Case Report

Cross sensitivity between ciprofloxacin and levofloxacin for an immediate hypersensitivity reaction

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ABSTRACT

Seven years old male child (24 kg weight) diagnosed as a case of sub acute appendicitis treated with ciprofloxacin, immediately developed multiple erythmatous papules. Reaction subsided after withholding ciprofloxacin and treatment with dexamethasone and chlorpheneramine maleate. It was developed again when treated with levofloxacin and subsided after withdrawal. IgE binding at 7th position of core structure of fluoroquinolones likely to be the mechanism. As all the fluoroquinolones have similar core structure, hypersensitivity to one may have cross sensitivity to other fluoroquinolones. It is advisable to avoid other fluoroquinolones and switch over to other group of antibiotics when hypersensitivity to one occurs.

Key words: Cross sensitivity, ciprofloxacin, fluoroquinolones, levofloxacin

INTRODUCTION

Cross sensitivity is defined as sensitivity to one substance that renders an individual sensitive to other substances of similar chemical structure.[1] Cross sensitivity has been reported commonly among various β lactam antibiotics and sulfonamides.[2,3] For the diagnosis of cross sensitivity, various methods like prick test, patch test and histamine release test are available. Oral challenge test is considered as the most reliable.[4] Due to broad antimicrobial spectrum, favorable pharmacokinetic properties and few adverse drug reactions, fluoroquinolones are widely used. Frequently reported adverse reactions with fluroquinolones are nausea, abdominal pain, diarrhea, dizziness, restlessness, headache, depression and somnolence or insomnia.[5] Hypersensitive reactions are rare (0.4% to 2%) due to fluoroquinolones.[4,6] Immediate type of reactions are more common than delayed type of reactions. Frequently reported immediate hypersensitive reactions are urticaria, anaphylactic shock, rashes and erythema.[4] Ciprofloxacin and norfloxacin are the most common drugs causing hypersensitivity reactions, while levofloxacin is the least common with incidence of 1 per million population.[4,7] Fixed drug eruption by ciprofloxacin with cross sensitivity to norfloxacin has been reported.[8] However, we could not find a case of immediate hypersensitivity reaction with levofloxacin or case report of cross sensitivity between ciprofloxacin and levofloxacin. Here with, we report a case of cross sensitivity between ciprofloxacin and levofloxacin for immediate type of hypersensitive reaction.

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CASE REPORT

Seven years old male child (24 kg weight) admitted in paediatric ward, Sir Takhtsinhji General Hospital, Government Medical College, Bhavnagar, Gujarat, India with complaints of fever, headache, vomiting and abdominal pain for 7 days. Fever was of high grade, intermittent and associated with chills, which was followed by colicky abdominal pain. He had a past history of similar attacks two times, at that time pain was relieved after oral treatment. There was no past history of drug allergy. Provisional diagnosis of subacute appendicitis was made.

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On examination, temperature was raised; tenderness was present in the right iliac fossa. Various investigations like hemoglobin, total and differential WBC count, platelet count, ESR, urine and stool examination were normal. Peripheral smear for malaria parasites, Mantoux test and Widal's test were negative. USG abdomen was suggestive of appendicitis. As per surgical opinion conservative treatment was started with ciprofloxacin infusion (20mg/kg/day in two divided doses), inj. metronidazole (30mg/kg/day, in three divided doses), inj. ondansetron (0.1mg/kg, as and when required) and tab. paracetamol (10mg/kg, as and when required). Five minutes after starting infusion of ciprofloxacin, patient developed itching followed by rashes at the site of infusion. On dermatological examination, multiple erythmatous papules and plaques were present on the arm and chest. Reaction started from the site of injection and spread upward involving whole arm up to chest. Infusion was stopped immediately and injection dexamethasone (0.5mg/kg) was given along with injection chlorphenaramine maleate (0.1mg/kg). After two hours rashes subsided and metronidazole infusion started. Patient was kept under observation, no adverse reaction seen with metronidazole. Levofloxacin (10mg/kg/day) was added in treatment in place of ciprofloxacin from next day under close observation. Immediately after levofloxacin infusion, itching and rashes in arm appeared so, infusion was withdrawn. This time reaction occurred within few seconds. No rescue treatment required and reaction abated after stopping the infusion. Ceftriaxone (100mg/kg/day) injection added in the place of fluoroquinolones along with metronidazole.

Reaction was probable according to naranjo's scale.[9] It was moderate in severity according to Modified Hartwig and Siegel's scale[10] and non preventable as per Modified Schumock and Thornton scale.[11]

DISCUSSION

All fluoroquinolones have similar core structure (4-oxo-1, 4-dihydroquinoline ring) with fluorine atom attached at position 6 except, first generation quinolone, nalidixic acid. Norfloxacin, a second generation fluroquinolone, is the result of replacement at C-7 methyl side chain with piperazine group, while replacement of N-1 ethyl group of norfloxacin with cyclopropyl group generates ciprofloxacin. Levofloxacin, third generation flouroquinolone, has modification of piperazine group with methyl group at C-7. Moxifloxacin is fourth generation flouroquinolone having methoxy group at C-8 position. Although changes in position 1, 7 and 8 generated different fluoroquinolones, core structure remains same.[12,13]

54.5% immediate type of reactions to fluoroquinolones are IgE mediated and occurs due to binding of IgE to 7th position of core structure of fluoroquinolones.[4] Patient had a past history of two similar attacks, at that time he might be treated with fluoroquinolones, which may resulted in production of IgE antibodies. As a result, treatment with fluoroquinolones this time might have caused the reaction. Ciprofloxacin and levofloxacin have similar core structure; this may be the reason for the cross sensitivity in this case. It is advisable to avoid other fluoroquinolones when hypersensitivity reaction detected to one and should be shifted to other class of antimicrobials. Overall risk of adverse effects especially hypersensitivity reactions with fluoroquinolones is low but due to widespread use, such rare hypersensitivity reactions should be kept in mind. Improvement in diagnostic tests like detection of IgE antibodies, cellular tests and skin test may help in preventing such adverse drug reactions.

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