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LETTER TO THE EDITOR

ADVERSE DRUG REACTIONS – HOW COMMON TO QUINOLONES ?

Sir,

(Received on March 25, 1996)

We read with interest the article entitled "Unwanted effects of ciprofloxacin in Indian Population" by Dr. J.K. Grover published in July 1993 issue (1).

The above mentioned study shows the adverse effects to ciprofloxacin in 326 patients receiving the drug for a period of two years. However, no attempt has been made to evaluate the epidemiological profile contrary to the statement in the abstract and, a sample study from this centre generalises the Indian population.

It has been stated in the abstract that the route of administration influenced the onset of ADRs and the severity was proportional to the dose. But, no where the dose of ciprofloxacin has been mentioned. In contrast, Lode (2) has reported that unlike oral route, parenterally administered ciprofloxacin does not cause dose related ADRs.

The author discussed that the nature of ADRs to ciprofloxacin in Indian population is the same as reported in the literature. However, in Table III, the reported percentage of ADRs in Japan is shown as 3%. Further, in the discussion, ADRs from Europe are stated as 3% and from Japan as 6.5% and Japanese are reported to show lesser incidence of ADRs to quinolones. Whether racial factor contributes to ADRs to quinolones?

The incidence of adverse reactions among patients receiving ciprofloxacin as reviewed by Ball (3) is reported as 3% in Europe, 6.5% in Japan and 13.4% in U.S., but more recent data by Schacht et al., 1988, show an overall incidence of 10.2% with little difference between the countries (3, 4). Sanders in an overview has reported the possible drug related adverse effects in 332 (14.8%) of 2236 courses of oral ciprofloxacin given to 2203 patients (5). Most of the reactions were mild and did not shorten the course of therapy. There was a tendency for such reactions to occur more frequently at higher dosages and in elderly. The common adverse effects were in the gastrointestinal system (34%), abnormality in laboratory tests on metabolic and nutritional parameters (19%) and CNS adverse effects (18%). Epilepsy, alocoholism and high serum theophylline level precipitated convulsions in four such cases.

In the discussion, it is mentioned that ciprofloxacin has lesser effect on the bowel flora, therefore, this drug has not been associated with superinfection with *Clostridium difficile*. However, the reference quoted i.e., Holt et al (6) shows the study on 6 male healthy volunteers. As quinolones tend to spare the anaerobic gut flora, they are less often associated with emergence of *Clostridium difficile* induced pseudomembranous enterocolitis. Though rare, it has been reported by Arcieri et al (7), Jungst and Mohr (8) and Dan and Samra (9). Sanders (5) has also reported one episode of pseudomembranous enterocolitis with ciprofloxacin which responded to metronidazole treatment and recovered without any sequelae (5).

The incidence of adverse drug reaction to quinolones tends to increase in higher age group. However, the graphical presentation (Fig. 1) showing percentage of ADRs in relation to age is not clear as the abscissa is not calibrated with class–intervals. It may be

mentioned here that convulsions have been associated with the use of quinolones (especially with pefloxaxcin, ciprofloxacin and ofloxacin) and there is a steep increase in the incidence of convulsions with ofloxacin after the age of 50 years (10).

It is reported in the article that adverse drug raction monitoring in India has yet to take roots. In this connection it may be stated that Sarkar et al (11) have reported ciprofloxacin induced gastrointestinal disturbances in 4 and bone pain in 2 out of 18 patients while treating enteric fever in paediatric age group with 15–20 mg/kg dose. Further, Kshirsagar (12) in a short report has mentioned ciprofloxacin induced muscular weakness which has also been reported by Sanders (5).

There are some major inaccuracies in quoting references in the article. Interested readers are suggested to refer the articles by Lode (2), Sanders (5), Hooper and Wolfson (13), Paton and Reeves (14).

In conclusion, as Davey has stated "state-of-the art technique for analysis of ADRs have not been applied to quinolones, despite the fact that these events might have been predicted from experiences with nalidixic acid" (10).

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