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Reappraisal of High-Dose Desferrioxamine Therapy

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It is now widely accepted that the best treatment for thalassemia major is a precocious and regular transfusional regimen with the aim of maintaining pretransfusional Hb levels of 10.5-11 g/dl [1]. Such an approach, by minimizing the growth disturbances and serious cardiac complications, has greatly improved the quality of life and survival of thalassemic patients. On the other hand, the hemosiderosis secondary to hypertransfusion regimen is a serious threat for a long life expectancy. This concern and the general assumption that desferrioxamine treatment has minimal side effects resulted in a generalized tendency toward the use of high doses of desferrioxamine. The reduction of serum ferritin below 1,000 µg/ml is considered an objective to pursue with determination [1].

We believe that now it is time for a pause of meditation. In the last few years, together with the increase of desferrioxamine doses, important side effects have been reported frequently. Potentially life-threatening infections from *Yersinia enterocolitica* have been reported with increasing frequency in thalassemic patients [2]. It has been postulated that the large amount of iron excreted through the intestine as a consequence of the chelation treatment may represent a growth factor for the bacteria.

Other alarming side effects, although rare, are cataracts [3], visual-field defects [4] and acute visual loss [5]; however, more subtle signs of visual and auditory neurotoxicity may be discovered with a certain frequency when accurate visual tests, visual evoked potentials and audiometry are performed [6]. The dose of desferrioxamine administered to patients with abnormal tests was significantly higher than in normals [6]. Growth velocity was significantly reduced in 47 of

71 prepubertal thalassemic children undergoing high-dose desferrioxamine treatment [Gabutti, pers. communication.]; growth resumed after dose reduction in 16 of 47 children.

It has been postulated that disproportionately high doses of desferrioxamine in relation to the amount of body iron result in high levels of unchelated drug, which may be toxic [6]. One of the mechanisms of toxicity, which has been quoted but not proved, is the chelation of trace elements such as zinc and copper [4, 6]. In our experience patients with good compliance to chelation therapy have low neutrophil zinc content and zinc levels, whereas urinary zinc excretion is significantly higher than in those patients with poor compliance to treatment [7]. Although convincing explanations are still lacking, the importance of complications associated to high-dose desferrioxamine therapy cannot be overlooked. Careful clinical surveillance programs, integrated by the use of neurophysiologic tests, should be undertaken in any center taking care of thalassemic patients in order to assess the true incidence of

important toxicities related to chelation therapy. In the meantime, we believe that, optimally, the serum ferritin levels of these patients should be increased by two or three times. The clinician should primarily consider the health of his patient instead of pursuing an ideal ferritin level.

References

Modell, B.; Berdoukas, V.: The clinical approach to thalas-saemia (Grune & Stratton, London 1984).
Robins-Browne, R.M.; Prpic, J.K.: Desferrioxamine and systemic yersiniosis. *Lancet* ii: 1372 (1983).

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Bloomfield, S.E.; Markenson, A.L.; Miller, D.R.; Peterson, C.M.: Lens opacities in thalassemia. *J. pediatr. Ophthalmol. Strabismus* 15: 154-156(1978).
Davies, S.C.; Marcus, R.E.; Hungerford, J.L.; Miller, M.H.; Arden, G.B.; Huehns, E.R.: Ocular toxicity of high-dose intravenous desferrioxamine. *Lancet* ii: 181-184(1983).
Borgna-Pignatti, C.; De Stefano, P.; Broglia, A.M.: Visual loss in patients on high-dose subcutaneous desferrioxamine. *Lancet* i: 681 (1984).
Olivieri, F.N.; Buncic, J.R.; Chew, E.; Gallant, T.; Harrison, R.V.; Keenan, N.; Logan, W.; Mitchell, D.; Ricci, G.; Skarf, B.; Taylor, M.; Freedman, M.H.: Visual and auditory neurotoxicity in patients receiving subcutaneous deferoxamine infusions. *New Engl. J. Med.* 314: 869-873 (1986).
7 Schilirò, G.; Russo, A.; Azzia, N.; Russo Mancuso, G.; Di Gregorio, F.; Romeo, M.A.; Fallico, R.: Leukocyte alkaline phosphatase: a useful marker of zinc status in β -thalassemic patients. (Submitted).