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Iron chelation in patients with transfusion dependent thalassemia: an insight on response to deferasirox

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Iron Chelation in Patients with Transfusion Dependent Thalassemia: An Insight on Response to Deferasirox

Sir,

Situated in South Asia, Pakistan is a home to over 180 million populations. With a carrier rate of 5% to 13% in the country,[1] an estimated 5000 to 9000 children are born annually with beta-thalassemia major. Bone marrow transplantation is expensive and restricted to a couple of large cities, therefore, majority of children are treated with regular blood transfusions.

Excess iron from transfusions deposits in liver, heart and endocrine glands leading to organ failures if not controlled and eliminated by chelation therapy.[2] Deferoxamine, the parent drug in use for last four decades requires parenteral administration whereas, deferiprone although orally active and well proven to be cardioprotective,[3] requires thrice daily administration and may cause idiosyncratic reactions like erosive arthritis and agranulocytosis.[3] These facts are the reasons for non-compliance and hence poor iron chelation. After the availability of deferasirox in Pakistan in 2008, physicians and patients considered it as an answer to their miseries. It is orally active and has bioavailability and half-life suitable for once daily dosing.[4] The most common side effects reported with deferasirox are gastro-intestinal events, skin rash and mild dose-dependent increase in creatinine and hepatic transaminase levels.

Our institute has a day-care centre which offers blood transfusion facilities to over 200 thalassemia major patients. Several thalassemics were started on deferasirox however, many of them discontinued it because of its questionable efficacy. Serum ferritin levels did not improve substantially in several patients. As it was a significant observation, we evaluated the efficacy of deferasirox in these patients. Thalassemics were included who reported a good compliance with the medicine and were free from any liver disease. Baseline serum ferritin levels (before starting deferasirox), dose of deferasirox, last available ferritin levels and duration of treatment were inquired and confirmed from medical records. For assessment of hepatic and renal functions, Alanine Aminotransferase (ALT) and serum creatinine levels respectively were performed before starting the drug and thence repeated at a variable time period of 1 - 6 months. Complete blood counts were evaluated for cytopenias before each transfusion (at 3 - 4 weeks interval). Furthermore, patients were examined for auditory, ocular, cardiac and gastrointestinal disturbances at their visits to outpatient clinic or in the day-care. Due to unavailability of more sophisticated methods like T2*MRI and Superconducting Quantum Interference Device (SQUID), serum ferritin level was used to assess reduction in iron overload. Parents/guardians of all patients were counselled in detail regarding possible benefits and adverse effects of deferasirox. All the patients were provided liberty to stop or change the medicine at any time.

A total of 63 patients were included for analysis. The mean age was 12.2 ± 7.2 years with male: female ratio of 1:1. The mean serum ferritin level before starting deferasirox was 5254.5 ± 3540.4 ng/ml (range 1276 - 19265) whereas it was 4701.8 ± 2989.8 ng/ml (range 538 - 17200) at the time of final analysis. The application of paired-samples T-test showed a difference of -552.7 ± 1677.2 ng/ml (p=0.01). The mean duration of the medicinal intake was 15.2 ± 15.9 months (range 5 - 65 months) and the mean dose of deferasirox was 22.9 ± 7.5 mg/kg/day. Ten (16%) patients reported gastro-intestinal disturbance mostly in first few weeks of starting the drug. No patient developed skin rash. Hepatic, renal, ocular, auditory and cardiac abnormalities were not observed in any patient.

High serum ferritin level in the study cohort reflects the poor iron chelation in majority of thalassemics in our country.[5] Nevertheless in current analysis, deferasirox resulted in decrease in ferritin levels with continued use (p=0.01) without any major untoward adverse effect. In search of an ideal iron chelator, the availability of deferasirox generated a hope for proper management and hence, better lifestyle for thalassemia major patients. Based on this observation and its concordance with the literature,[4] we recommend the continued use of deferasirox in patients with thalassemia major particularly in those who are non-compliant with other regimens.

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