CHAPTER IV

RESULTS AND DISCUSSION

I Serum Gentamicin Levels and Pharmacokinetic Parameters of Thai Patients

Sixty admitted patients who met the criteria of this study were analyzed . Table 1 showed the characteristics of the patients, table 2 showed the dosage regimen administered to patients and their corresponding serum gentamicin levels. Also included in table 2 was each patient's treatment time, the combination drugs given, his or her disease and the results of treatment of the 60 patients evaluated, fifteen patients (25%) were treated with gentamicin alone, while forty-five patients (75%) were treated concomitantly with other antibiotics. The percentages of concomitant drugs used were as follow :

Table 1 Characteristics of Patients.

Patient Number	Age (Year)	Sex	IBW(kg) *	TBW(kg) **	Height(cm)	Scr(mg/dl) ***
1	82	F	50.10	50.00	155.00	.50
2	73	F	50.02	41.50	156.00	.70
3	67	M	62.88	50.00	164.00	.80
4	27	M	59.20	45.00	160.00	.90
5	72	F	49.18	40.00	154.00	1.00
6	43	M	68.40	51.00	170.00	1.00
7	26	F	54.70	52.00	160.00	.60
8	36	F	51.94	59.00	157.00	.80
9	51	F	57.46	65.00	163.00	.40
10	27	M	67.02	82.50	168.50	.80
11	59	F	48.26	49.00	153.00	.50
12	85	F	41.82	45.00	146.00	.80
13	19	M	59.20	53.00	160.00	.60
14	36	F	54.69	61.00	160.00	.90
15	42	M	64.72	53.00	166.00	.80
16	64	F	58.38	59.50	164.00	.90
17	42	M	64.72	57.00	166.00	1.00
18	52	F	35.38	39.50	139.50	1.10
19	61	M	64.72	56.00	166.00	1.20
20	19	M	69.32	55.00	171.00	1.40
21	60	F	49.18	62.00	161.00	1.30
22	19	M	60.12	52.00	161.00	.80
23	52	M	56.90	52.00	157.50	1.40
24	24	M	57.46	55.00	163.00	.60
25	55	M	69.42	63.00	176.00	.90
26	18	M	61.04	43.00	162.00	.80
27	55	F	45.50	51.00	150.00	.80

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Patient Number	Age (Year)	Sex	IBW(kg) *	TBW(kg) **	Height(cm)	Scr(mg/dl) ***
28	21	F	53.32	49.80	158.50	.80
29	63	F	51.02	64.00	156.00	1.10
30	21	F	51.94	82.00	157.00	.90
31	19	F	52.86	45.00	158.00	.60
32	28	F	57.46	60.40	163.00	1.50
33	27	F	51.94	45.70	157.00	.60
34	40	M	57.20	57.50	160.00	.50
35	27	F	49.18	50.00	154.00	.60
36	55	M	50.00	54.00	150.00	.60
37	59	M	58.28	37.00	159.00	.40
38	47	M	57.36	50.00	158.00	.70
39	21	F	48.26	41.00	153.00	.70
40	33	M	65.64	54.00	167.00	.60
41	24	M	63.80	60.00	165.00	1.00
42	59	M	58.28	49.50	169.00	.80
43	40	M	54.00	53.00	160.00	.80
44	27	M	54.00	50.00	160.00	.80
45	56	F	43.67	52.00	148.00	.60
46	44	M	61.96	49.00	163.00	.90
47	58	F	50.10	51.00	155.00	1.10
48	78	F	45.04	38.00	149.50	.70
49	51	M	64.72	49.00	166.00	.70
50	21	F	52.40	52.50	157.00	1.10
51	19	M	57.20	45.00	160.00	.70
52	48	F	48.26	52.00	153.00	.30
53	21	F	52.86	62.00	158.00	.80

