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Hemodialysis Properties of Clindamycin (7-Chloro-7-Deoxylincomycin)

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The effect of hemodialysis (Kolff-type machine) on clindamycin blood levels in anuric patients was studied. At 1 hr after oral ingestion of drug, blood levels ranged from 1.23 to 5.17 μg/ml and fell thereafter. Half-times for peripheral removal were 3.36 μg/ml ± 0.22 when subjects were "off" dialysis and 3.14 μg/ml ± 0.09 during dialysis. Their difference was not statistically significant, indicating that hemodialysis does not affect the blood level of clindamycin. In all studies, significant levels of the antibiotic were present at 12 hr.

The emergence of maintenance hemodialysis from the experimental to the therapeutic phase has emphasized the necessity of making available sufficient information on the dialysis properties of new drugs as they are being introduced.

Clindamycin is a new antibiotic derived from lincomycin. Although the bacterial spectrum is similar for both antibiotics, in vitro studies indicate that clindamycin is more active than lincomycin (4; L. B. Hogan and W. J. Holloway, Abstr. Intersci. Conf. Antimicrobial Agents Chemotherapy, 8th, New York, p. 10, 1968; R. J. Santos et al., Abst. Intersci. Conf. Antimicrobial Agents Chemotherapy, 8th, New York, p. 10, 1968). Preliminary data also indicate that orally administered clindamycin is better absorbed and has fewer side effects than lincomycin (6, 7, 8, 10). Because infection and appropriate antibiotic therapy play such an important role in the management of uremic patients, this study was undertaken to determine the effect of hemodialysis on clindamycin blood levels.

MATERIALS AND METHODS

Antibiotic assay method. 7-Chloro-7-deoxylincomycin (clindamycin) was assayed by the cylinder plate method (5) with a six-point standard curve on eight replicate plates. Five samples and one assay control standard per sample plate and four replicate sample plates were used. The assay organism was *Sarcina lutea* ATCC 9341 (liquid nitrogen frozen suspension). One liter of sterile Penassay agar (Difco) was inoculated at 0.1% with *S. lutea*. For the primary standard, an 880-μg base equivalent per mg was used. Concentrations of 16, 8, 4, 2, 1, and 0.5 μg/ml of serum were used in Hylan commercial pooled human serum. As a secondary standard, predose specimens were spiked at 8, 4, 2, and 1 μg/ml with the above standard when possible. The serum specimens were assayed undiluted. All of the specimens from a single subject were assayed on the same day and calculated against secondary standards. Zero is equal to or less than 0.4 μg/ml.

Artificial kidney. A Kolff-Travenol hemodialyzer was used (1, 9). This dialyzer utilizes a disposable unit consisting of two cellophane tubes in parallel arrangement, enveloped in fiberglass screens and wrapped around a central core. Dialysate fluid is pumped between the layers of the blood-filled tubing so that dialysis or exchange takes place. The flow of blood through the artificial kidney machine (Sarns pump used) per minute varied from 200 to 400 ml/min. The hydrostatic pressure measured at the filter chambers varied from 140 to 220 mm of Hg.

TABLE 1. *Creatinine clearances of patients with chronic glomerulonephritis*

Patient	Urine	Creatinine Clearance
	ml/24 hr	*ml/min*
G.B.	0	0
G.H.	0	0
P.L.	0	0
C.T.	115	0.25
J.G.	380	1.5

All of the patients had internal arteriovenous fistulae (2) and were dialyzed by the venipuncture technique (3).

Patients. Four adult male and one adult female subjects with end-stage renal disease were studied. These patients were on the chronic hemodialysis program of this center and were dialyzed twice weekly (Table 1).

