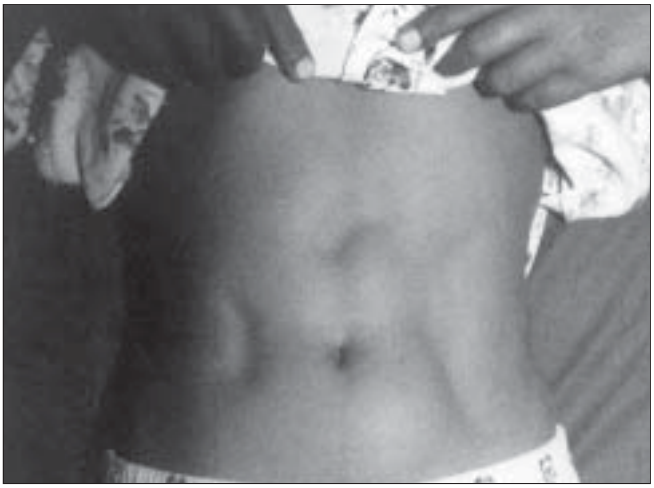

Figure 1: Atrophy of the subcutaneous fat as seen on abdomen

last 3 years. The lipoatrophy has not progressed further, and she has achieved better control of her blood sugar level with purified insulin injections and strict adherence to dietary advice.

Insulin lipoatrophy presents as depressed plaques, histologically showing atrophy of the subcutaneous fat.[2] It is an allergic phenomenon, thought to be due to immune complex deposition. IgG and insulin have been demonstrated in lipoatrophic tissues, and circulating anti-insulin antibody titres are commonly high. It is treated by injections of highly purified soluble insulin, which floods the site with antigen and solubilizes the complexes.[1]

Lipoatrophy localized to injection sites occurs particularly with longer acting preparations. It is becoming more and more infrequent with the use of modern insulins.[1]

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Treatment of Schamberg's disease with pentoxifylline

Sir,

I read with great interest article by Gandhi et al[1] and would like to offer some comments.

The authors have cited the report of Kano et al and have presumably designed their trial on its basis.[2] Kano et al administered pentoxifylline 300 mg daily for 8 weeks to 3 patients with Schamberg's disease and reported significant clinical improvement after 2-3 weeks. Despite its anecdotal nature, this report attracted wide attention. But, subsequent studies have reported different results. Based on their findings on 2 patients, Basak and Ergin found both the suggested dosage and the duration of therapy (pentoxifylline 400 mg daily for 3 weeks, subsequently increased to 600 mg daily up to 8 weeks) to be inadequate and unable to induce clearing of lesions.[3]

Based on these reports, we performed a multicentric, randomized, investigator-blinded, parallel group, therapeutic trial to compare the effects of oral pentoxifylline 1200mg daily in 3 equally divided doses versus topical betamethasone dipropionate cream 0.05% applied as a thin film locally twice daily on 112 patients, since topical steroids are the traditional therapeutic modality in this disorder.[4] The total treatment period was 8 weeks and follow up was for another 24 weeks. We found that pentoxifylline had a beneficial effect and was more effective than topical betamethasone. However, its effect diminished in many patients at follow-up at six months and we concluded that a 2 month period of therapy was inadequate.

Hence we recommend an even longer period of therapy. This seems to be rational because the dosage regimen followed in our trial was similar to the conventional dosage of pentoxifylline in vascular disorders.[5] Though the cause of Schamberg's disease is not known in almost 75% of cases,[6] capillary stasis has been proposed as a major factor behind the capillaritis. Gravity and

increased venous pressure have been identified as important localizing factors in many cases.[7] In an earlier study, we too found a concomitance of Schamberg's disease and stasis dermatitis in 13 cases and on retrospective analysis found a history of prior Schamberg's disease in 8 out of 14 cases of stasis dermatitis.[8] So the dosage employed in our study would have been able to take advantage of the combined rheological and immunological actions of pentoxifylline.

In view of these facts, the findings of Gandhi et al, who used pentoxifylline in the dose of 400 mg daily and noticed a marked improvement (50%) in 50% of the study population (n = 20), is surprising. The gradation of clinical improvement denoting the percentage of clearance of lesions (< 25%, 25-50% and > 50%) is unclear, to say the least. What do these figures stand for? Is it the number of lesions or is it the area occupied by the lesions? If it signifies the number of lesions, as it apparently does, then it throws up a few more questions. It is well known that Schamberg's disease is typified by punctate macules developing into confluent patches, papules and plaques and petechiae with indistinct margins, mainly on the lower extremities.[9] If the disease is not characterized by multiple distinct lesions, it is meaningless to talk about clearance of a certain number of individual lesions. If the percentage of clearance is taken to be that of the total area occupied by the lesions, we are beset with another problem: Schamberg's disease is made up of lesions of irregular shapes and sizes; what then was the method adopted by the authors to calculate the area?

Another concern regarding the methodology is the assessment of clinical improvement, which was done by two different observers independently at 2-weekly intervals. It is a moot point whether any change is clinically discernible in Schamberg's disease within 2 weeks and thus whether such frequent assessment is necessary. Besides, it is not clear if each patient was assessed twice by two different observers at each point of time and if that were not so, how the problem of inter-observer bias was addressed in the trial. It has also not been mentioned whether the observers had been properly blinded to minimize intra-observer bias.

The authors have mentioned the phenomenon of spontaneous clearance of lesions in Schamberg's disease. As the incidence of such clearance is not documented, the only way to test the efficacy of any therapeutic modality would be a placebo-controlled study.

Pentoxifylline is recommended by the authors as the first-line therapy of Schamberg's disease on the basis of their results. In a nutshell, the results were improvement of 50% (n = 10) patients to the extent of clearance of > 50% lesions in a small trial (n = 20). Even if we ignore the ill-defined measures of clinical improvement, such a conclusion based on the results of such a trial seems unfair.

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