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Patient Number	Age (Year)	Sex	IBW(kg) *	TBW(kg) **	Height(cm)	Scr(mg/dl) ***
54	17	M	68.40	52.00	170.00	.70
55	17	M	61.04	49.00	162.00	.90
56	20	M	80.36	50.00	183.00	.60
57	38	F	57.46	50.55	163.00	.60
58	23	F	50.10	49.00	155.00	.90
59	19	M	61.04	48.00	162.00	.60
60	48	F	54.70	43.00	160.00	.50
mean±SD	40.917±	F = 31	56.325±	52.290±	159.69±	0.8±0.25
	19.095	M = 29	7.927	8.591	7.097	
(Range)	(17-85)		(35.38-	(37.0 —	(139.5-	(0.3-1.5)
			80.36)	82.5	183)	
n = 60	n = 60	n = 60	n = 60	n = 60	n = 60	n = 60

* IBW = Ideal Body Weight

** TBW = Total Body Weight

*** Scr = Serum Creatinine

Table 2 Dosage Regimen and Measured Serum Gentamicin Concentration.

Patient Number	LD* (mg)	MD** (mg)	Interval (hour)	Dose/kg/day (mg)	Peak (µg/ml)	Trough (µg/ml)	$C_{t2.5}$ (µg/ml)	Treatment Time (day)	Concomitant Drug	Disease 2	Result 1
1	80	60	8	3.60	4.67	1.55	3.53	9	-	5	p
2	60	50	8	3.61	5.28	.76	3.09	12	-	1	+
3	80	40	8	2.40	2.63	.63	1.70	-	Genta/P.G.S.	5	p
4	-	60	8	4.00	4.49	.90	2.57	8	Genta/Ceph	2	-
5	-	40	8	3.00	5.10	1.75	3.34	17	Genta/Clin	2	-
6	80	70	8	4.12	2.77	.22	1.73	-	Genta/Ceph	2	.
7	-	80	8	4.62	4.68	1.02	3.05	10	Genta/P.G.S.	2	+
8	-	80	8	4.62	5.25	1.05	3.95	14	Genta/Ampi	7	+
9	80	60	8	3.13	3.23	.26	1.82	-	Genta/P.G.S.	6	.
10	-	100	8	4.48	5.26	.38	1.87	6	Genta/Ampi	8	+
11	-	60	8	3.73	4.67	.82	2.54	7	Genta/Ceph	8	-
12	80	50	12	2.37	3.12	1.29	3.00	7	Genta/Ceph	8	+
13	75	60	8	3.40	3.80	.30	1.90	6	Genta/P.G.S.	1	+
14	-	80	8	4.39	3.27	1.67	3.10	-	Genta/P.G.S.	2	.
15	80	60	8	3.40	3.37	.48	2.00	-	-	1	.
16	-	60	8	3.08	3.20	1.00	2.45	7	Genta/P.G.S.	2	-
17	-	80	8	4.21	8.23	.59	4.03	9	Genta/Clin	4	+
18	-	60	12	3.39	5.46	1.02	4.19	11	-	1	+
19	80	80	8	4.29	5.51	2.16	4.51	14	Genta/Ampi	3	-
20	-	60	8	3.27	6.89	5.01	6.30	10	Genta/Ampi	1	+
21	-	60	8	3.66	5.75	2.49	4.91	8	-	1	+
22	-	60	8	3.46	3.01	.36	1.91	5	Genta/Clin	4	+
23	-	50	8	2.88	3.94	1.40	3.07	10	Genta/Ampi	7	+
24	-	80	8	4.36	3.90	-	1.81	12	Genta/Clin	4	+
25	-	80	8	3.81	5.51	.64	2.98	-	Genta/Ceph	8	.
26	-	60	8	4.19	3.74	.72	2.30	-	Genta/Ampi	8	.

