Safety: A Primary Concern in Thalidomide Use in Thalassemia

I read with interest the article by Chandra, et al. [1] published in the journal recently. Authors have presented their data on the efficacy and safety of thalidomide in adolescents with transfusion-dependent thalassemia (TDT). It is an excellent effort and much awaited publication keeping in view the quantum of thalassemia in India, the high cost of bone marrow transplant (BMT), and the scarce data on use of thalidomide in TDT. However, I would like to highlight a few issues in the study.

The primary concern with use of thalidomide in TDT remains safety rather than efficacy. A study period of six months is too short for a disease requiring long-term therapy with thalidomide. During a study of any new drug for a disease, the criteria for stoppage of trial are pre-defined for ensuring safety [2]. In their study, 8/37 developed infection with one death (due to unrelated causes), and 10/37 developed neutropenia (one severe grade-III neutropenia) and one grade-IV renal injury. Such a high incidence of neutropenia is unexplained by co-administration of deferiprone alone [3]. Considering the small sample size, continuing the trial despite severe adverse reactions may warrant more details.

The very low baseline mean hemoglobin F (HbF) and the steep rise in the study [1] is not supported by the literature. Mean baseline HbF levels were 2.95% and have risen to 49.2% after six months of thalidomide therapy. The baseline levels are generally higher (10-60%) in adolescents in the studies of HbF inducers in thalassemia [4]. Also in clinical studies, on an average, a 20% rise is seen in responders of HbF-inducer agents in thalassemia [5].

The baseline mean packed cell volume in the study cohort was 75 mL/kg in last 6 months, which seems quite modest for adolescent children with thalassemia (12-18 years) as their requirement is high due to growth and pubertal spurt. Even the sample size calculation in the study was based on assumption of 220 mL/kg/year. Therefore, was there a selection bias as the cases were randomly enrolled?

**REFERENCES**


**REPLY**

We are thankful to the reader for appreciating the need for developing drugs for thalassemia. The learned reader has reiterated the same safety issues which we had already mentioned in the last paragraph of our paper, including the need for larger studies addressing safety of thalidomide [1]. We restricted the study for 6 months on account of financial reasons.

As regards adverse effects (AEs), reader’s attention is drawn to a recent study on another fetal haemoglobin (HbF) inducer luspatercept. In this study, 96% patients had one or more AE with 29% having AE grade 3 or more, 15% having serious AE with...