

Concentration of Clindamycin in Human Bone

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Thirty patients undergoing total hip replacement received clindamycin beginning the day before surgery. Mean clindamycin concentrations during surgery were 7.33 ± 3.37 $\mu\text{g/ml}$ in serum and 2.63 ± 1.76 $\mu\text{g/g}$ in bone; mean ratio of bone-serum concentration was 0.40 ± 0.30 .

As part of a study undertaken to evaluate the role of prophylactic therapy with clindamycin in patients undergoing total hip replacement (1), the results of which were inconclusive because there were no early or late hip-joint infections in either the treated or control group of patients, we had the opportunity to determine concentrations of clindamycin in human bone.

Patients received 300-mg doses of clindamycin phosphate intramuscularly every 8 h beginning at 4:00 p.m. on the day before surgery. Serum and bone specimens were obtained simultaneously during surgery 1 h after the previous dose of clindamycin and were assayed for clindamycin concentrations by the cylinder-plate method in Penassay seed agar (Difco) with *Sarcina lutea* (ATCC 9431) as the assay organism (2). The method standardized by Norden (5) for measuring antibiotic bone concentrations was employed to determine concentrations of clindamycin in the bone specimens. The bone specimens were dissected free of soft tissue, split lengthwise, and scraped free of marrow. The bone was dried and any remaining marrow was removed. After freezing at -70 C, the bone was crushed to a fine powder; the powder was weighed and suspended in 0.1 M phosphate buffer, pH 7.8. After agitation for 5 h at 4 C, the supernatant fluid was assayed for clindamycin. Zones of inhibition were equal when reference antibiotic was suspended in buffer or buffer containing bone from patients not given antibiotics. The assays of clindamycin concentrations were reproducible in bone samples from any individual patient.

Bone specimens were obtained from 30 patients given clindamycin; bone concentrations of clindamycin were determined in 27 patients. Serum and bone concentrations of clindamycin

during surgery, together with age and orthopedic diagnosis for each patient receiving clindamycin, are shown in Table 1. Mean serum clindamycin concentration at the time of hip removal was 7.33 ± 3.37 $\mu\text{g/ml}$. Mean bone clindamycin concentration was 2.63 ± 1.76 $\mu\text{g/g}$. The mean ratio of bone-serum clindamycin concentration was 0.40 ± 0.30 .

There are few reports of determinations of antibiotic concentrations in human bone. Use of a standard method of measuring antibiotic bone levels such as that developed by Norden (5) is essential to provide reproducible data. Holloway et al. (3), studying lincomycin in the treatment of patients with osteomyelitis caused by *Staphylococcus aureus*, found an average bone lincomycin level of 3.3 $\mu\text{g/g}$ and an average bone-serum concentration ratio of approximately 0.16; all patients had good clinical responses to lincomycin. In experimental animals with osteomyelitis due to *S. aureus*, lincomycin was more effective than cephalothin at the end of week 2 of therapy, though both were equally efficacious at the end of week 4 (5). The mean ratio of bone-serum clindamycin concentration in our patients (0.40) was greater than the reported ratios for oxacillin (0.05 to 0.20) (4) or lincomycin (0.16) (3). Further studies are needed to evaluate the efficacy of clindamycin in the treatment of osteomyelitis and in the prophylaxis of infection following total hip arthroplasty.

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TABLE 1. Serum and bone concentrations of clindamycin at surgery

Patient	Age (years)	Orthopedic diagnosis ^a	Clindamycin concn		Ratio bone-serum concn
			Serum (µg/ml)	Bone (µg/g)	
1	67	OA	3.39	1.38	0.41
4	58	OA	6.93	^b	
7	68	OA	1.02	0.21	0.21
9	70	OA	3.60	1.34	0.37
10	71	OA	4.20	3.50	0.83
13	76	OA	15.36	1.15	0.07
14	77	AN	4.70	1.80	0.38
15	59	OA	7.42	2.90	0.39
16	76	OA	5.75	8.18	1.42
18	58	AN	9.32	4.00	0.43
24	61	OA	11.62	1.35	0.12
25	42	OA	7.18	3.48	0.48
28	63	OA	5.66	1.81	0.32
30	56	RA	8.58	1.35	0.16
33	58	RA	1.22	0.32	0.26
38	71	OA	8.29	3.82	0.46
40	73	OA	8.07	4.43	0.55
41	70	AN	6.17	3.12	0.51
42	52	MC	8.41	3.54	0.42
45	73	PF	8.43	1.36	0.16
46	58	OA	8.67	1.80	0.21
50	68	OA	7.08	0.73	0.10
52	60	OA	9.35	2.89	0.31
55	73	OA	7.38	1.93	0.26
57	67	OA	10.06	^b	
59	71	OA	10.62	4.48	0.42
65	74	OA	5.02	5.28	1.05
66	74	OA	15.59	3.59	0.23
67	70	OA	6.54	1.40	0.21
68	64	PF	4.39	^b	
Mean ± SD deviation ^c			7.33 ± 3.37	2.63 ± 1.76	0.40 ± 0.30

^a OA, osteoarthritis; RA, rheumatoid arthritis; AN, avascular necrosis; PF, previous failure at hip pinning; MC, metastatic carcinoma.

^b Sample damaged.

^c SD, standard deviation.

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