To study the incidence of anemia in HIV-infected children on zidovudine-based highly active antiretroviral therapy regimen

Sir,

With increasing access to highly active antiretroviral therapy (HAART) to children, a complete understanding of the side effects of the drug is more relevant than ever before. Zidovudine (AZT) is a nonnucleoside reverse-transcriptase inhibitor (NNRTI) which is a part of the HAART regimen being prescribed to the children under the NACO program. Side data of AZT have been studied earlier, but the effect on pediatric population, especially in India, is scant. We studied the profile of anemia in the children receiving AZT-based HAART.

This study was conducted in the antiretroviral treatment (ART) center of a tertiary level teaching institute over a period of 12 m from July 2014 to June 2015. All the children in the age group of 1–18 years who were started on AZT-based HAART during the first 6 m of the study were included in the study. Written informed consent was taken from the parents/guardians. A detailed history was taken and complete physical examination was done at the time of enrollment. NACO guidelines were followed for initiation of AZT-based HAART in children if the hemoglobin was ≥9 g%. Baseline hemoglobin (Hb), CD4 count, and other relevant investigations were done. The children were followed up every 2 m, when the compliance was ensured, and a thorough assessment was done including a hemoglobin level. Anytime the Hb dropped below 9 g%, AZT was replaced by stavudine. Other obvious causes of anemia such as malaria were ruled out. Hb <6 g% was taken as a cutoff for packed cell transfusion. The children were followed up for 12 m.

A total of 79 children were started on AZT-based HAART during the first 6 m of the study period. The male:female ratio was 4.2:1, and the mean age at enrollment was 8.7 ± 3.7 years. The mean Hb at the time of enrollment was 10.94 ± 0.67 g/dL. Out of these, 36 (45.5%) children developed anemia (Hb <9 g%) and 10 children needed a packed cell transfusion. The mean baseline Hb in children who developed anemia was significantly lower (10.57 ± 0.52 g/dL) than children who did not develop anemia (11.26 ± 0.61 g/dL), P < 0.001. The baseline characteristics such as age, sex, and WHO staging of the disease were not significantly associated with the development of anemia. The mean time to development of anemia was 6.4 ± 2.2 m, and the mean drop in hemoglobin was 3.84 ± 1.49 g%. The anemia was normocytic in 20, macrocytic in 12, and microcytic in 4 children. The mean hemoglobin and the cumulative incidence of anemia in children started on AZT are given in Table 1.

McKinney et al. in a multicenter study of AZT in children on advanced HIV disease found that 61% of children had one or more episodes of anemia (Hb <7.5 g %).[2] Bunupuradah et al. while studying the predictors of severe anemia in Asian HIV-infected children on ART found that the use of AZT was significantly associated with increased risk of early severe anemia (P = 0.013).[3] Agarwal et al. in their study reported anemia (Hb <8 g%) in 16.5% of patients on HAART, and they included patients >15 years in their study.[4] The drop in Hb was 6.3 ± 1.4 g/dL and the mean duration for fall in Hb was 3.66 ± 3.9 m, and the majority (58%) of the patients had macrocytosis. The drop in Hb was earlier and more marked compared to our study which could be because of the different age groups in the two studies. They did not find any significant association of body weight, CD4 count, or WHO clinical staging with an increased risk of anemia. Various studies have shown a significant association between low baseline Hb, low baseline CD4, and low body weight with the development of anemia in children on AZT-based HAART.[5,6] We also found a significant relation between the baseline Hb and the incidence of anemia.

The children started on AZT-based HAART need to be closely monitored for the development of anemia. Replacement of the drug leads to quick reversal and correction of anemia.

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Table 1: Mean hemoglobin and cumulative incidence of anemia in children started on zidovudine

| Time      | Mean hemoglobin (g %) (±SD) | Cumulative number of children with anemia (n) |
|-----------|-----------------------------|---------------------------------------------|
| At enrollment | 10.94±0.67                     | 0                                           |
| 2 m       | 10.71±1.30                    | 0                                           |
| 4 m       | 10.12±1.36                    | 23                                          |
| 6 m       | 9.56±1.52                     | 29                                          |
| 8 m       | 9.97±1.38                     | 14                                          |
| 10 m      | 10.30±1.52                    | 7                                           |
| 12 m      | 10.66±0.52                    | 0                                           |

5D=Standard deviation
Conflicts of interest
There are no conflicts of interest.

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REFERENCES
1. NACO. Department of AIDS control, Ministry of Health and Family Welfare, Government of India Annual Report; 2013-14. Available from: http://www.naco.gov.in. [Last accessed on 2015 Apr 04].
2. McKinney RE Jr., Maha MA, Connor EM, Feinberg J, Scott GR, Wulfsohn M, et al. A multicenter trial of oral zidovudine in children with advanced human immunodeficiency virus disease. The Protocol 043 Study Group. N Engl J Med 1991;324:1018-25.
3. Bunupuradah T, Kariminia A, Chan KC, Ramautarsing R, Huy BV, Han N, et al. Incidence and predictors of severe anemia in Asian HIV-infected children using first line antiretroviral therapy. Int J Infect Dis 2013;17:e806-10.
4. Agarwal D, Chakravarty J, Chaube L, Rai M, Agrawal NR, Sundar S. High incidence of zidovudine induced anaemia in HIV infected patients in eastern India. Indian J Med Res 2010;132:386-9.
5. Ssali F, Stöhr W, Munderi P, Reid A, Walker AS, Gibb DM, et al. Prevalence, incidence and predictors of severe anaemia with zidovudine-containing regimens in African adults with HIV infection within the DART trial. Antivir Ther 2006;11:741-9.
6. Curkendall SM, Richardson JT, Emons MF, Fisher AE, Everhard E. Incidence of anaemia among HIV-infected patients treated with highly active antiretroviral therapy. HIV Med 2007;8:483-90.