Accidental Overdose of Intravenous Ofloxacin with Benign Outcome

RICHARD B. KOHLER,1* NANCY ARKINS,1 AND KENNETH J. TACK2

Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana 46202, 1 and R. W. Johnson Pharmaceutical Research Institute, Raritan, New Jersey 088602

Received 4 January 1991/Accepted 29 March 1991

A patient accidentally received approximately 3 g of ofloxacin intravenously. She experienced only moderately severe central nervous system symptoms, which resolved within 9 h. The peak serum ofloxacin level was 39.3 μg/ml, approximately seven times the usual peak level. Ofloxacin may possess a considerable safety margin in humans.

Fluoroquinolones are broad-spectrum orally absorbed and intravenous antimicrobial agents used for a variety of localized and systemic infections. Although generally well tolerated, members of this class can be associated with adverse reactions, including a wide range of central nervous system side effects (4, 6–8, 12).

Little is known about the toxicity of these drugs in humans when given in amounts larger than recommended, i.e., with overdose, possibly because gastrointestinal tolerance may be limiting and parenteral formulations are not yet widely available. We cared for a woman who received a dose of ofloxacin, approximately seven times that which was intended.

A 26-year-old woman with asthma was admitted to the hospital for treatment of acute left-upper-lobe pneumonia as part of an evaluation of intravenous ofloxacin. As specified by the study protocol, ofloxacin treatment (400 mg intravenously every 12 h) was begun. She tolerated this without incident and improved clinically. During the ofloxacin infusion on the morning of the fourth day of therapy, she developed drowsiness, nausea, hot and cold flashes, subjective facial infusion and swelling, slurring of speech, and mild to moderate disorientation; she stated that she felt as though she were drunk. Because of these complaints, the infusion was discontinued after approximately 45 min, at which time approximately three-fourths of the infusion had been administered. Her vital signs remained unchanged from their baseline. Other medications which the patient was receiving were inhaled albuterol and beclomethasone and oral terbutaline and theophylline; her theophylline level at that time was 8 μg/ml.

All complaints except dizziness and nausea resolved within 1 h after the infusion was discontinued. The dizziness, most bothersome with standing, resolved in approximately 9 h. She felt normal the following morning.

After the infusion was discontinued, it was discovered that 4,000 mg of ofloxacin, rather than 400 mg, had been added to the infusion bag. Thus, the patient received approximately 3.0 g of ofloxacin before the infusion was discontinued. A serum sample obtained 15 min after completion of the infusion revealed an ofloxacin level of 39.3 μg/ml; in 7 h, the level had fallen to 16.2 μg/ml, and by 24 h, it had fallen to 2.7 μg/ml.

Laboratory testing (complete blood count with differential, electrolytes, hepatic enzymes, uric acid, and creatinine) revealed no clinically significant abnormalities immediately following and 1, 3, and 14 days after the infusion was terminated. A urinalysis on the evening of the infusion contained numerous erythrocytes, but these were attributed to menstrual flow and were absent 14 days later.

This patient received a dosage of ofloxacin approximately 7.5 times the recommended dose. Her levels in serum were over seven times the average maximum level of 5.5 μg/ml seen with normal subjects at steady state. Her adverse reactions, including nausea, may all have been due to central nervous system effects and are consistent with those attributed to the fluoroquinolones.

Neurological disturbances occur in 1 to 4.7% of patients receiving modern fluoroquinolones (4, 6, 12). Central nervous system side effects include restlessness, insomnia, hallucinations, agitated and confused states, depression, nightmares, headache, dizziness, vertigo, visual and olfactory disturbances, ataxia, tremor, and paresthesias (4, 6–8, 12, 13). Rarely, seizures occur (2, 3, 10). In mice and rats, quinolones inhibit attachment of γ-aminobutyric acid to its receptors on brain neurons (1, 5, 9, 11). Because γ-aminobutyric acid functions as a neurotransmitter, at least some quinolone-related central nervous system side effects, particularly those related to neurostimulation, may be related to this mechanism.

Although our patient did experience central nervous system side effects, the absence of seizures or development of other serious side effects suggests that a considerable margin of safety exists in humans when ofloxacin is used at a dosage of 400 mg twice a day. The margin of safety for dosing ofloxacin and other quinolones in a young, otherwise healthy woman may be considerably greater than that in elderly patients, patients with reduced renal function, and patients with preexisting central nervous system disorders. Firm conclusions regarding the margin of safety of ofloxacin, even in healthy young individuals, cannot be drawn from observations with one patient. However, it is not likely that high doses similar to that which our patient received will be administered intentionally to humans, and knowledge regarding the tolerance of humans to high doses of quinolones will require building on reports such as this one.

REFERENCES

* Corresponding author.