

PENTOXIFYLLINE MAY BE USEFUL IN THE TREATMENT OF TYPE 2 LEPROSY REACTION

Sir,

Leprosy reactions (LR) are among the most significant complications during the development of leprosy.

Up to now thalidomide and cortisone are the main drugs used in the treatment of Type 1 (reversal reaction) and Type 2 (erythema nodosum leprosum) LR.

Thalidomide and cortisone are the drugs of choice in the treatment of erythema nodosum leprosum (ENL), and cortisone is the only treatment for reversal reaction. The results are quite good with these drugs, but, side-effects are significant. Mainly for this reason the World Health Organization (WHO) recommended that, 'priority should be given to finding an acceptable alternative to these drugs'.¹

According to present knowledge pentoxifylline (PF) could be useful in the treatment of LR^{2,3} because it interferes on the level of TNF- α and IL-1. TNF- α and IL-1 are probably associated with the development of leprosy reactions.⁴

Pentoxifylline (Trental[®]), also known as 1-(5-oxohexyl)-3,7 dimethylxanthine, 1-(oxohexyl) theobromine, is a methylxantine derivative with properties similar to theobromine, caffeine, and theophylline.^{2,3} It has potent haemorrhologic properties. Although doctors using a new drug are under an obligation to check the contraindications, it may be helpful if the authors included a short note that oxpentifylline is contraindicated in patients who show drug allergy to theophylline and caffeine, and that care should be exercised in patients with coronary artery disease or orthostatic hypotension, as the drug has a hypotensive effect.

Recently we observed a patient with Type 2 reaction treated with PF.⁵ The good results prompted us to treat more LR patients with PF.

From July 1994 to January 1995 we treated a further 8 patients presenting with Type 2 and Type 1 reaction with PF.

Patients and methods

Four patients with Type 2 reaction and 3 with Type 1 reaction were treated with oral pentoxifylline (400 mg three times a day). Another patient with Type 2 reaction started with the same dosage but as no response was observed the patient received IM injections of 100 mg PF, 3 times a day, for 3 days followed by oral PF, 400 mg four times a day (see Table 1).

Table 1. Summary of clinical data and efficacy of pentoxifylline in the treatment of lepra reaction.

Patient no.	Sex	Age (yr)	Classification LL or B*	Type of reaction	Efficacy of pentoxifylline
1	m	19	LL	Type 2	good
2	m	25	LL	Type 2	good
3	m	42	LL	Type 2	good*†
4	m	70	LL	Type 2	good
5	m	28	LL	Type 2	good
6	F	44	BB	Type 1	fair
7	M	47	BV	Type 1	no response
8	M	40	BV	Type 1	no response

* LL, lepromatous leprosy; B, borderline leprosy.

† This patient failed to respond to pentoxifylline 400 mg/three times a day but improved with injections of 100 mg every 8 hours for 3 days followed by oral PF 400 mg/four times a day.

Reactions were diagnosed clinically, and bacilloscopies and biopsies were performed for all of the cases. These patients were under treatment or had completed multidrug therapy (MDT).

ENL or Type 1 plaque lesions were disseminated. Fever, malaise and joint pain were associated with ENL.

No patient had significant nerve enlargement or other indications for urgent treatment with cortisone.

Results

All patients but one presented with progressive regression of ENL related symptoms such as fever, malaise and articular pain in 2 to 5 days, and involution of ENL lesions was observed in 2 to 4 weeks.

A patient with Type 2 reaction that did not improve with 400 mg, 3 times a day, responded well to three intramuscular (IM) injections a day of 100 mg PF, for 3 days, followed by oral PF, 4 times a day.

In only one patient with Type 1 reaction was there a slow regression of plaque lesions.

No side-effects related to PF were observed.

Discussion

In spite of the efficacy and good tolerance of WHO-MDT, LR still represents a serious constraint during the development of leprosy. The well known side-effects of thalidomide and cortisone, the two main drugs used in the treatment of leprosy reaction, constitute the main difficulties in the management of LR.

Therefore, there is an urgent need to find alternative drugs for the treatment of LR.

According to Sarno⁴ the elevated concentrations of TNF- α and IL-1 may be implicated in LR.

Pentoxifylline should be an alternative drug for the treatment of LR because this agent suppresses monocyte production of TNF- α and inhibit leukocyte stimulation by TNF- α and IL-1.^{6,7}

In a previous report⁵ we treated a Type 2 reaction with PF. The good response of joint pains and malaise followed by a progressive involution of ENL lesions prompted us to treat further LR patients with PF.

The treatment of LR with PF gave satisfactory results particularly in Type 2 reaction. The

general symptoms improved in 2 to 5 days and ENL progressively disappeared in 2 or more weeks.

The results observed in Type 2 reaction are less impressive than those verified with thalidomide or cortisone but it does seem to be an alternative treatment.

The progressive regression of Type 1 reaction in 1 patient could be a spontaneous regression and so far it is very difficult to affirm that improvement was related to PF. After 3 days of PF treatment the reversal reaction lesions did not change or worsen in 2 of the patients. Thus we interrupted PF and cortisone was introduced.

According to the present observations, it seems that pentoxifylline must be used for weeks or months for the effective control of Type 2 reaction, more or less in the same way as we do with thalidomide. Our follow-up is limited to 2–4 months.

We think it is necessary to utilize higher dosages of IM pentoxifylline for the treatment of patients with severe Type 2 reactions or cases that do not improve with standard recommended doses of PF.

In conclusion, according to the present study, pentoxifylline demonstrated interesting effects on the treatment and control of Type 2 reaction and should be better studied as an alternative drug for the management of leprosy reactions.

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