Gentamicin and Tobramycin Penetration into Synovial Fluid

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The penetration of gentamicin and tobramycin into the synovial fluid of 12 patients with nontraumatic joint effusions was studied. Simultaneous serum and synovial fluid specimens taken after the intramuscular or intravenous administration of an antimicrobial agent were assayed. Synovial fluid levels of antibiotic were >50% of serum levels in all subjects studied. In five patients, synovial fluid levels were equal to or exceeded simultaneous serum values. These results suggest that intra-articular injection of aminoglycoside antibiotics is not necessary in the treatment of infectious arthritis.

Previous reports have documented the penetration into synovial fluid of many commonly used antimicrobial agents (1, 5, 6). However, very little data are available on gentamicin and tobramycin penetration (2, 4).

This report details our study in which we measured simultaneous serum and synovial fluid levels of gentamicin and tobramycin in patients with joint effusions of nontraumatic etiology.

The patient population consisted of adult subjects with nontraumatic joint effusion. This population included eight cases of rheumatoid arthritis and four cases of degenerative joint disease. All patients were free of known renal impairment. Informed consent was obtained from all. Synovial fluid cell counts and total protein contents are summarized in Table 1.

Eleven subjects received a single intramuscular injection of either gentamicin (group I) or tobramycin (group II). The dose varied from 1.0 to 1.5 mg/kg. One subject received a 1.0-mg/kg dose of gentamicin by the intravenous route (group I). In subjects receiving intramuscular injections, a simultaneous serum and synovial fluid sample was obtained for antimicrobial assay between 60 and 120 min after injection. The patient receiving intravenous gentamicin had a simultaneous sample drawn 30 min after infusion. In addition, one patient from groups I and II had a second simultaneous specimen taken at 210 and 240 min after intramuscular injection, respectively.

Serum and synovial fluid assays for gentamicin and tobramycin were performed by the agar diffusion technique. All assays were done in duplicate, and results are expressed as a mean value. Synovial fluid-to-serum ratios were calculated.

All patients had detectable levels of gentamicin and tobramycin in synovial fluid. Although individual values varied from patient to patient, all had synovial fluid levels at least 50% of simultaneous serum levels. Indeed, five patients had synovial fluid levels that equalled or exceeded serum values. In the two patients with second simultaneous specimens, gentamicin and tobramycin were still present. Penetration of these antimicrobial agents was independent of the type of arthritis studied (Table 2).

Knowledge of the penetrability of antimicrobial agents into the synovial fluid is important in planning an adequate therapeutic program for patients with infectious arthritis. Nelson (5) and Parker and Schmid (6) demonstrated that many commonly used antimicrobial agents, except erythromycin, penetrated adequately into the synovial fluid in cases of infectious arthritis. Baciocco and Iles (1) found that kanamycin

TABLE 1. Synovial fluid cell count and total protein

Group no.	Patient no.	Leukocyte count/mm ³	Protein (g/dl)
I	1	26,000	5.9
	2	12,500	5.9
	3	250	5.8
	4	100	3.8
	5	7,250	6.1
	6	25	ND ^a
II	1	16,500	3.9
	2	7,250	6.0
	3	27,500	4.6
	4	12,750	5.7
	5	100	3.7
	6	12,250	5.9

^a ND, Study not performed.

TABLE 2. Results of serum and synovial fluid assays for gentamicin and tobramycin

Group no.	Patient no.	Diagnosis	Antibiotic dose (mg/kg)	Route	Time ^a (min)	Synovial fluid level (μg/ml)	Serum level (μg/ml)	Synovial fluid/serum levels (%)
I	1	RA ^b	1.5	IM ^c	60	2.9	5.4	54
	2	RA	1.0	IM	90	2.4	2.4	100
	3	DJD ^d	1.5	IM	{ 90 210	{ 3.5 3.3	{ 6.5 4.1	{ 54 81
	4	DJD	1.5	IM		4.4	3.0	147
	5	RA	1.0	IM	120	2.4	2.8	86
	6	DJD	1.0	IV ^e	30	5.4	5.8	93
II	1	RA	1.5	IM	90	4.5	4.3	105
	2	RA	1.5	IM	{ 120 240	{ 2.3 1.6	{ 2.9 1.0	{ 71 160
	3	RA	1.0	IM		1.6	1.6	100
	4	RA	1.0	IM	90	1.3	1.7	76
	5	DJD	1.5	IM	90	3.4	5.6	60
	6	RA	1.0	IM	90	2.2	2.3	96

^a Time specimens obtained after antibiotic administration.^b RA, Rheumatoid arthritis.^c IM, Intramuscular.^d DJD, Degenerative joint disease.^e IV, Intravenous.

entered synovial fluid in adequate amounts. However, their subjects had traumatic joint effusions, and most of the synovial fluids were either serosanguinous or grossly bloody. Chou et al. (2) and Marsh et al. (4) have reported one case each of infectious arthritis in which gentamicin was shown to penetrate synovial fluid in amounts adequate to inhibit the causative microorganisms.

Our study of patients with nontraumatic joint effusion indicates that gentamicin and tobramycin readily penetrate into synovial fluid after intramuscular or intravenous administration. Synovial fluid values obtained were at least 50% of simultaneous serum levels and equalled or exceeded serum levels in five patients. These values obtained with a single intramuscular or intravenous injection, especially at the 1.5-mg/kg dosage, are of sufficient magnitude to inhibit many bacterial pathogens (3). The data do not preclude the use of a second antimicrobial agent (e.g., carbenicillin for *Pseudomonas aeruginosa*) when indicated, judicious use of surgical intervention, or determination of synovial fluid antimicrobial activity during therapy. Although studies involving

multiple-dose pharmacokinetics are indicated, our results suggest that aminoglycoside antibiotics, like most other antimicrobial agents, do not require intra-articular instillation in the treatment of infectious arthritis.

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