LETTERS TO THE EDITOR

PENICILLAMINE INDUCED CHEILOSIS

Approximately 60% of patients with Wilson's disease and cystinuria have been reported to develop skin rashes when treated with d-penicillamine A number of other manifestations like vesicles, bullae, cysts, milia, elastosis perforans serpiginosa and pemphigus foliaceus have also been described. Cheilosis is seen uncommonly. We observed an eitht-year-old boy having Wilson's disease manifesting as difficulty in speech, difficulty in walking and in using the left upper limb, dysarthric speech, Kayser-Fleischer rings in both eyes, weakness in the proximal group of muscles, poor hand grip, rigido-spasticity on the left side, involuntary athetoid movements, and enlarged liver. Investigations showed erythrocyte sedimentation rate to be 45 mm. Serum was fairly opalescent. Caeruloplasmin level in serum was 1.7 mg%. Serum copper level was measured to be 221 micrograms per 100 ml. Zinc turbidity test showed 12.6 units. Patient's mother refused bone marrow studies. Rest of the investigations were within normal limits. A diagnosis of Wilson's disease was made and the patient treated with oral d-penicillamine in a dosage of 250 mg three times a day. On the eighth day of treatment, the patient developed cheilosis and was referred to us. A diagnosis of penicillamine drug reaction was made and the drug withdrawn until the cheilosis subsided. It was again started in small, gradually increasing doses and maintained thereafter without any recurrence of cheilosis.

Penicillamine induced skin eruptions can be of two types, viz, (1) eruptions of early onset, and (2) eruptions of late onset. Early onset eruptions appear within two weeks of starting the treatment and clear when the drug is withdrawn temporarily and usually do not reappear when the drug is restarted. The late onset eruptions are characterised by appearance of the rash after a year or more with high dose of the drug. The lesions improve if the dose is reduced. Some workers have reported cheilosis as an uncommon manifestation following penicillamine therapy.

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ROLE OF ZINC IN ERYTHEMA MULTIFORME

I have gone through the article entitled "Oral zinc in recurrent erythema multiforme with depigmentation" published in the Ind J Dermatol Venereol and Leprol, 1984; 50 : 10-12. I wish to make the following observations :

(1) The authors have studied cases with a preceding history of herpes simplex, while erythema multiforme in each case appeared later. The primary disease, therefore, was herpes simplex. Hence the title could preferably have been something like "Oral zinc in recurrent herpes simplex with recurrent post-herpetic erythema multiforme and resultant depigmentation", specifying the main disease.

(2) The authors have combined the history of all the three cases which looks odd with similar type of history and clinical features. No reference to upper respiratory infection has

been made by the authors as the same of long duration (4-6 weeks) has been implicated in such cases.[1]

(3) In dermatologic disorders like venous leg ulceration and acne vulgaris controlled studies on oral zinc have failed to demonstrate any effect superior to that of a placebo.[2,3] No beneficial results have also been obtained in other conditions like alopecia areata and psoriasis.[4,5] It is recommended only in cases with pre-existing zinc deficiency.[6]

(4) Dosages of oral zinc used in this study seem to be higher than those recommended recently. It has been brought forward that zinc deficiency symptoms are easily controlled by oral administration of 15-25 mg of zinc daily[7] and in dermatological conditions like acrodermatitis enteropathica 2 mg/kg/day of oral zinc should suffice. The usual dose recommended for iatrogenic zinc depletion (ZD) is about 50-150 mg of elemental zinc daily.[6] Moreover, the risk of producing copper deficiency leading to anaemia and leucopenia particularly in patients receiving prolonged higher doses (100-150 mg zinc daily) has to be kept in mind.[6] It seems the authors have not demonstrated the serum zinc level in these cases which could otherwise have been helpful to detect zinc deficiency if any in these cases.

(5) Erythema multiforme is a self-limited eruption and usually subsides in 2-3 weeks.[8] As observed by the authors, the duration of the reaction pattern has not been much reduced after oral zinc therapy which shows this therapy is not in anyway helpful in erythema multiforme. The authors have not attempted to demonstrate the immune complexes too from the lesions of the skin before and during the therapy to prove their work.

(6) The authors have attached much more importance to the depigmentation noted in erythema multiforme when actually that was noted only after the skin lesions resolved and cannot be designated as depigmenting type of erythema multiforme, as this is done generally when a disease is in its active form. Hypomelanotic areas occur following resolution of areas of eczema and of psoriasis[9] and is the routine genesis of the disease with probably a loss of functional melanocytes.

It is, therefore, inferred that the effects of oral zinc in erythema multiforme are neither beneficial nor convincing. It is likely that it may be of some value for herpes simplex indirectly affecting post herpetic erythema multiforme (PHEM) because of its anti-viral effect as mentioned by some workers,[10,11] but that has been proved by studies conducted in vitro. It is however to be elucidated if this therapy is of any significance with respect to viral infections in man.[7] It has also not been clarified by the authors as to why oral zinc therapy has been preferred over topical zinc therapy used by a number of workers for herpes simplex with beneficial effect,[1,12] actually when oral zinc has to be used for a period not less than 3 months it is not regarded safe when used in higher doses Repigmentation seen in some hypopigmented patches of erythema multiforme has been attributed to zinc therapy but the mechanism involved has not been fully explained to reveal if this affects melanogenesis in any way, or the process is spontaneous.

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Reply

I am thankful to Dr. Lal for taking interest in our article. We have been using oral zinc (220 mg $ZnSO_4$ per day) in cases of leprosy for more than 2 years and have not come across any side effect, except mild gastric irritation in a few patients.[1] Recently, we have studied the effect of oral zinc therapy on HDL-C and total cholesterol and have found that in the dosage mentioned above, it does not decrease HDL-C levels (unpublished).

Reasons for trying zinc in our cases were : it inhibits DNA polymerase of herpes simplex virus, it inhibits complement dependent immune complex reaction, and it has anti-inflammatory action. The beneficial effect of our regimen could be judged by the fact that there was no recurrence subsequently.

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Reference

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