Comparison of the Distribution of Tobramycin and Gentamicin in Body Fluids of Dogs

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Tobramycin serum, thoracic lymph, renal lymph, and urine concentrations were measured in mongrel dogs after intravenously administered 5, 10, and 20 mg/kg doses. These were compared with intravenous gentamicin delivered at 5 and 20 mg/kg. Both drugs achieved similar concentrations in serum and thoracic lymph. At 20 mg/kg, tobramycin showed consistently higher renal lymph and urine concentrations than gentamicin. At 5 mg of tobramycin per kg, renal lymph and urine concentrations were higher than with gentamicin only within the 1st h after administration. Thereafter the difference was no longer significant. These data suggest that on the basis of distribution in the body fluids of dogs, tobramycin is a reasonable alternative to gentamicin.

The clinical value of the aminoglycoside antibiotic, gentamicin, is undisputed. Its distribution in serum, urine, thoracic duct lymph, renal capsular lymph, and interstitial fluid has been well established, primarily through the work of Chisholm and Gingell and their co-workers (3, 4, 9, 10). A new aminoglycoside, tobramycin, the sixth of eight antimicrobial factors produced by Streptomyces tenebrarius, is now available for investigation. This antibiotic is basically similar to gentamicin in structure, protein binding, and antibacterial spectrum (11, 12, 15, 16, 18, 20). Studies suggest that it may be more effective against certain strains of pseudomonas and that it may manifest less ototoxicity than gentamicin (1, 2, 17). These characteristics would make tobramycin a welcome addition to the antibiotic armamentarium, especially if its distributional characteristics are the same as gentamicin. The present study was performed in order to measure and compare the rate of distribution and excretion of tobramycin and gentamicin in the body fluids of normal dogs.

METHODS AND MATERIALS

Five groups of mongrel dogs, weighing from 17 to 22 kg, were anesthetized with pentobarbital and underwent cannulation of the thoracic duct and a renal capsular lymphatic vessel with PE 50 and PE 10 polyethylene catheters, respectively. A urethral catheter was placed for urine collections. Intravenous saline was administered throughout the experiments at a rate of 30 ml/h into a femoral vein. Three groups of nine dogs each received 5, 10, or 20 mg of tobramycin per kg as an intravenous bolus. Two groups of five dogs each were similarly treated with 5 and 20 mg of gentamicin per kg. Samples of serum, thoracic duct lymph, renal capsular lymph, and urine were collected at 15, 30, 45, 60, 180, 240, and 300 min. The specimens were analyzed for tobramycin or gentamicin by an agar well diffusion method by using Bacillus globigii as the test organism (14, 19, 21). Prior to analysis all urine specimens were buffered to pH 8 with phosphate buffers. Statistical studies consisted of computer-calculated means, standard errors, and an analysis of variance comparing the 5 and 20 mg/kg tobramycin and gentamicin groups, respectively.

RESULTS

The distribution of tobramycin at 20, 10, and 5 mg/kg, as well as gentamicin at 20 and 5 mg/kg, in serum, thoracic lymph, renal lymph, and urine, is depicted in Fig. 1 to 4, respectively.

The peak serum tobramycin concentrations (Fig. 1) were 55, 30, and 14 μg/ml at 15 min for the 20, 10, and 5 mg/kg doses, respectively. The 20 mg/kg gentamicin dose peaked at 60 μg/ml at 30 min, whereas the 5 mg/kg dose achieved a peak concentration of 11 μg/ml at 15 min. No statistically significant difference was found by comparing tobramycin and gentamicin serum concentrations at both the 20 and 5 mg/kg doses, P > 0.05. The rate of disappearance of the two drugs corresponded to a half-life of approximately 70 to 80 min.

The thoracic lymph concentrations are shown.
mg/kg, tobramycin urine concentrations were significantly and uniformly greater than the gentamicin concentrations, \( P < 0.01 \); however, at the 5 mg/kg dose, the difference was apparent only at 45 and 60 min, but not thereafter.

**DISCUSSION**

It is presently accepted that kidney lymphatics drain that organ’s interstitial space (8, 13). Renal lymph antibiotic levels have been the most successful method of estimating the actual tissue concentrations. Gingell et al. as well as Cockett and his colleagues have used this method extensively (5-7, 9, 10). Knowledge of an antibiotic’s concentration in the kidney’s interstitial space is of extreme importance when it is being considered in the treatment of pyelonephritis which begins as an interstitial inflammatory process (5). Prompt, high levels of an antibiotic in renal lymph and urine are desirable when dealing with such infections. These have been well demonstrated for gentamicin by Gingell and co-workers (10). Our data in Fig. 2. Peak tobramycin concentrations were uniformly achieved at 15 min, whereas the 20 mg/kg gentamicin dose again peaked at 30 min. The differences between tobramycin and gentamicin in thoracic lymph at both the 20 and 5 mg/kg doses were not statistically significant, \( P > 0.05 \).

Renal capsular lymph concentrations are displayed in Fig. 3. Tobramycin renal lymph concentrations were slightly higher than those found in serum at the 20 and 10 mg/kg doses. Gentamicin at 20 mg/kg showed uniformly higher renal lymph than serum concentrations, whereas at the 5 mg/kg dose the difference was prominent only during the first 120 min and was less striking thereafter. In comparing the two drugs, it was found that at the 20 mg/kg dose, tobramycin renal lymph concentrations were significantly greater than gentamicin renal lymph concentrations, \( P < 0.01 \). At the 5 mg/kg dose this difference was significant only at 15 min, \( P < 0.01 \).

Urine concentrations, which were prompt and high for both drugs, are depicted in Fig. 4. At 20
show similar results with tobramycin. Because the pharmacological behavior of tobramycin is known to be very similar to gentamicin, these findings are not surprising (11, 12, 15, 16, 18, 20).

A comparison of the two drugs nevertheless reveals some differences. At the 20 mg/kg dose, renal lymph levels were consistently higher for tobramycin than for gentamicin, even though the serum and thoracic lymph levels did not differ significantly. At the 5 mg/kg dose, differences in renal capsular lymph were apparent only at 15 min, at which time tobramycin exceeded gentamicin. Thereafter, no other significant differences were obtained. Tobramycin urine levels were uniformly higher than those for gentamicin only at the 20 mg/kg dose; however, both were of sufficient magnitude so as to be considered bacteriostatic for even resistant microorganisms.

The reasons for the above differences between the two antibiotics in renal lymph and urine levels are not readily apparent. In humans, both drugs are excreted unchanged in the urine by glomerular filtration (18). Although the literature contains conflicting reports, recent work by Gordon and his colleagues suggests that neither tobramycin nor gentamicin are protein bound (11). A difference in protein binding or renal excretion of these antibiotics in dogs is unlikely, especially because their half-lives in serum are similar.

Our data demonstrated conclusively that tobramycin levels in serum, thoracic lymph, renal lymph, and urine compare favorably with those of gentamicin. There is some evidence that the renal lymph and urine levels of tobramycin are higher than those of gentamicin. This characteristic suggests that tobramycin is an acceptable alternative to gentamicin in cases of pyelonephritis.

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LITERATURE CITED