Effect of Azlocillin on Uric Acid Levels in Serum

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Uric acid levels in serum were observed to fall precipitously in a group of 20 hospitalized asthmatic patients receiving azlocillin, bronchodilators, and steroids. None of the 20 hospitalized controls receiving the antiasthma therapy without azlocillin showed any decline in their uric acid levels. The levels for the azlocillin-treated group fell from a mean of 6.4 mg/dl to mean of 2.3 mg/dl, whereas those for the control group initially were 7.0 mg/dl and fell only to a mean of 6.5 mg/dl.

From 1980 to 1982, 40 patients admitted to The Bronx Lebanon Hospital Center with bronchial asthma were randomly assigned to receive either 20 g of azlocillin per 24 h (5 g every 6 h) intravenously or a placebo (saline) as part of a study investigating the role of antibiotics in acute bronchial asthma. Both groups received the usual anti-asthma therapy, which included intravenous theophylline and steroids, oral terbutaline, and inhaled isethoarine. All patients were afebrile throughout their stay, with no roentgenographic evidence of acute pneumonia. The groups were similar with respect to age, sex, severity of asthma, cough, fever, sputum production, sputum color, sputum Gram stain, sputum bacterial colony counts, and sputum culture. Renal and liver function tests were normal for all patients.

The azlocillin group consisted of six males and nine females between the ages of 18 and 80 years, with a mean age of 37 years. Their weights ranged from 42.2 to 86.6 kg, with a mean weight of 58.7 kg. The placebo group consisted of 9 males and 10 females ranging in age from 18 to 62 years, with a mean age of 40 years, and their weights ranged from 53 to 99 kg, with a mean weight of 71.8 kg.

Both the patients and the treating physicians were unaware of which treatment was being used until after the trial was over. When the fall in uric acid levels in serum was noted by the project director, who was not involved in the care of the patients, this information was also withheld from the treating physician.

Measured by the phosphotungstate method, the average level of uric acid in serum obtained before beginning azlocillin therapy was 6.4 mg/dl, with a standard deviation of 1.9. In the placebo group it was 7.0 mg/dl, with a standard deviation of 1.8. All uric acid levels in serum from all days of treatment fell during azlocillin therapy to a mean of 2.3 mg/dl, with a standard deviation of 1.3, whereas the mean of all levels in the control group was 6.5 mg/dl, with a standard deviation of 2.8. No clinical signs or symptoms that could be attributed to this fall of uric acid levels in serum were observed.

The observed fall in uric acid levels was serendipitous, since the levels were measured only sporadically throughout the course of therapy and not all subjects were tested at similar times. Consequently, the results obtained do not easily lend themselves to any meaningful statistical analysis.

Azlocillin is a new antibiotic of the acylureido-penicillin group with a wide spectrum of antibiotic activity encompassing that of the cephalosporins and penicillins. The pattern of its absorption, distribution, and excretion is similar to those of carbenicillin and ampicillin, with a serum half-life of 25 to 50 min and with 50 to 75% of the drug found unchanged in the urine within 6 h. Extensive testing (including uric acid levels in serum) has shown that azlocillin in the dose which we used causes no renal, hepatic, cardiovascular, or biochemical abnormalities in subject populations (3), except for the fall of uric acid levels in serum, which was not reported previously. A computer search of the literature did not turn up further data on the effects of penicillin on uric acid levels in serum.

It is known that penicillin and its congeners are secreted by the renal tubules (4). Hypouricemic drugs increase the secretion of uric acid by either inhibiting its tubular reabsorption or enhancing its secretion (1). Pyrazinamide, probenecid, phenylbutazone, and salicylate inhibit the secretion of uric acid in
low doses and inhibit its reabsorption in high doses (5). High-dose penicillin therapy has been observed to reduce uric acid levels in serum (H. Neu, personal communication). The sudden fall of these levels can best be explained by a renal effect of azlocillin perhaps similar to that of probenecid. This fall has been recently noted by another investigator, who also observed that uric acid levels return to normal within 24 h after discontinuation of azlocillin therapy (2). Metabolic studies are currently under way in an attempt to further elucidate the renal mechanism responsible for the fall of uric acid levels in serum seen in patients on azlocillin.

**LITERATURE CITED**


