Sleep disturbance in children treated with ofloxacin

Dr C UPTON (Norfolk and Norwich Hospital, Norfolk NR1 3SR) writes: Fluoroquinolones are not licensed for use in children but are the only drugs that act orally against *Pseudomonas aeruginosa*.[1] They are therefore used widely in children with cystic fibrosis and pseudomonas infection. Their use has increased since the finding that treatment with oral ciprofloxacin and nebulised colistin can delay chronic carriage of pseudomonas when given after the organism is first isolated.[2] This has become standard practice. This hospital's pharmacy recently changed the fluoroquinolone on its formulary from ciprofloxacin to ofloxacin. I report here severe sleep disturbance in three children with cystic fibrosis treated with ofloxacin.

P aeruginosa was cultured from a routine outpatient pharyngeal swab from a 6 year old boy. Treatment was started with nebulised colistin 500 000 U twice daily and oral ofloxacin 400 mg twice daily. His sleep became very disturbed (he slept a maximum of only five hours a night), and he developed a light sensitive rash. Nevertheless, we continued the treatment for three weeks, and the symptoms subsequently settled.

P aeruginosa was cultured from samples taken after a viral illness in another 6 year old boy. He started taking nebulised colistin 500 000 U twice daily and oral ofloxacin 200 mg twice daily. He returned after two weeks complaining of nightmares and severe sleep disturbance. Ofloxacin was stopped and colistin continued for a further week, during which the symptoms settled. A subsequent respiratory exacerbation was treated with ciprofloxacin 500 mg twice daily, but he did not develop any sleep disturbance.

After a course of intravenous antibiotics for a respiratory exacerbation due to *P aeruginosa* a 10 year old girl had a persistent cough, which was treated with nebulised colistin 500 000 U twice daily and oral ofloxacin 400 mg twice daily. She returned 10 days later complaining of an inability to sleep. Colistin was continued but her oral treatment was changed to ciprofloxacin 500 mg twice daily. Her symptoms settled immediately.

None of the three patients had previously received fluoroquinolone treatment. All continued to receive vitamin supplements and pancreatic enzymes, and the second and third patients also received prophylactic oral flucloxacillin. Doses of these drugs were unchanged and symptoms had not previously occurred with them. The temporal relation makes it almost certain that the symptoms were due to ofloxacin. The last two patients slept well while subsequently taking ciprofloxacin. Both drugs are effective orally against pseudomonas infection in cystic fibrosis in adults.[3] Sleep disturbance is a recognised but rare complication of fluoroquinolone treatment, but it has not been related to one specific drug in adult practice.[1,3] These observations suggest that sleep disturbance is common in children receiving ofloxacin and that ciprofloxacin is usually well tolerated.

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Enalapril and bullous eruptions

Drs P D MULLINS and S L CHOUDHURY (Countess of Chester Hospital, Chester CH2 1BQ) write: An 83 year old man with cardiac failure had his treatment changed for convenience from captopril 12·5 mg three times a day to enalapril as a single nocturnal dose. He took one dose of 10 mg and 36 hours later developed a bullous rash on both legs; this cleared quickly after enalapril was stopped. The figure shows the rash four days later, when it was fading. The rash did not recur when captopril treatment was restarted.

Angiotensin converting enzyme inhibitors are reported to account for 19% of serious dermatological reactions,[1] of which between 4%[2] and 12%[3] concern patients treated with captopril. Such reactions are less common with other ACE inhibitors. This is postulated to be because captopril has a sulphydryl group. Enalapril does not contain a sulphydryl group, and reports suggest that enalapril can be safely substituted for captopril if captopril causes hypersensitivity reactions.[4] A single reported case of bullous rash (pemphigus) induced by enalapril was postulated to be due to its molecular similarities with captopril.[5] Bullous eruption in our case cannot be explained either by the presence of a sulphydryl group, as in captopril, or by molecular similarities between captopril and enalapril as the rash did not recur after captopril was reintroduced. We conclude that prescribing for patient convenience can have drawbacks.

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5 Shelton RM. Pemphigus foliaceus associated with enalapril. *J Am Acad Dermatol* 1991;24:503-4.

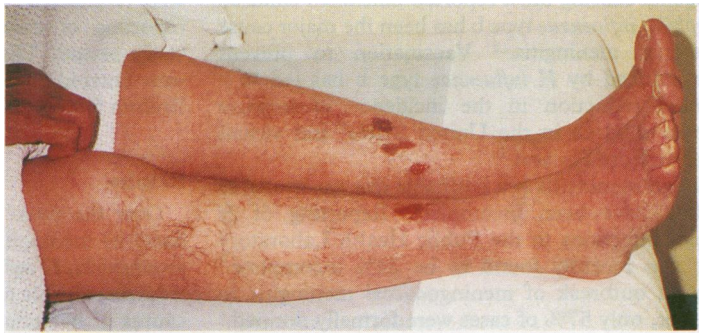
Acute hemiparesis associated with ciprofloxacin

Drs A ROSOLEN, P DRIGO, and L ZANESCO (Department of Paediatrics, University of Padua, 35128 Padua, Italy) write: Oral ciprofloxacin is used in various clinical conditions for its wide range of activity and lack of cross resistance with other non-quinolonic antibiotics. Despite its overall safety,[1,2] adverse effects such as seizures[3] and psychoses[4] have been described when ciprofloxacin was given alone or with co-trimoxazole and theophylline.[5] We report an episode of hemiparesis associated with a migrating involvement of cranial nerves that was probably due to ciprofloxacin in a patient with leukaemia.

A 15 year old girl receiving treatment for standard risk acute lymphoblastic leukaemia that had not affected the central nervous system was admitted with a headache and low fever a week after discontinuing a four day course of low dose intravenous cytarabine (75 mg/m²) and three days after a course of oral mercaptopurine (60 mg/m²). Physical examination showed nothing abnormal, apart from some tenderness over the left cheek and the left maxillary sinus. Erythrocyte sedimentation rate was 70 mm in the first hour. We then started treatment with ciprofloxacin 250 mg twice a day. Two days later, a few hours after the fourth dose of ciprofloxacin, she developed an acute left hemiparesis that affected homolateral facial muscles and was associated with partial loss of taste, dysarthria, and dysphonia. The Babinski sign was bilaterally positive.

The patient underwent an intense work up in order to clarify her clinical condition and consequently failed to take two doses of ciprofloxacin during the next 24 hours. On the same day all neurological abnormalities gradually diminished, and after a few hours she performed all neurological tests almost normally. The following evening, roughly one hour after restarting ciprofloxacin, she had a new episode of left hemiparesis, dysphagia, dysarthria, right facial paraesthesia, and deficit of the left 12th cranial nerve and of the 10th cranial nerve bilaterally. Reflexes were normal. Computed tomography of the brain and evoked potentials (visual and auditory) did not show any abnormality, and a lumbar puncture ruled out the possibility that her leukaemia had affected the central nervous system. Since the patient was in continuous complete remission and since ciprofloxacin was the only drug being given when the symptoms arose, treatment was discontinued and complete clinical normalisation was observed within the next 24 hours.

The relation between symptoms and ciprofloxacin administration strongly suggests that ciprofloxacin was the cause. The rapid onset and the migrating pattern of the neurological abnormalities could imply a vascular mechanism affecting the brain stem. The fact that ciprofloxacin may cause such severe symptoms should be kept in mind in the differential diagnosis of disease in any patient who is prone to accidents that affect the central nervous system.



Bullous eruptions associated with enalapril treatment four days after enalapril was discontinued

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