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Alpha Interferon in the Treatment of Mixed Cryoglobulinaemia Patients

Clodoveo Ferri, Emanuele Marzo, Giovanni Longombardo, Francesco Lombardini, Francesco Greco and Stefano Bombardieri

INTRODUCTION

MIXED CRYOGLOBULINAEMIA (MC) is an idiopathic systemic disease characterized by a typical clinical triad - purpura, weakness, arthralgias - and by a variable visceral involvement secondary to the tissue deposition of circulating immune complexes [1]. The therapeutic approach to MC largely depends on the extension and severity of organ involvement. Steroid and/or plasma exchange [2, 3] and low antigen-content diet therapy [4] have been usefully employed in large series of MC patients.

Alpha interferon has been used in this disease with encouraging results, as reported in a previous open study [5]. The aim of the present work is to investigate the effect of alpha interferon in a controlled trial performed in a large MC series. Preliminary results obtained during the first 4 months of the trial are reported here.

PATIENTS AND METHODS

The randomized, cross-over study included 22 patients (14 female and eight male, mean age 55 ± 7 years) with active manifestations of MC. Until now, 10 patients have been treated with interferon alfa-2b (2 million units daily for 1 month, then every other day for 5 months). Pretreatment 6-methylprednisolone dosages (4-8 mg/day) remained unchanged in all cases.

Clinical and immunological evaluation of the effects of alpha interferon treatment was performed using the following parameters: complete physical evaluation and routine blood chemistry; liver enzymes; renal, neurological and vascular involvement; systemic manifestations (Raynaud's phenomenon, Sjögren's syndrome, etc.); cryocrit, haemolytic complement activity; peripheral lymphocyte subsets; and anti-hepatitis C virus (HCV) antibody levels.

RESULTS

Response

The main clinico-serological and immunological variations before and after alpha interferon are shown in Figures 1-3 and in Table 1. There was a significant improvement in purpura score ($P < 0.005$) in interferon-treated patients while control patients remained unchanged (Fig. 1). Similarly, in treated patients, there was a significant fall both in serum glutamic

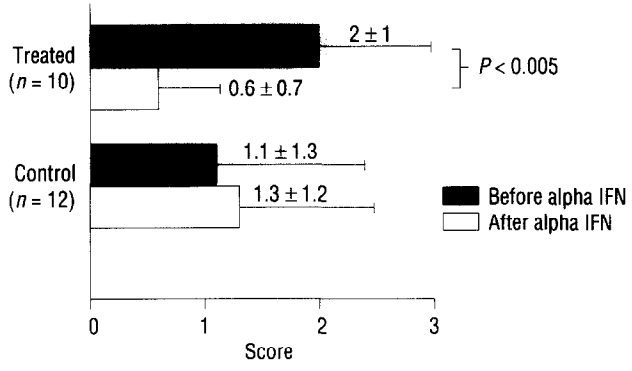

Fig. 1. Purpura score (0-3).

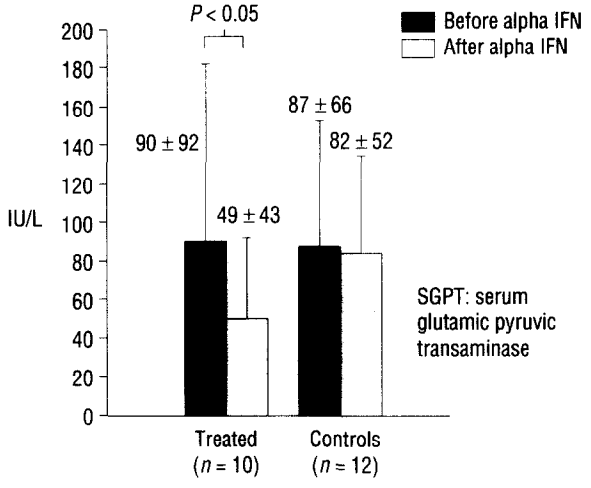

Fig. 2. Serum glutamic pyruvic transaminase levels (normal = < 40 IU/L).

Table 1. Variations in CD4/CD8 ratio and anti-HCV positivity before and after alpha interferon and in control patients

No. of patients	CD4/CD8 ratio 1.3-2.1	Anti-HCV+ (% of pts)
10 treated	1.3 ± 0.5/1.8 ± 0.4*	50/20†
12 controls	ND	58/58

ND = not done; Anti-HCV = antibody to hepatitis C virus.
*$P < 0.025$.
†$P < 0.001$.

