ART TOXICITY

ANTIRETROVIRAL TOXICITY IN CHILDREN

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Antiretroviral (ARV) toxicity is an important issue that must be fully appreciated by prescribing doctors. While the benefits of therapy are well documented, toxicity is of concern and may be extremely serious, occasionally resulting in fatality. However, most side-effects are not serious and are reversible.

There are two ways in which children may be exposed to ARVs. One is in utero or postnatal exposure as a result of vertical transmission prophylaxis (VTP), and the other is treatment for symptomatic HIV infection.

SYMPTOMATIC INFECTION

Castelli-Gattinara et al.1 presented a comprehensive review of ARV toxicity at the XIV International AIDS Congress in Barcelona in July 2002. As this is, to my knowledge, the largest review of ART toxicity in children, it is worth close attention. The Italian Multicentric Collaborative Study1 was conducted between 1998 and 2000 and included 29 institutions.

Four hundred and eighty-four patients were enrolled in the study (male/female ratio 0.9). The median age was 6.4 years (range 1 month – 18 years). The median follow-up was 709 days, but again there was a wide range (8 – 1 381 days). The clinical and immunological profile (Fig. 1) suggested less severe disease than is commonly seen in South Africa. In the Italian group 71% of patients were either asymptomatic (N) or mildly symptomatic (A). In contrast, 68% of children first presenting at the Tygerberg Family Clinic are either stage B (moderate) or C (severe). The importance of this observation is that the adverse drug reaction (ADR) profile may be different in South Africa, perhaps due to a more severe disease profile.

ADRs were graded from 1 (mild) through 4 (severe) according to a World Health Organisation (WHO) classification. ADRs were experienced by 190 children, representing 39.3% of the total. There were 289 reactions, of which 42 were grade 3 or 4 (14.5%). The grade 3 and 4 ADRs are shown in Table I. Two persistently reported adverse reactions were diarrhoea and raised creatinine. There was only 1 death attributed to the ARV medication.

The four most common ADRs are shown in Fig. 2. They were lipid abnormalities (20%), bone marrow toxicity, liver function abnormalities (elevated aspartate aminotransferase/alanine aminotransferase (AST/ALT) and skin rashes.
(<10%). Less frequent side-effects were renal stones, lipodystrophy and gastrointestinal disturbances, including nausea and vomiting (N/V).

Lipodystrophy and lipid abnormalities were more common in children over 10 years of age, and there was a marginally higher incidence in females. This observation is of importance as these abnormalities, currently rare in children in South Africa, will become more important with longer use of ARVs.

Another important observation was that the relative risk of ADRs increased quite significantly when more than three drugs were used simultaneously (Fig. 3).

Many ADRs can be linked to specific ARVs. Examples are listed in Table II.

In conclusion, ARV toxicity is of concern, especially when wider access to these drugs is becoming possible. It would be very helpful to have a mechanism for multi-centre data collection in order to monitor toxicity and efficacy. This could possibly be coordinated through a national body such as the Medical Research Council or a university-based department of pharmacology.

REFERENCES