LETTERS

Lack of Tobramycin Distribution into Saliva

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Several drugs distribute into saliva, and the concentration of some of these drugs in saliva correlates directly with their concentration in the serum (1–4). The assay of saliva levels may therefore be useful for clinical drug monitoring thus eliminating the need for venipuncture. We wanted to determine whether tobramycin, therapy could be monitored with the use of saliva samples.

Materials and Methods

Tobramycin was assayed by high pressure liquid chromatography (HPLC). The procedure was similar to that reported previously by Anhalt and Brown (5) in which post-column derivatization is used to produce fluorescent products. We used a peristaltic pump (Cole-Parmer Co., Chicago, IL) to deliver 0.5 ml/min of *o*-phthalaldehyde reagent and an Ultrasphere-ODS column (4.6 × 150 mm) from Altex Scientific, Berkeley, CA with a mobile phase flow rate of 1.5 ml/min Amikacin was used as internal standard, and peak heights were determined by an integrator (Hewlett-Packard Co., Avondale, PA).

Six paired serum and saliva samples (2–3 ml each) were obtained from three patients who were already receiving tobramycin therapy (80–120 mg every 8–12 hours) and were at steady state. Serum and saliva samples were collected at one hour after (peak level) and one-half hour prior to (trough level) tobramycin administration and the samples were frozen until assay. The samples were prepared for HPLC by the addition of 50 µl (5 µg) of the internal standard amikacin, to 950 µl of each sample. This mixture was passed through a 1.5 × 0.6 cm CM-Sephadex column which then was rinsed with 1.5 ml of 0.2 M sodium sulfate solution. This was followed by 200 µl of a 0.2 M solution of sodium sulfate in 10 mM NaOH and then by another 800 µl, in which the two aminoglycosides were eluted. A standard curve (detectable range 0.5–10 µg/ml) was prepared by averaging the peak height ratios of duplicate samples (two injections per sample) of drug-free serum and saliva spiked with tobramycin.

Results and Discussion

Weakly basic drugs which are not highly protein bound, such as tobramycin, should have a saliva/serum concentration ratio greater than one because of the difference in pH between saliva and serum, if they enter the saliva by a passive process (3, 6, 7). Even though the concentration of tobramycin in the serum samples were 3.9, 3.2, 2.5, 1.1, 0.7 and < 0.5 µg/ml, tobramycin was not detected in any of the saliva samples. We conclude, therefore, that for practical clinical application tobramycin does not distribute into saliva, since saliva taken at both peak and trough sampling times from patients at steady state failed to contain detectable tobramycin levels even though the drug was detected in the serum.

While this work was in progress another group reported (8) that neither gentamicin nor tobramycin appeared in saliva to any significant extent. Our results support that conclusion.

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