFS patients are warranted.

Keywords: chronic fatigue syndrome, Isoprinosine®, IFN-γ, IL-12, IL-10, IL-2, Natural Killer Cells

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INTRODUCTION.

The 1988 and 1994 Center for Disease Control criteria for chronic fatigue syndrome (CFS), include a requirement for several symptoms, such as severe fatigue, exercise intolerance, myalgia, cognitive deficit and a variety of neuropsychological symptoms (1,2). Many studies suggest the involvement of the immune system in the pathogenesis of CFS (3-8). Unfortunately, there is no established treatment for CFS, although several therapies, including a variety of immunomodulatory therapies, have been attempted (9-17).

Isoprinosine® (inosine pranobex) is a synthetic purine derivative consisting of the p-acetamidobenzoic acid salt of N,N-dimethylamino-2-propanol (DIP.PAcBA) and β polymorph of inosine in a 3:1 molar ratio. It is an immunopharmacologic agent with both immunomodulatory and antiviral properties. Isoprinosine® has been licensed since 1971 for the treatment of cell mediated immune deficiencies associated with various viral infections (18-20). The exact mechanism for these actions is not fully understood. However,