REVIEW ARTICLE

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OVERVIEW AND EXPERIENCE WITH THE USE OF FLUOROQUINOLONE IN CHILDREN IN THE TROPICS

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ABSTRACT

The use of fluoroquinolone is contraindicated in children because of the potential complication of arthropathy. In spite of this, the role of ciprofloxacin is becoming increasingly significant. We report two cases in which organisms that did not respond to the use of some other potent antibiotics clearly responded to the use of ciprofloxacin .A general overview of the fluoroquinolones is also highlighted. It is concluded that ciprofloxacin is a very useful agent in the management of serious infections in children and available data clearly supports its use where the efficacy outweighs any considerable risk. Fluoroquinolone is therefore recommended in children, where it offers a clear therapeutic advantage over other classes of antibiotics but not for routine empirical use.

Introduction

The demographic and subsequent economic pressures in developing nations have contributed to the increasing levels of antibiotic resistance among both commensals and pathogenic bacteria. This has made empirical options available to diminish by the day. In spite of this, the role of ciprofloxacin in paediatric infection is becoming increasingly significant (1). Anecdotal observations have shown that certain patients who will otherwise not respond to conventional antibiotics show rapid response with ciprofloxacin. In-vitro laboratory analysis has also consistently shown responsiveness of these organisms to ciprofloxacin. In a study of UTI in hospitalized patients, a lot of the organisms were found to be susceptible to

ciprofloxacin.(2). Yet it is largely contraindicated in children because of rare but well documented cases of joint damage (3-5). This article therefore aims to highlight two remarkable cases in practice where certain antibiotics failed but ciprofloxacin worked satisfactorily with no residual joint damage seen clinically both at discharge and follow-up.

Case reports

Case 1

A 9-year-old boy presented with history of progressive post-trauma swelling of the left hip and knee joint and fever of 3 days duration. There was inability to use those joints. Physical examination revealed obvious tender and warm swelling of the left hip and knee joints with decrease range of movement across them. The child was anaemic with PCV of 16%. Needle aspiration of the left hip swelling yielded pus. An assessment of septic arthritis was made and sultamicillin and gentamicin were commenced. He was also transfused raising the PCV to 23%. Fever and pain did not subside with this antibiotics rather abscesses further developed in the anterior chestwall, left forearm and right leg. Meanwhile aspirate from left knee and hip yielded profuse growth of staphylococcus aureus sensitive to pefloxacin, erythromycin, gentamicin, ofloxacin, cefuroxime and ciprofloxacin. Ciprofloxacin was commenced after the child had completed 7 days of sultamicillin and gentamicin with no clinical improvement. Incision and drainage of the abscesses were carried out at the time ciprofloxacin was commenced. Fever subsided fully by 6th day of ciprofloxacin therapy, there was no further spread of abscess and remarkable reduction of pain was noticed by the third day of therapy. He completed 3 weeks of ciprofloxacin and was discharged home. No residual joint damage occurred clinically as full functions returned to both the knee and hip joints.

Case 2

A 10 months old female child who presented with history of fever and multiple abscesses on the left gluteal region and lower part of the right thigh. There was limitation of movement at the knee joint raising the suspicion of a septic arthritis. However radigraphh study of the right knee revealed widening of the joint spaces with no bony involvement. Furthermore, at surgery, pyomyositis of the muscle of the right lower thigh region rather than septic arthritis was found. Incision and drainage of the gluteal abscess was also carried out. Meanwhile she had been commenced on sultamicillin and gentamicin since admission. The culture and sensitivity result of the pus obtained from the pyomyositis and the left gluteal region yielded profuse growth of coliform sensitive to gentamicin, ofloxacin, cefuroxime, ceftriaxone and ceftazidime. Despite the result, both antibiotics were continued since it was sensitive to gentamicin. Both of them had to be discontinued after 10 days when it was noticed that the fever did not completely subside and the right lower thigh continued to be tender. Ciprofloxacin was introduced and fever subsided after 48 hours. He received it for 11 days and became clinically stable. At follow-up the improvement was sustained

