Effect of Oral Activated Charcoal on Tobramycin Clearance

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To evaluate the effect of activated charcoal on aminoglycoside pharmacokinetics, six healthy volunteers received tobramycin intravenously with and without multiple oral doses of activated charcoal. Activated charcoal did not have a statistically significant effect on any pharmacokinetic parameter. We conclude that activated charcoal does not enhance tobramycin clearance in subjects with normal renal function when concentrations in serum are within the therapeutic range.

Tobramycin is an aminoglycoside antibiotic that can cause concentration-dependent ototoxicity and nephrotoxicity (17). Aminoglycosides are eliminated by glomerular filtration, and aminoglycoside clearance correlates well with creatinine clearance. In patients with normal renal function, the elimination half-lives of the drugs are 2 h or less. In these patients, toxic concentrations fall rapidly to nontoxic levels. In renal impairment, aminoglycoside clearance is reduced (half-life up to 30 to 40 times normal in uremia) (17). Therefore, toxic concentrations in these patients persist, and the potential for ototoxicity or nephrotoxicity may be increased.

Because of its adsorbent properties, activated charcoal is commonly administered orally to reduce the absorption of orally ingested drugs and poisons. Recent literature indicates that activated charcoal administered orally or by nasogastric tube can enhance the clearance of intravenously administered drugs, such as phenobarbital, digoxin, methotrexate, and other agents (1, 2, 4, 7, 9, 12, 13). However, activated charcoal is not without risk. Its use has been associated with charcoal aspiration, resulting in the adult respiratory distress syndrome and necessitating a prolonged hospitalization in the intensive care unit in one patient (personal observation) and death in another (H. H. Harsch, Letter, N. Engl. J. Med. 314:318, 1986). We therefore sought to evaluate the effect of orally administered activated charcoal on tobramycin clearance.

Six healthy nonsmoking volunteers (one female and five males of ages 25 to 39) were enrolled in the study after informed consent was obtained. The study protocol was approved by the Human Subjects Review Board. All subjects had normal physical examinations, urinalysis, and hematological and chemical studies. All were within 20% of their ideal body weights (mean weight, 78 kg). The subjects abstained from alcohol-containing beverages and medications for 72 h before and 24 h after tobramycin administration. All subjects underwent repeat laboratory tests within 72 h after the study.

In a randomized crossover sequence, subjects received 2.5 mg of tobramycin (donated by Eli Lilly & Co.) per kg of body weight, dissolved in 100 ml of 5% glucose solution, by intravenous infusion over a 30-min period with orally administered activated charcoal or an equal volume of water.

When administered, 50 g of activated charcoal was given just before and 15 g was given 2, 4, and 6 h after the start of the tobramycin infusion. Subjects also received 300 ml of magnesium citrate (containing 1.745 g of magnesium citrate per oz [29.573 ml]) as a cathartic along with the 1-h dose of activated charcoal.

Blood was taken from an indwelling intravenous cannula immediately before and at 1, 1.5, 2, 3, 4, 6, and 8 h after the start of the tobramycin infusion. The samples were allowed to clot and were centrifuged for 15 min at 800 × g, and the serum was collected. Urine was collected just before and from 0 to 2, 2 to 4, 4 to 8, 8 to 12, and 12 to 24 h after each tobramycin dose. The urine volume was recorded, and a sample was saved for assay. All blood and urine samples were frozen within 1 h of collection and were stored at −20°C until assayed.

Samples were allowed to thaw at room temperature on the day of the assay. Tobramycin concentrations in the plasma and urine samples were determined by homogeneous enzyme immunoassay (EMIT). The intraday coefficients of variation were 4.7% (4.0 µg/ml) and 6.4% (8.7 µg/ml). All assays for each subject were run on the same day.

The data were analyzed by model-independent pharmacokinetic methods (5).

Statistical analysis of the data was performed by using the paired Student t test and the Wilcoxon signed-rank test. Probability values of <0.05 were considered significant (18).

Tobramycin pharmacokinetic parameters with and without activated charcoal administration are shown in Table 1. Multiple doses of orally administered activated charcoal did not produce a statistically significant effect on the mean value of any parameter. The mean tobramycin clearances were 7.9 and 8.5 liter/h with and without activated charcoal administration, respectively. Clearance was unchanged or lower and elimination half-life was the same or greater in five of the six subjects with charcoal, although this was not statistically significant. Totals of 84.9 and 93.5% of the administered dose were recovered in urine samples with and without activated charcoal coadministration, respectively. Tobramycin renal clearance was lower in five of the six subjects with charcoal administration.

Tobramycin clearance was not affected by the administration of activated charcoal. Volume of distribution, urinary recovery, and renal clearance of unchanged drug were lower in four of our subjects when activated charcoal was given.
but these relationships did not achieve statistical significance. The small changes noted may have been due to a decrease in glomerular filtration caused by volume contraction from the cathartics.

Oral activated charcoal has been shown to enhance the elimination of other drugs from the body, including agents that do not undergo enterohepatic recycling, such as theophylline (1, 2, 4, 7, 9, 12, 13). The increase in drug clearance results from the adsorption of the drug onto the charcoal after diffusion into the gastrointestinal lumen from the circulation (10, 14). This process would be even more effective in patients with toxic drug concentrations, since the diffusion gradient into the lumen would be greater. This phenomenon has been demonstrated by a greater increase in theophylline clearance in patients with liver disease (15) and a greater increase in digoxin clearance in a patient with renal impairment (13) compared with subjects with normal organ function.

Levy (10) postulated that drugs removed by peritoneal dialysis would be good candidates for clearance with activated charcoal. Tobramycin removal by peritoneal dialysis has ranged in various studies from 23 to 69% and 16.5% to 26% after intermittent and continuous ambulatory peritoneal dialysis, respectively (3, 6, 8, 11, 14, 16), but was not removed by activated charcoal in our study. However, the results obtained in our normal subjects cannot be compared with those found in patients with renal failure.

We were unable to demonstrate an effect on tobramycin pharmacokinetics with activated charcoal administration in subjects with normal renal function and tobramycin concentrations within the therapeutic range. However, these results cannot be extrapolated to patients with toxic concentrations in serum or renal dysfunction. The use of activated charcoal in these populations warrants further study.

LITERATURE CITED