

Ofloxacin-induced reversible arthropathy in a child

Sir,

Ofloxacin, a potent fluoroquinolone antibiotic, is used in various gram-positive and gram-negative bacterial infections. Common adverse drug reactions (ADR) to ofloxacin include nausea, vomiting, abdominal discomfort, diarrhea, headache, dizziness and insomnia. Tendinitis, a rare complication documented in adults, is potentially serious because of the risk of tendon rupture. Ofloxacin is concentrated in human bone and cartilage and the tissue half life is longer than that in serum.^[1] It has been reported that fluoroquinolones do damage growing cartilage and can cause arthropathy affecting major joints in animals. Articular cartilage erosion, changes in the cartilage matrix and increased synovium, have been reported in immature rats and juvenile dogs.^[2,3] In humans, ofloxacin-induced arthropathy has been reported in pediatric patients treated for multidrug-resistant tuberculosis, other infections and cystic fibrosis.^[4,5] Thus, fluoroquinolones are not routinely recommended for use in children and adolescents in countries like the UK and USA. However, arthropathy is reversible on drug withdrawal, serious joint damage has not been reported and pediatric formulations of ofloxacin are widely available in India. In this context, we report a case of ofloxacin-induced arthropathy in a child who received the drug as first line treatment for typhoid fever.

An eight-year-old boy presented with high-grade continuous fever for one week. Routine hemogram was normal and Widal test was positive for *Salmonella typhi* O antigen at 1:160 dilution. Enteric fever was diagnosed. The child was treated on outpatient basis with ofloxacin 15 mg/kg/day orally in two equally divided doses and paracetamol for fever. The fever subsided on the sixth day of treatment and ofloxacin was continued till the tenth day. On the seventh day of treatment, the child complained of pain in the right hip and experienced difficulty in walking. There was local tenderness and pain was elicited on medial rotation of hip joint. X-ray showed no bony or joint space abnormalities. A repeat routine hemogram was also normal. Patient was given ibuprofen 30 mg/kg/day in divided doses. He improved gradually and recovered fully in two weeks. Other joints, like knees, elbows and wrists, were not affected.

The child suffered an acute episode of hip arthropathy. Ofloxacin was the most likely cause. The only other drug the patient received – paracetamol – is not known to produce arthropathic symptoms or cause joint damage. On the contrary it may be useful in arthritic pain. There are also no significant drug interactions between paracetamol and ofloxacin. In our case, there was reasonable temporal relationship between event and drug exposure. Pain and

functional disability subsided gradually on withdrawal of suspect drug. Rechallenge was not attempted. The arthropathy is unlikely to have been due to disease because symptoms appeared when fever was subsiding. Therefore, this event can be considered as 'probable' or 'likely' reaction by the WHO and Uppsala Monitoring Centre standardized case causality assessment criteria. Analyzed by the Naranjo's ADR probability scale, the score was 7, which also makes it a 'probable' event.

Among reported cases of arthralgia and arthropathy induced by fluoroquinolones in man, symptoms generally began few days following commencement of the drug and resolved within several days of cessation of treatment. In some instances, however, symptoms continued for longer periods – up to three months. Various joint sites have been affected. In our case, hip involvement was unilateral and full recovery took two weeks.

The mechanism of fluoroquinolone arthrototoxicity is unknown. Quinolones accumulate in cartilage and because they form chelate complexes with divalent cations, they may induce a functional deficiency of magnesium that leads to cartilage damage.^[6] The drug may interfere with mitochondrial activity in immature articular chondrocytes.^[7] It is also possible that quinolone-induced arthropathy and quinolone-induced tendinitis are different manifestations of the same toxic effect on cellular components of connective tissue structures.^[8]

Physicians in general and pediatricians in particular need to be aware of the possibility of ofloxacin arthropathy. If it does occur, the drug should be withdrawn and symptomatic management offered till the subject recovers.

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