Antibiotic administration. Before treatment began, 12 ml of blood was drawn to serve as the zero-hour level. All subjects received 150 mg of 7-chloro-7-deoxylincomycin by mouth every 6 hr for 48 hr,

TABLE 2. *Blood levels of clindamycin (μg/ml) in patients on hemodialysis*

Patient	Predialysis (1 hr after dose)	Hr postdialysis/hr after dose										BUN[b]	
		1/2	2/3	3.5/4.5	5/6	6/7	7/3	8/9	—[a]/10	—[a]/12	—[a]/24	Predialysis	Postdialysis
G.H.	1.97	2.99	3.12		1.77		0.74		0.77	0.66	0.0	90	20
C.T.	2.81	2.39	1.16	0.72	0.68	0.56		0.41	0.57	0.53	0.4	98	40
J.G.	4.69	3.39	2.41	1.92	1.23			0.81	0.73	0.74	0.46	98	37
G.B.	5.17	3.87	2.74	2.13	1.72		1.14		0.99	0.90		102	28

[a] Dialysis stopped.
[b] Blood-urea-nitrogen, expressed as mg/100 ml.

TABLE 3. *Blood levels of clindamycin (μg/ml) in patients off dialysis*

Patient	Hr after dose						
	1	3	4.5	6	10	12	24
G.H.	2.61	2.50	1.49	1.30	0.96	0.96	0.58
C.T.	1.23	1.00	0.74	0.61	0.45	0.42	0.0
J.G.	5.06	2.26	1.76	1.48		0.64	0.46
G.B.	4.21	2.52	2.02	1.61		0.92	0.51

preceding the drawing of blood samples. Five-milliliter amounts of blood were drawn at the following intervals after the last capsule was taken: 1, 3, 4.5, 6, 10, 12, and 24 hr. Two extra samples were taken from patients while they were being dialyzed; these were at 1 hr after the start of dialysis and a postdialysis sample. All blood samples were separated by centrifugation, and the serum was promptly frozen until assays could be performed.

RESULTS AND DISCUSSION

The dialyzability of clindamycin was examined in four of the five patients. In one instance, patient P.L. discontinued the drug because of abdominal pain, diarrhea, nausea, and vomiting after receiving only two doses. We were not convinced that these symptoms were due to the drug. Patient G.H. actually had an increased blood level while on dialysis. This may have been owing to gastric retention and continued absorption of the antibiotic secondary to known duodenal disease.

Table 2 shows serum levels of clindamycin for patients on hemodialysis; Table 3 shows a series of levels for the same patients off dialysis. Hemodialysis appears to play no significant role in the removal of this drug from the blood. The progressive decrease in serum concentrations of clindamycin is virtually the same on or off hemodialysis.

The peak blood level for this drug is 1 hr or less after ingestion. The initial blood levels for these patients ranged from a high of 5.17 μg/ml to a low of 1.23 μg/ml. In all studies, significant blood levels of clindamycin were present at 12 hr. In five of the eight patient studies, blood levels were still detectable at 24 hr. A 24-hr specimen could not be obtained in one of the patients, and two others showed zero level at 24 hr. The data were plotted on semilog paper and the half-time was calculated graphically. The half-life for clindamycin "off" dialysis is 3.36 ± 0.22 and "on" dialysis is 3.14 ± 0.09. The average half-life for clindamycin in subjects with normal renal function is 2.55 hr (*personal communication*).

TABLE 4. *Comparison of half-time of clindamycin in each patient on and off hemodialysis*[a]

Subject	Half-time off dialysis	Half-time on dialysis	Difference
J.G.	3.20	3.13	0.07
C.T.	3.53	3.25	0.28
G.B.	3.12	3.00	0.12
G.H.	3.63	3.17	0.46
Average half-time	3.36	3.14	0.232 (mean difference)

[a] Standard deviation = ±0.176.

Of the five patients who participated in the study, four were anuric and one was severely oliguric. The one oliguric patient's urinary output during hemodialysis was so small that it would have been fruitless to carry out a urinary recovery of clindamycin. Individual half-times for "on" and "off" dialysis studies are listed in Table 4. The difference in half-time during hemodialysis and without dialysis is not statistically significant ($P = > .05$).

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