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Patient Number	LD* (mg)	MD** (mg)	Interval (hour)	Dose/kg/day (mg)	Peak (µg/ml)	Trough (µg/ml)	$C_{t2.5}$ (µg/ml)	Treatment Time (day)	Concomitant Drug	Disease 2	Result 1
27	-	60	8	3.96	3.58	.70	2.64	14	Genta/P.G.S.	8	+
28	-	80	8	4.82	7.93	.42	3.39	10	-	1	+
29	-	60	8	3.53	5.49	3.16	4.30	22	Genta/Ampi	7	+
30	-	80	8	4.62	4.62	2.76	3.61	8	Genta/Clin	4	+
31	-	80	8	5.33	4.91	.99	3.49	12	Genta/Ampi	1	.
32	-	60	8	3.13	3.92	1.19	3.04	7	Genta/Clin	4	+
33	-	80	8	5.25	5.55	.25	2.86	12	Genta/Ampi	8	+
34	80	60	8	3.13	3.89	.91	1.43	8	Genta/P.G.S.	8	+
35	-	80	8	4.88	3.37	-	1.42	5	Genta/Ampi	8	-
36	80	60	8	3.60	4.37	.98	2.10	7	Genta/P.G.S.	8	.
37	80	60	8	4.86	2.91	.66	1.47	24	-	6	+
38	-	60	8	3.60	3.93	.69	2.37	7	Genta/P.G.S.	3	+
39	-	60	8	4.39	4.80	1.61	2.33	5	Genta/Cloxa	8	-
40	-	80	8	4.44	4.09	.23	1.93	18	-	2	.
41	-	80	8	4.00	4.04	.75	2.82	21	Genta/P.G.S.	3	+
42	-	60	8	3.64	4.81	.81	2.65	18	Genta/Cloxa	3	+
43	-	80	8	4.53	3.95	.52	2.40	6	-	1	-
44	-	80	8	4.80	5.08	.30	1.59	14	Genta/Clin	4	+
45	80	60	8	4.12	4.91	1.59	3.88	14	-	1	+
46	-	80	8	4.90	4.38	1.07	3.45	7	Genta/Cloxa	5	p
47	-	80	8	4.79	6.27	2.19	5.29	7	-	1	+
48	-	60	8	4.74	5.97	1.19	3.90	8	-	2	.
49	-	60	8	3.67	3.62	.39	1.75	7	Genta/Ampi	7	+
50	80	60	8	3.44	4.95	2.12	4.30	8	-	2	+

Continued...

Patient Number	LD* (mg)	MD** (mg)	Interval (hour)	Dose/kg/day (mg)	Peak (µg/ml)	Trough (µg/ml)	$C_{t2.5}$ (µg/ml)	Treatment Time (day)	Concomitant Drug	Disease 2	Result 1
51	-	80	8	5.33	5.74	1.84	4.81	10	Genta/P.G.S.	3	+
52	-	60	8	3.73	6.87	.72	3.76	14	Genta/Ampi	8	+
53	-	80	8	4.54	5.50	1.19	3.92	6	Genta/P.G.S.	8	+
54	-	60	8	3.46	3.33	.35	1.51	-	Genta/Cloxa	2	.
55	-	60	8	3.67	4.26	.55	2.69	14	Genta/P.G.S.	3	+
56	-	60	8	3.60	3.37	.50	2.25	7	Genta/Cloxa	6	-
57	-	80	8	4.480	5.21	.45	3.55	7	Genta/Cloxa	4	+
58	-	60	8	3.67	4.78	.50	3.10	14	-	1	+
59	80	60	8	3.75	4.19	.26	2.22	6	Genta/Cloxa	2	+
60	-	60	8	5.58	6.22	.75	3.22	6	-	1	+

1 Result p = Prophylaxis (n = 3)
+ = Improved (n = 37)
- = No Improved (n = 9)
. = Not Complete Follow up (n = 11)

2 Disease 1 = Urinary Tract Infection (n = 14)
2 = Septicemia (n = 11)
3 = Infective Endocarditis (n = 6)
4 = Cellulitis (n = 7)
5 = Prophylaxis (n = 3)
6 = Pneumonia (n = 3)
7 = Hapatobiliary Infection (n = 4)
8 = Miscellaneous Infection (n = 12)

