LETTER TO EDITOR

TOXICITIES DUE TO HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY (HAART) IN HIV-POSITIVE CHILDREN: NEED FOR FURTHER MEDICAL RESEARCH

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According to the National AIDS Control Organization (NACO) estimates,[1] approximately 50,000 children below 15 years are infected by HIV every year. With the AIDS epidemic slowly spreading its tentacles, the figures are only expected to grow in the future. Management of these patients includes confirmation of their HIV-positive status, following which they undergo comprehensive history-taking, clinical examination, staging of HIV is according to WHO guidelines[2] and CD4 count (HIV-positive children of age < 15 years form a priority group for CD4 testing). On the basis of these they are started on anti-retroviral therapy (ART). Currently the preferred 1st line ART regimen for this age group is a combination of two Nucleoside Reverse Transcriptase Inhibitors (NRTI) plus one Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI). Such a combination of three (or more) anti-retroviral drugs is called Highly Active Anti-Retroviral Therapy (HAART).

The anti-retroviral drugs are associated with a wide range of toxicities, ranging from self-limiting low-grade intolerance, to life-threatening adverse drug reactions. These toxicities are well-documented with respect to the adult population and detailed guidelines for the management are also available.

The "age old" adage of paediatrics that "children *are not miniature adults*" should be kept in mind when prescribing HAART drugs to the children. These toxicities are a matter of concern because they often lead to interruption or stoppage of ART, thereby increasing morbidity and mortality in HIV-positive paediatric population. It is also inevitable[3] that children with HIV-1 infection will be exposed to ARVs for an ever-increasing length of time throughout post-natal growth and development, and the cumulative toxicities will be different from that observed in adults receiving HAART.

Anti-retroviral drugs are already known to cause osteopenia, growth failure and insulin resistance in children.[4] In a cross-sectional study[5] on 152 HIV-infected children and adolescents, at the Pediatrics Immunodeficiency Division, University Hospital, Universidade Estadual de Campinas, mild liver toxicity was observed in 19.7% of the HIV-infected children and adolescents on ART. A review article[6] on children exposed to HAART in utero have reported complications including lactic acidosis and mitochondrial toxicity, as well as cardiomyopathy.

In India, very few studies have been conducted which deal with the drug toxicities of HAART in children exclusively. In one such study[7] conducted at a pediatric and prenatal HIV clinic in a tertiary general hospital in Mumbai, India, on HIV-positive children in the age group of 5 months-14 years were started on HAART, of which 16% developed hepatotoxicity with elevated liver enzyme levels at least five times the baselines values, 12% had raised serum amylase without symptomatic pancreatitis,12% had Zidovudine induced anemia, 9% had

Nevirapine induced rash, 2% had Didanosine induced pain in abdomen, 2% had Stavudine induced angioedema, and 2% had hepatic steatosis. The values in the above mentioned study is radically different from that in adult's population.

In the present setting, only a certain number of investigations are done to monitor toxicities in the children on HAART (even these are mostly based on toxicities of adults), during their follow-up visits. Further research noting aberrant/unpredictable toxicities (if any) that show up consistently in several patients, would provide a thrust towards including the necessary investigations for these toxicities in the routine follow-up, in addition to the investigations presently being done. This would help in better management of morbidity and mortality issues among pediatric patients in future.

India with its wide variety of genetic make-ups hold a possibility of uncovering many new adverse drug reaction due the HAART drugs that might not have been detected in earlier clinical trials. Researchers and HIV physicians need to come together in India and do research on this aspect of HIV care urgently. More data on this aspect is definitely the need of the hour for effective control of the HIV/AIDS epidemic.

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