Discussion

In the two children highlighted, there was satisfactory clinical response to ciprofloxacin where sultamicillin and gentamicin failed. The organisms were sensitive to the third generation cephalosporin but the patients could not afford it, hence the consideration of a much cheaper alternative, which informed the trial of ciprofloxacin. Even though we were aware it was contraindicated in children, we were also aware that other workers have successfully tried it in children.(6) it therefore turned out that a less often used drug in children became useful. Ciprofloxacin is likely to have worked in those patients because of limited use of ciprofloxacin in the paediatric age group. It is still not recommended as a first line antibiotic, but it should be employed especially in gram-negative septicaemia when all the regular antibiotics have failed. In case 1, the fever clearance time following the use of ciprofloxacin was 6 days while in case 2 it was about 48 hours. It is worth noting that the first patient with septic arthritis developed it prior to commencement of ciprofloxacin. None of them developed arthropathy after the use of ciprofloxacin. No treatment or associated event was recorded in any of the patient both during admission or at follow up. This is consistent with findings of other workers who used bigger sample size (6). However our own sample revealed no single case of treatment associated event compared to 10.9% of children receiving oral ciprofloxacin/18.9% among IV recipients in a group of 1795 children who received treatment courses of IV or oral ciprofloxacin. Overall arthralgia occurred in 31 ciprofloxacin treatment courses (1.5%) and majority of events were of mild to moderate severity and resolved without intervention (6). More than 60% of the arthralgia was in children with cystic fibrosis. We cannot as of yet assemble such a large cohort of patients on either ciprotab or ciprofloxacin since there is still a high skepticism on its use in children in our environment. We dared to use it in our children for lack of a plausible alternative. A review of the journals indicates its use in children and the rate of adverse event pattern was similar to that observed in adults.

The recommendation that fluoroquinolone should not be used in children resulted from findings in juvenile animal of cartilage damage after administration of high doses. Histopathological examination of the joint surface of affected animals revealed the loss of cartilaginous matrix and chondrocytes and cavitation within the intermediate zone of cartilage accompanied by cartilage fibrillation or chondrocyte clustering or loss of the surface layer which covers the cavitations (loss of outer wall of the cavity (3). The possibility of mutagenesis and joint damage restricted the use of fluoroquinolones in children to serious life saving indication only The joint damage usually resolves gradually after drug withdrawal and is more frequent with pefloxacin. In practice quinolone is an option for children only when the expected benefit outweighs the risk of joint damage. In the rare cases in which flouroquinolone is justified, ciprofloxacin is the drug of first choice. Pefloxacin should be avoided.

Fluoroquinolones are generally very safe antibiotics, which do not cause severe or life threatening adverse reactions. The most f frequent side effects are gastrointestinal reactions (nausea, dyspepsia and vomiting) and CNS reaction such as dizziness, insomnia and headache. Many of the more severe CNS reactions seem to be due to metabolic interaction with theophylline especially when enoxacin is used. Of the potential serious side effects, photosensitivity has been reported in varying frequencies with the different fluoroquinolones. Caution is necessary when this group of drug especially pefloxacin is prescribed

to patients who will have intense exposure to ultra-violet light during treatment (4).

The quinolones are active against both gram positive and gram-negative bacteria. It is particularly active against gram-negative bacteria including salmonella, shigella, campylobacter, neisseria, bacillus anthracis and pseudomonas. It has only moderate activity against gram-positive bacteria such as streptococcus pneumonia and enterococcus faecalis. It is also active against chlamydia and some mycobacterium.

It should be used with caution in patients with a history of epilepsy or condition that predispose to seizures, in G6PD deficiency, myasthenia gravis (because of risk of exacerbation) in pregnancy, during breastfeeding. It may induce convulsion in patients with or without history of convulsion. Taking NSAIDs at the same time may also induce them. Tendon damage including rupture has been reported rarely in patients receiving quinolones. Tendon rupture may occur within 48 hours of starting treatment; hence its use is contraindicated in patients with history of tendon disorders related to quinolone use. The risk of tendon rupture is increased by the concomitant use of steroids. If tendonitis is suspected, the quinolone should be discontinued immediately. It is given by mouth 10-30 mg/kg in two divided doses or by IV infusion 8-16mg/kg daily in 2 divided doses.

In conclusion, ciprofloxacin is a very useful agent in the management of serious infection in children. Data clearly support its use where the efficacy outweighs any considerable risk. It should also be chosen for indications in which they offer a clear therapeutic advantage over other classes of antibiotics rather than as agent whose broad spectrum prompts routine empirical use.

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