Monitoring Adverse Drug Events: Need for an Active Surveillance System

The issue of use of nimesulide as an anti-pyretic agent in children has generated a lot of debate in the last 24 months and I must compliment Piyush Gupta and H.P.S. Sachdev for conducting and reporting a systematic meta-analysis regarding safety of oral use of nimesulide in children. They have concluded that for short-term use (≤ 10 days) in children, nimesulide is as 'safe' or 'unsafe' as other analgesics-antipyretics(1). Meta-analysis provides one of the strongest scientific evidence for a research question. However, type B adverse drug reactions, which are bizarre reactions that cannot be predicted from the known pharmacology of the drug, are extremely rare occurrences. A large sample size would be required to pick up such reactions(2,3). At least 30000 people need to be treated with a drug (and their data analyzed) to be sure that a reaction with an incidence of 1 in 10000 is not missed(4). These events and reactions are best detected through post-marketing surveillance(5). Therefore, the government should establish a countrywide network operating on a continuous basis, for monitoring the safety of newly introduced, if not all, drugs. At present, departments of Clinical Pharmacology at select medical colleges and only a few centers are working in this area(6). These centers are collecting data regarding adverse drug events only from a few physicians working in the same institution. Although these efforts are laudable, they are not able to generate the kind of data, which could form the basis of corrective measures. As we are unable to generate data pertaining to side effects of drugs in our own population, we are heavily dependent on the data generated in other countries and advisory notes issued and regulatory actions taken by regulators elsewhere. And when the regulators world over are divided in their opinion about safety of a drug, Indian drug regulators are in a dilemma regarding allowing its continued production and marketing. In this context it should also be noted that adverse drug reactions (ADRs) of different type or severity might occur in Indian population due to socio-cultural and ethnic factors(6), making it imperative upon us to generate Indian data.

Previously, new drugs were introduced in the Indian market after a gap of several years. Hence the physicians and regulators here were able to draw upon the data generated in the countries that were using the drug for those years. It has been observed that the lag has now decreased considerably(7). This makes it even more pertinent for us to have an indigenous system to detect adverse drug events. The centers under the nation-wide pharmacovigilance system should collect data regarding adverse drug events from clinicians, pharmacists, nurses and lay people. The apex center under the system could collate the data and perform analytical, advisory and regulatory functions. It could put up alerts and advisory notes for the clinicians regarding ADRs and safety of drugs. At present, the clinicians are not aware of the valuable contribution that they can make in monitoring drug safety. Hence, the pharmacovigilance program should also take up educational activities in collaboration with professional bodies like the Indian Academy of Pediatrics, to inform and enlighten clinicians about the need for and advantages of an active reporting system for monitoring drug safety.

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Role of *Entamoeba histolytica* in Acute Watery Diarrhea in Hospitalized Under-five Children

Acute diarrhea is a major cause of morbidity and mortality among children in developing countries and Rotavirus and Enterotoxigenic *E. coli* (ETEC) are the most frequent etiological agents(1,2). Although, *E. histolytica* is an uncommon cause of acute watery diarrhea in under-five children, anti-protozoal drugs (with or without antibiotics) continue to be used in this setting(3). This has been further compounded by the recent increase in the number of formulations containing antiparasitic agents with antibiotics. This case control, tertiary-care hospital based study was conducted to elucidate the role of *E.histolytica* in the causation of acute watery diarrhea in hospitalized under-five children in our setting.

The study was carried out over a three-month period (1 June-30 August, 2001) among the pediatric inpatients of Dr. R.M.L. Hospital, New Delhi. All the patients satisfying the inclusion criteria were included in the study.

Inclusion criteria. Less than 5 year of age and acute watery diarrhea of less than 72-hour duration.

Exclusion criteria. Dysentery, mucoid diarrhea, and history of receiving any antiparasitic drug in the ten days prior to admission. Age and sex-matched controls were selected from among the hospital in-patients, provided they had not had diarrhea in the previous month and, had not received any antiparasitic drug in the last ten days. Information regarding age, sex, place of residence and source of water supply was obtained in a proforma. From each case and control, at least (approx.) 5 mL or 5 g of faeces was collected in a clean, sterile container, marked and dispatched by hand to the pathology laboratory. These samples were examined by one of the authors (RBY) within