

Severe anaphylactoid reaction to nalidixic acid

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We present the case of a 58-year-old non-atopic woman who suffered an adverse reaction to orally administered nalidixic acid, which had been prescribed for the treatment of a urinary tract infection. The single-blind oral provocation test was positive; the patient presented the clinical features of an anaphylactoid reaction 3 min after administration of nalidixic acid. Both the skin test and the histamine release test were negative. These results suggest that we are dealing with an anaphylactoid reaction not described before with this drug.

Key words: anaphylactoid reaction; nalidixic acid; oral challenge.

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Nalidixic acid (1-ethyl-1,4-dihydro-7-methyl-4-oxo-1,8-naphthyridine-3-carboxylic acid) (Fig. 1) is one of the chemotherapeutic agents widely used in the treatment of urinary tract infections (9, 11). It has a molecular weight of 232.2 D. and a biological half-life between 1.5 and 2 h (5). Its two most important metabolites are 7-hydroxynalidixic acid and 7-carboxinalidixic acid; the former possesses antibacterial properties similar to those of nalidixic acid (3, 8), whereas the latter is biologically inactive. The drug's therapeutic action depends upon the inhibition of bacterial DNA replication.

The documented adverse reactions to nalidixic acid have been: hyperglycemia and central nervous system disturbance (4), photosensitivity (2), hemolytic anemia (12), thrombocytopenic purpura (6), hemorrhagic gastroenteritis (13), arthralgias, exanthemata, fever (1), disseminated lupus erythematosus (10), pruritus, eosinophilia, reversible leukopenia, etc. (16).

The aim of the present study is to report the occurrence of an anaphylactoid reaction following the oral administration of nalidixic acid.

Case report

A 58-year-old non-atopic woman with a long history of recurrent urinary tract infections was

seen by our Allergy Service for evaluation of an adverse reaction after administration of nalidixic acid. Two weeks before, within 10 min of the first oral dose of a 500 mg tablet, the patient developed "tingling of the lips", facial angioedema, generalized urticaria and dyspnea. Her symptoms were relieved with steroids and antihistamines administered in the emergency room. She did not know whether or not she had previously received the drug.

Laboratory findings

The patient's blood chemistry, as well as her whole blood count and blood picture were normal; there was no evidence of eosinophilia. Total IgE was 10 IU/ml.

The investigations described were performed 3 months after the adverse reaction.

Routine skin tests (prick test) with a battery of commercially available allergens were negative. Likewise, prick and intradermal tests with nalidixic acid (concentrations of 100 and 500 mg/ml) were negative.

A histamine release test, by the automated fluorimetric method (7), was negative with nalidixic acid (1:5 w/v in phosphate buffered saline).

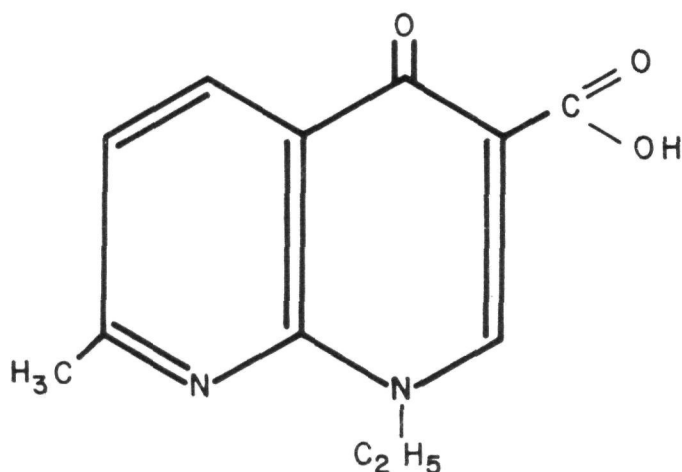


Fig. 1. Nalidixic acid.

Subsequently, a single-blind oral provocation test was performed. This took place in a laboratory containing the necessary resuscitation equipment and medication for treating any possible adverse reaction. Three minutes after ingestion of an initial dose of 62 mg nalidixic acid (Wintomylon - Sterling Winthrop, S.A. Spain), the patient developed buccal paresthesia, dysphagia, dyspnea, lingual edema, generalized urticaria and a fall in arterial blood pressure; the symptoms subsided 30 min after parenteral administration of adrenaline, antihistamines and corticosteroids.

To discard the possibility that the reaction could have been produced by one of the other components in the Wintomylon tablet (brown iron oxide, cellulose and lauril sodium sulphate), oral provocations were performed as described above, each with negative results.

Comments

Even though the patient did not know whether she had been previously treated with nalidixic acid, we cannot ignore the possibility as she had been treated for recurrent urinary tract infections with numerous chemotherapeutic agents. This observation, together with the short latency period and the small dose required to reproduce the above mentioned symptomatology on oral provocation, suggest an anaphylactic reaction. However, the low level of total IgE together with the negative

results of the skin and histamine release tests were at variance with our suspicion.

The complexity of the mechanisms mediating adverse reactions to drugs and the unreliability of the tests presently employed in the diagnosis of such reactions are well recognized. A provocation test utilizing the suspected agent is the only test which can provide information regarding the prophylactic measures to be adopted in order to avoid future reactions. It should be taken into account that such a test entails a certain amount of risk (2).

According to the results of the laboratory investigations, it seems unlikely that we are dealing with an anaphylactic reaction mediated by IgE. Thus the possibility of an anaphylactoid reaction should be considered. In the literature reviewed, we were only able to find a verbal reference of a reaction to nalidixic acid (3), described as anaphylactic; we do not know whether specific tests were carried out to confirm this diagnosis.

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