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Case Reports

REPORT OF THREE CASES OF CIPROFLOXACIN-INDUCED HEMOLYTIC ANEMIA IN G6PD DEFICIENT PATIENTS

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INTRODUCTION

Glucose 6-phosphate dehydrogenase (G6PD) is an enzyme for the integrity of the hexose monophosphate shunt. Drug induced hemolytic anemia in the presence of G6PD deficiency was recognized by Carson and coworkers in 1956. The antimalarial drugs of the primaquine groups were found to cause hemolytic anemia.[7] One year later Browne found that this complication occurred more frequently in certain ethnic groups such as coloured races, and 10 percent of male American blacks.[3] Deficiency in G6PD activity is also more prevalent among Indians, Chinese and Mediterranean inhabitants such as Greeks, Italians, and Maltese.[6] The effect of G6PD deficiency is to shorten the survival of red blood cells when exposed to certain types of oxidative stress. Such stresses may be due to ingestion of broad beans in favism, infection, acidosis (as in diabetes) and the neonatal state. The most common cause of hemolytic anemia in G6PD deficient patients has been the administration of certain drugs.[2]

We report three cases of hemolysis due to the ingestion of ciprofloxacin.

Case report

Three male patients were given ciprofloxacin, 500 mg two times a day, for treatment of ampicillin-resistant pneumonia. Table I shows patients' age, gender, time of occurrence of hemolysis and previous history of G6PD deficiency.

In all three cases, after the appearance of jaundice and dark colored urine, patients were hospitalized. Fluorescent spot test was used to measure the plasma level of G6PD quantitatively. Table II shows laboratory values and tests performed on the patients.

Table I. Patient parameters and occurrence of hemolysis. Ciprofloxacin dosage and previous history of G6PD deficiency.

Patient number	Age	Gender	Time of hemolysis after receiving drug (days)	Dosage	Previous history of G6PD deficiency
1	35	male	3	500 mg/bid	+
2	28	male	4	500 mg/bid	...
3	37	male	2	500 mg/bid	+

Table II. Patients' laboratory results and G6PD level.

Patient number	Hb g/dL	WBC	Bilirubin (total) mg%	Bilirubin (direct) mg%	AST U/L	ALT U/L	Alk. Ph. IU/L	G6PD level
1	10	11,000	8	1.5	19	45	136	Severely deficient
2	8	10,500	12	1.8	15	10	75	Partially deficient
3	10.5	10,700	6	1.3	23	34	120	Severely deficient

Following hospitalization, ciprofloxacin was discontinued and patients received procaine PCN, 800,000 IU/q12h, IM.

Patient number 2 received fresh blood in addition to PCN because of a low hemoglobin (8 g/dL) and hemodynamic instability. After 5-7 days jaundice decreased and the patients were discharged.

DISCUSSION

Ciprofloxacin is a fluorinated quinolone, and is an analogue of nalidixic acid. Ciprofloxacin is active against a variety of Gram positive and Gram negative bacteria. Quinolones block bacterial DNA synthesis by inhibiting DNA gyrase, hence preventing the relaxation of supercoiled DNA that is required for normal transcription and duplication.[1]

Drug-induced hemolytic anemia has been recognized for some time. Antimalarial agents including quinine, pyrimethamine and quinolones were among the first drugs shown to cause such a problem. Analgesic drugs such as acetanilide, aspirin, amidopyrine and phenacetin are included in this category.[3] Although nalidixic acid has been shown to cause acute hemolytic anemia,[2] its congener ciprofloxacin has not been shown to cause such a problem. Therefore our patients appear to be the first reported cases of ciprofloxacin-induced hemolytic anemia.

Owing to the high frequency of G6PD deficiency in the northern parts of Iran, a quantitative test for G6PD deficiency is recommended prior to the use of quinolones in suspected individuals.

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