EDITORIAL

Combination of Oral Iron Chelators for Thalassemia

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In a developing country like India, research on newer treatments modalities – that are cheaper and yet effective – is the need of the hour. Regular packed red cell transfusions and effective chelation is the cornerstone of treatment for patients with thalassemia major. Repeated blood transfusions lead to iron overload. In this issue of *Indian Pediatrics*, Gomber, *et al*. [1] highlight that a combination of two oral iron chelators (deferasirox and deferiprone) is better than single oral iron chelator in removing excess iron in these patients. In this study, 49 multi-transfused children with thalassemia received daily chelation therapy with either deferiprone alone (75 mg/kg/d in 3 divided doses), deferasirox alone (30 mg/kg/d single dose) or their daily combination (same dose as monotherapy) for 12 months. The combination therapy was more efficacious in causing fall in serum ferritin levels compared to deferiprone and deferasirox monotherapy (P=0.035 and P=0.040, respectively). No significant adverse reactions were noticed in either the monotherapy or the combination group.

Another prospective, single-center, open-label, uncontrolled study from India, has also documented similar findings in 36 children [2]. Previously, one randomized trial, few clinical case reports and case series have also reported the efficacy and safety of this combination in about 70 children [3-7]. Data from the randomized study [7] showed that while both forms of combination therapy, 'deferasirox and deferiprone' and 'deferiprone and desferrioxamine', were effective in reducing iron overload in multi-transfused thalassemia major, patients who received 'deferasirox and deferiprone' showed a higher decline in serum ferritin, greater improvement in cardiac T2*MRI, higher treatment satisfaction, better compliance, and more improvement in quality of life than those who received 'deferiprone and desferrioxamine', with no increased toxicity.

Thalassemia major has a huge impact on quality of life [8]. Iron overload is a major contributor to this problem. The data from present study [1] and others [2-7] have many implications. Most children with thalassemia would have chances of prolonged survival consequent to the better cardiac and liver functions due to effective chelation. A more effective chelation would lead to a better quality of life due to better growth, skin colour, endocrine functions and energy levels [7]. Also, the combination of two oral iron chelators is cheaper and easier to administer as compared to intravenous desferrioxamine, and thus compliance is likely to be good [2]. This combination may be a good option for heavily iron overloaded patients, particularly those are difficult-to-chelate with a suboptimal response to monotherapy. Hematopoietic stem cell transplant (HSCT) is the only curative option for patients with thalassemia major but outcomes are worst in Pesaro Class III patients (who have high iron overload) with overall success rate of 60% [9]. The major cause of mortality is veno-occlusve disease due to high iron content in the liver. This newer and more effective chelation regimen given before HSCT could lead to better outcomes in class III patients.

However, few cautions are needed like watching out for agranulocytosis and arthritis due to deferiprone and liver, and renal derangements due to deferasirox [2]. The present study needs to be replicated in a multi-centric setting with well-controlled dresign and larger numbers, for combination oral chelation to become a standard of care in thalassemia management.

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