Correspondence to: C. Ferri.
C. Ferri is at the Rheumatology Unit, University of Pisa, Ospedale S. Chiara, Pisa, Italy.
E. Marzo, G. Longombardo and F Lombardini are at the Rheumatology Unit, University of Pisa, Ospedale S. Chiara, Pisa, Italy, F. Greco is at the Blood Centre, Ospedale S. Chiara, Pisa, Italy and S. Bombardieri is at the Clinical Immunology Unit, University of Pisa, Pisa, Italy.

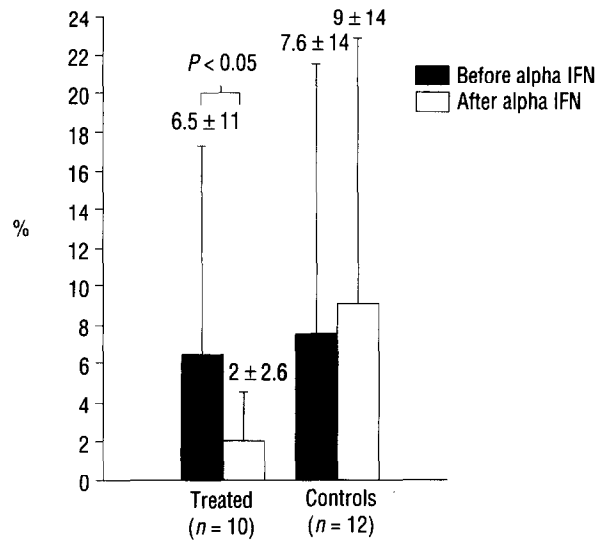

Fig. 3. Serum cryocrit levels.

pyruvic transaminase (SGPT) levels ($P < 0.05$) (Fig. 2), and in serum cryocrit ($P < 0.05$) (Fig. 3). Patients receiving alpha interferon also showed a significant improvement in CD4/CD8 ratio ($P < 0.025$); in half of the patients, this parameter was below the normal range at the beginning and was normalized after 1 month of treatment. After alpha interferon, anti-HCV antibodies disappeared in three of five patients ($P < 0.001$), while in the control group they remained unchanged (Table 1).

Drop out

Only one of the 10 patients treated with alpha interferon dropped out, after a 3-week period, because of worsening peripheral neuropathy.

CONCLUSIONS

Alpha interferon positively affected clinical manifestations of MC, such as severity and frequency of purpura, and signs of liver involvement (increased SGPT levels) that were present in 60% of cases. These results were mirrored by changes in immunological parameters. Although preliminary, these results suggest that alpha interferon may be considered an interesting therapeutic approach, able to affect, at different levels, the pathogenetic mechanism(s) of MC and improve some clinical manifestations of the disease.

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Molecular Events in B-Cell Activation and Growth: Sensitivity to Alpha Interferon

Erik Lundgren, Håkan Hedman, Göran Landberg, Fanyi Chiang, Göran Roos and Rhiannon Sanders

INTRODUCTION

IN ORDER TO determine molecular targets for alpha interferon and other agents on B-cells, we have studied important molecular events in normal peripheral B-cell activation and growth. The purpose was to identify interferon-sensitive events as a platform for further studies on interferon-sensitivity of B-cell tumours.

Correspondence to: E. Lundgren.
E. Lundgren is at the Institute of Cell Molecular Biology, University of Umeå, Umeå, Sweden.
H. Hedman, G. Landberg, G. Roos and R. Sanders are at the Institute of Cell Molecular Biology, University of Umeå, Umeå, Sweden.

MATERIALS AND METHODS

Isolation of primary B-cells

Buffy coats were obtained from healthy donors. The isolation process consisted of lymphoprep separation of mononuclear cells, anti-CD19 immunomagnetic beads, and complement lysis of T-cells. The final cell population contained less than 0.1% CD2 positive cells.

Growth of B-lymphocytes

B-lymphocytes were grown with anti-IgM antibodies, phorbol ester (PDB)/Ca-ionophor (ionomycin), cocultivation with lymphokines, and membranes from activated T-cells.