* LD = Loading Dose

Drug	Number of Patients (percent)
Gentamicin + Ampicillin	13 (21.666%)
Gentamicin + Penicillin G Sodium	14 (23.333%)
Gentamicin + Cloxacillin	7 (11.666%)
Gentamicin + Clindamycin	7 (11.666%)
Gentamicin + Cephalosporin	4 (6.666%)

During this study, 25% of patients (15 out of 60) started gentamicin with loading dose and followed with maintenance dose, and 75% (n = 45) of patients started with maintenance dose. From these patients (n = 60), 13.333 percent of the dosage regimen given were according to Hull and Sarubbi dosing guideline while 86.666 percent followed traditional practice. The physician tended to use standard or conventional dosage regimen (dose and interval) and the majority dosage regimen were 60 or 80 mg/dose in every 8 hours. Physicians in Chulalongkorn Hospital haven't applied pharmacokinetics to the gentamicin dosage regimen calculation and they did not concern about the differences in the accepted gentamicin therapeutic range for different diseases.

Forty-nine patients were followed up for their clinical results. The patient was indicated as showing positive result if he or she was cured without changing the drug(s) used. Thirty-seven patients showed sign of improvement, nine patients showed negative improvement and three cases were treated for prophylaxis. For those

patients who showed improvement in the treatment, the approximate average treatment time was 11 days (11.25 days).

I.1 Serum gentamicin levels and the therapeutic range

Mean measured peak and trough concentrations were in the desired concentration range (4 to 8 µg/ml for peak concentration and 0.5 to 1.5 or 0.5 to < 2 µg/ml for trough concentration) which were required in treatment to attain therapeutic results. When individual data was considered, many patient gentamicin levels were out of the desired range. Among 60 patients included in this study, 22 patients had measured peak concentration before the desired range 4 µg/ml, one above 8 µg/ml and 25 patients had measured trough concentration out of desired range (< 0.5 µg/ml, n = 14 and > 1.5 µg/ml, n = 11). Seven patients had high trough concentration, i.e., exceeded 2 µg/ml. Only 23 patients were in acceptable therapeutic range.

Table 3A showed that when drug dosage regimen was given according to the present traditional practice and general guideline, percentage of patients whose gentamicin serum levels were within the therapeutic range was 61.666 when the peak level only was considered, and was 61.666 when the trough level only was considered, while the percentage was 38.333 when both peak and trough levels

were considered. The acceptable peak concentration; 4 to 8 µg/ml and trough concentration; 0.5 to 1.5 µg/ml or 0.5 to less than 2 µg/ml were considered.

Table 3B showed that when patients who received gentamicin without any concomitant drug only were considered, seven out of fifteen patients had gentamicin serum levels within the therapeutic range when both the peak and trough levels were considered. Twelve out of the fifteen patients had the peak gentamicin serum levels within the therapeutic range while nine out of the fifteen patients got the trough gentamicin serum levels within the therapeutic range.

At the same time, the clinical outcome as related to the therapeutic range was also presented in table 3A and 3B.

When all patients were considered, the percentage of improvement were 83.333%, 61.90% and 68.42% if the peak concentration only, the trough concentration only and both peak and trough concentrations were within the therapeutic range, respectively. For sub-therapeutic range, there were 68.75%, 100% and 100% improvement if the peak concentration only, the trough concentration only and both peak and trough concentrations were in the sub-therapeutic range respectively, and for over-therapeutic range, there were 100% and 85% improvement if the peak concentration

Table 3 Percentage of Patients Whose Serum Gentamicin Level Were within the Therapeutic Range.

A : All patients were included.

