Volume 63, Number 4
Printed in the U.S.A.

CORRESPONDENCE

This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters. The mandate of this JOURNAL is to disseminate information relating to leprosy in particular and also other mycobacterial diseases. Dissident comment or interpretation on published research is of course valid, but personality attacks on individuals would seem unnecessary. Political comments, valid or not, also are unwelcome. They might result in interference with the distribution of the JOURNAL and thus interfere with its prime purpose.

Is Pentoxifylline a Viable Alternative in the Treatment of ENL?

TO THE EDITOR:

The adequate management of leprosy reactions continues to be a challenge in all leprosy control programs. Although reactions embody a complex clinical situation for most patients, field conditions do not always offer the special attention they need. Nonsteroidal anti-inflammatory drugs are frequently prescribed, even for severe clinical complications, since a tailored scheme with corticosteroid is not considered reliable. Thalidomide, the chosen drug for treatment of the type 2 reaction (erythema nodosum leprosum, ENL) in leprosy, is not available in many countries and requires controlled usage.

Recently, many reports have pointed out the presence of high tumor necrosis factor-alpha (TNF-α) levels in the sera of ENL patients([2, 4, 5]), suggesting that this pleiotropic inflammatory cytokine might be responsible, at least in part, for the clinical signs and symptoms of leprosy reactions. Pentoxifylline, a drug recommended for the amelioration of blood flux in the context of the microcirculation, has been prescribed regularly by physicians for patients suffering from peripheral arterial disease and/or cerebral insufficiency. Several reports have indicated that the beneficial effects of pentoxifylline might be due to the inhibitory effect that this drug exerts on TNF-α production by inhibiting the synthesis of TNF-α messenger RNA (mRNA)([1, 6]).

In an attempt to determine whether pentoxifylline may be used as an alternative therapy for the management of leprosy reactions, we carried out a preliminary clinical trial. This report describes clinical observations concerning the use of pentoxifylline in 15 multibacillary leprosy patients (from the Leprosy Out-Patient Unit, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil) who were undergoing acute inflammatory reactional episodes.

Histopathologically, the patients (10 males, 5 females) were classified as lepromatous (LL; N = 10) and borderline lepromatous (BL; N = 5) leprosy, according to the Ridley-Jopling classification([3]). The patients were distributed into: a) 12 patients who presented with systemic ENL and b) 3 patients who presented with only extensive edema of the arms and/or feet. Among the ENL patients, two had a long history of recurrent ENL with unsuccessful corticosteroid therapy. Clinical and histopathological criteria were used to diagnose type 2 reactions. For treatment of the inflammatory manifestations, all 15 patients were prescribed 400 mg of pentoxifylline (Hoechst do Brasil, S.A.), three times a day for a 2-month period. Patients were observed once a week in the first month of treatment and every 15 days in the period thereafter.

Our most outstanding finding was that within 3 days after initiation of treatment with pentoxifylline all patients experienced from some degree of relief to almost total regression of their systemic symptoms, which included fever, malaise, headache, and insomnia. In addition, a decrease in the inflammatory aspects of ENL skin lesions

was noted after 7–14 days. Moreover, no side effects were observed in any of the patients.

Two patients responded very well to pentoxifylline with no further complaints. Five patients responded satisfactorily to the drug, but during the first month of treatment developed a few ENL nodules in the absence of any systemic manifestations. Within 1 to 2 weeks, these nodules regressed, and no other complications were noted. Only one patient developed a severe ENL episode in the fifth week of pentoxifylline treatment. Improvement of his clinical condition was only assured after adding 400 mg of thalidomide. Another patient presented with a recurrence of ENL 20 days after the interruption of pentoxifylline treatment. The drug was then re-introduced and regression of the symptoms was observed immediately.

In order to completely overcome the reactional episode in three patients, it was necessary to add steroids (20 mg of prednisone/day) to the pentoxifylline treatment. It is worth noting that 1 of these 3 patients had neuritis, which was controlled only after steroid treatment.

In the three patients with limb edema, treatment with pentoxifylline was found to be very effective. After 7 days of therapy, a significant reduction was noted; by the second week, total reversion of the edema had been completed.

An histological examination of the ENL lesions was performed in four patients. Biopsies were taken before and after 15 days of pentoxifylline treatment. All patients presented with a heavy bacillary load in the ENL specimens, as well as in the leprosy lesions. In the ENL lesions, the majority, if not all of the bacilli had a granular appearance. An inflammatory infiltrate built up by mononuclear and some polymorphonuclear cells extended from the upper dermis toward the hypodermis that also showed capillary proliferation. A large amount of feathery macrophages loaded with bacilli was present. Thickness of the epidermis and the absence of the Unna layer were also noted.

The biopsies taken after 15 days of pentoxifylline treatment showed a marked reduction in the inflammatory infiltrate and in the number of blood vessels. Macrophages loaded with bacilli did not show feathery aspects, and formed clusters surrounded by connective tissue. After this preliminary clinical experience, a clinical trial is being set up under a strictly controlled protocol in order to confirm our initial observations. These data suggest that pentoxifylline might be useful for the treatment of leprosy patients undergoing type 2 reactions.

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Acknowledgment. We would like to extend our thanks to E. R. Leite for typing the manuscript and for efficient secretarial help.

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