Letters to the Editor

Oral Iron Chelators

I read with interest the recent editorial on this topic(l) and have the following clarifications to seek:

(i) Regarding the side effect of LI (1,2 dimethyl-3-hydroxy-pyrid-4-one), the editorial states 'there is no evidence that it is related to rheumatoid arthritis or SLE like syndromes(l) whereas another review states that 'a large percentage of patients developed severe arthritis and serological evidence of SLE like disease(2). Which one of the above two statements is true?

(ii) According to the editorial 'However, in view of the life threatening complications faced by most thalassemics secondary to iron overload, use of this drug is imperative'(l). But at the same time, the other review states that 'due to coincidence of some very puzzling occurrences (in the form of various side effects) it is not advocated in any country yet for regular use'(2). Should we use this drug regularly or not?

(iii) The editorial states 'unfortunately none of other iron chelators including HBED and 90 other alfa-ketho-hydroxypyridines tested in animals appear promising enough for clinical use'(l). However, the other review article states 'out of these, HBED has proved very effective in animal trials with hardly any toxic effect'(2). Which statement is correct?

(iv) Whether LI can be used below 2 years age or not and if the answer is in affirmative, will it be available as liquid or chewable form? If not then probably for all practical purposes, children below 5 years of age will be deprived of the benefit of this drug.

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Reply

I thank Dr. Bhattacharyya for making some interesting observations related to differences between the two publications 'oral iron chelators'. To the best of our knowledge there is a single anecdotal report of arthritis being attributed to SLE in a case of thalassemia major receiving deferiprone(l). Both prior to and subsequent to this case report, patients receiving deferiprone have been tested for the laboratory evidence of SLE, rheumatoid arthritis and other immunological markers in Indian, Canadian, British and the Swiss trials(2-6). Stored seras prior to and subsequent to treatment of deferiprone have also been analyzed(6). An extensive animal

experiment was also carried out by Porter and his group in large number of mice where escalating doses of deferiprone were injected intraperitoneally and blood was periodically tested for occurrence of immunological parameters under discussion (personal communication). The consensus is that multi-transfused thalassemics have variable serological positivity with respect to anti-nuclear antibody and rheumatoid factor(7). There has been no significant increase in number of titers and there is no convincing clinical evidence of anything like SLE or rheumatoid arthritis in over 800 patients who have received deferiprone Worldwide(2). In fact the anecdotal case report itself has been unconvincing to most of the participants of the International Study Group.

Regarding-use of deferiprone on regular basis, the drug has been cleared by the Drug Controller and formally marketed in India from March 1995. As of today, 450 patients have been prescribed deferiprone after it's official launching. In view of myelotoxicity and joint toxicity the drug has been kept under postmarketing surveillance with patients receiving one month supply at a time, subsequent to which the clinician incharge has to certify regarding normal hemopoiesis and lack of arthropathy. These 450 patients include patients from Bangla Desh, Sri Lanka, Pakistan, Singapore, Thailand and of course, India. The drug can be used regularly by all those who cannot take adequate doses of desferrioxamine due to one or other reason. It may be discontinued if complications like granulocytosis or chronic neutropenia occur (1-2% of patients) and also if significant arthropathy develops (10-25%).

We agree that HBED has been found to be effective in animal trials. However the cost involved in its preparation and lack of data regarding toxicity has taken away the workers' interest in it(8).Deferiprone can be and has been used under the age of 2 years. Liquid preparations of deferiprone are not stable for significant duration and hence not yet available. The contents of capsules have been mixed with honey, fruit juices, milk and even water and taken by patients both during the trial and subsequently after its marketing practically all around. There has been no difference in efficacy and no increase in gastrointestinal adverse effects.

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