Our experience of the use of thalidomide in the steroid-dependent severe erythema nodosum leprosum

Sir,

Severe, chronic, recurrent erythema nodosum leprosum (ENL) is a serious problem. Patients are in need of effective and safe treatment because there is a danger of steroid dependence. Thalidomide has been shown to be highly effective in the treatment of refractory ENLs.[1] A number of dosage regimens of thalidomide, an expensive drug, have been tried.[1-3] We describe our experience of the use of a new dosage regimen of thalidomide in the management of steroid-dependent severe ENLs.

We conducted the study from March 2004 to July 2007. Fifteen patients (including three women of child-bearing age and one child) with recurrent episodes of necrotic or chronic steroid-dependent severe ENLs were enlisted. Steroid dependence signified that on tapering the prednisone dose below 10 mg OD, the patients either got new ENLs or had a worsening of their pre-existing ENLs. The average steroid dose received by all the patients ranged from 10 to 60 mg daily. Other drugs that were taken before starting thalidomide included antimalarials, clofazimine, colchicine, pentoxyphylline and aspirin. Except steroids, the above-mentioned drugs were stopped when the patients were started on thalidomide. Informed consent was taken. Women were explained about the teratogenic effects of thalidomide and the contraceptive precautions to be used, according to the guidelines set by the United States Food and Drug Authority.[2] Laboratory studies, which included urine testing, hemoglobin estimation, white blood cell and differential cell counts and liver and renal function tests were carried out periodically. The duration of ENLs ranged from 7 months to 4 years. The number of recurrent ENLs ranged from two to 12 episodes. Eight cases presented during multidrug treatment (WHO-MDT) of leprosy, five cases presented after WHO-MDT and two cases presented directly with ENLs. Thalidomide was initially started as 100 mg thrice daily for 1–2 months. The exact duration of treatment depended on the response of the patient. If the patient's symptoms, ENLs and laboratory data improved, the dose was reduced to 100 mg twice daily for 2 months and then to 100 mg once daily for 2 months. The patients were then maintained on 50 mg of thalidomide per day until complete remission. A 6-year-old girl was started on thalidomide at 100 mg twice daily, considering her age. The use of thalidomide for the treatment of ENLs in such a young patient has not been reported.

At the end of the study, 12 patients (80%) were in remission and thalidomide and steroids were stopped. Early institution of thalidomide (within 1 month of ENL onset) in one of these patients induced faster remission and prevented further ENLs. The remaining patients required thalidomide for longer durations (more than 1 year). The total duration of treatment ranged from 80 to 738 days [Table 1]. The duration of maintenance dose ranged from 2 to 10 weeks. Our study demonstrated few side effects, such as constipation in three patients, pedal edema in three patients and drowsiness in one patient.

The duration of thalidomide treatment in the initial

Table 1: Type of ENL cases and duration of thalidomide treatment

Patient number	Duration of thalidomide treatment (days)	ENL presentation
1	266	After MDT, classical type
2	217	After MDT, classical type
3	175	During MDT, classical type
4	365	After MDT, necrotic type
5	738	During MDT, necrotic type
6	564	During MDT, necrotic type
7	256	During MDT, necrotic type
8	189	During MDT, classical type
9	190	After MDT, classical type
10	147	During MDT, necrotic type
11	133	During MDT, classical type
12	343	During MDT, classical type
13	255	After MDT, necrotic type
14	80	With ENL, necrotic type
15	120	With ENL, necrotic type

MDT, multidrug treatment; ENL, erythema nodosum leprosum.

phase (100 mg thrice daily for 1–2 months) and the maintenance dose phase was dependent on the clinical response of the patient. However, the remaining part of the study involved using thalidomide in a fixed dosage regimen (100 mg twice daily for 2 months and 100 mg once daily for 2 months). This was in contrast to a study by Parikh *et al*,[3] where the dosing solely depended on the clinical response of the patient. They started thalidomide at 100 mg four times a day and then the dose was reduced to thrice, twice and once per day depending on the patient's clinical improvement. The duration of this study ranged from 12 to 643 days and the maintenance dose was the same as in our study, 50 mg/day.[3] In addition, we observed that if the patients were on high-dose steroids for a long duration, they took more time to improve. A similar observation was made by Parikh *et al*.[3] The reason for this is perhaps that steroids suppress the activity of the adrenal cortex temporarily and a certain time lapse may be necessary before that activity is resumed.[4] Villahermosa *et al*, in 2005, had conducted a randomized double-blind, controlled trial involving two groups receiving 100 and 300 mg of thalidomide. The 300 mg dose group had a slower tapering of the drug over a 6-week period and a more effective response.[5] This was consistent with our observations that better response occurs with higher initial doses and slow tapering. Most of the studies advocate thalidomide use in chronic steroid non-responders, but we have seen an effective response with early initiation of treatment. Hence, we advise to not only hit hard but also hit early with thalidomide for treatment of ENLs because it elicits a quick and effective response. However, thalidomide cannot be used as the only first-line drug for the treatment of ENLs. Steroids have to be used to control systemic symptoms. The drawback of our study is that our observations are based on a small sample of cases. The limiting factors for the use of thalidomide, especially in developing countries, are availability, cost and strict monitoring. If these are overcome, patient morbidity can be reduced to a minimum.

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