Serum Gentamicin Level		Number of Patients(n)	Percentage	Number of Patients had Clinical Result 1	Number of Patients showed Improvement	Percentage of Improvement
Within Therapeutic Range	Peak	37	61.666	30	25	83.33
	Trough	37	61.666	30	21*	70.00
	Both	23	38.333	19	13	68.42
Sub-therapeutic Range	Peak	22	36.666	16	11	68.75
	Trough	14	23.333	9	9**	100.00
	Both	6	10	3	3	100.00
Over-therapeutic Range	Peak	1	1.666	1	1	100.00
	Trough	7	11.666	7	6***	85.00
	Both	-	-	-	-	-

1. Number of patients who had clinical result were not include prophylaxis patients.

* Thirteen patients of twenty-one had peak concentrations within therapeutic range. (61.90%)

** Six patients of nine had peak concentrations within therapeutic range. (66.666%)

*** Patients had peak concentrations within therapeutic range. (100%)

B : Patients who recieved gentamicin without any concomitant drug only were considered.

Serum Gentamicin Level		Number of Patients(n)	Percentage	Number of Patients had Clinical Result 1	Number of Patients showed Improvement	Percentage of Improvement
Within	Peak	12	80	9	9	100
Therapeutic	Trough	9	60	7	6*	85.710
Range	Both	7	46.666	5	5	100
Sub-therapeutic	Peak	3	20	2	1	50
Range	Trough	3	20	1	1**	100
	Both	1	6.666	-	-	-
Over-therapeutic	Peak	-	-	-	-	-
Range	Trough	2	13.333	2	2**	100
	Both	-	-	-	-	-

1. Number of patients who had clinical result were not include prophylaxis patients.

* Five patients of six had peak concentrations within therapeutic range. (83.333%)

** Patients had peak concentrations within therapeutic range. (100%)

only and the trough concentration only were over the therapeutic range respectively

Patients who received gentamicin without any concomitant drug were considered, percentage of improvement (n = 15) were 100%, 85.71% and 100% when the peak concentration only, the trough concentration only and both peak and trough concentrations were within the therapeutic range, respectively. For sub-therapeutic range, there were 50% and 100% improvement when the peak concentration only and the trough concentration only were in the sub-therapeutic range respectively. For over-therapeutic range, there were 100% improvement when the trough concentration only was over the therapeutic range.

When the peak concentration only was considered the percentage of improvement was higher among the patients whose peak serum levels were within the therapeutic range as compared to those patients whose peak serum levels were in the sub-therapeutic range whether or not the concomitant drug was taken into consideration. However, when the trough concentration only or when both peak and trough concentrations were considered, the same relationship could not be observed. Physicians always recommended concomitant use of other antibiotic with gentamicin, further collection of data was needed before any strong conclusion could be made. If the clinical outcome was poor, physicians would often adjust the other

antibiotic in steady of changing the dosage regimen of gentamicin. Gentamicin was therefore continued on the same dosage regimen until the course of using gentamicin was completed, though gentamicin serum levels were low. The danger of suboptimal therapy in serious infections has been reported in gram-negative sepsis (60). Adjustment of dosage regimen when serum gentamicin level was out of the accepted therapeutic range will save both the expense of changing to the other more expensive drug also the time required for gentamicin using.

I.2 Comparison between the measured versus the predicted gentamicin serum concentration

The disposition of gentamicin which is influenced by both absorption and elimination of drug, has a substantial interpatient variation. At least 36 to 48 hours after initiating of the individualized dosage, peak, trough and post (two hours after infusion finished) concentrations were determined. Peak and trough serum gentamicin concentrations were showed in Figures 1 and 2. The phase median or mode value of measured peak and trough serum gentamicin concentrations were ranged 3 to 4 μg/ml and 0 to 1 μg/ml, respectively.

The means measured peak and trough serum gentamicin concentrations were 4.626 ± 1.206 μg/ml (means ± SD) and 1.053 ± 0.853 μg/ml respectively, while the means predicted peak and trough serum gentamicin

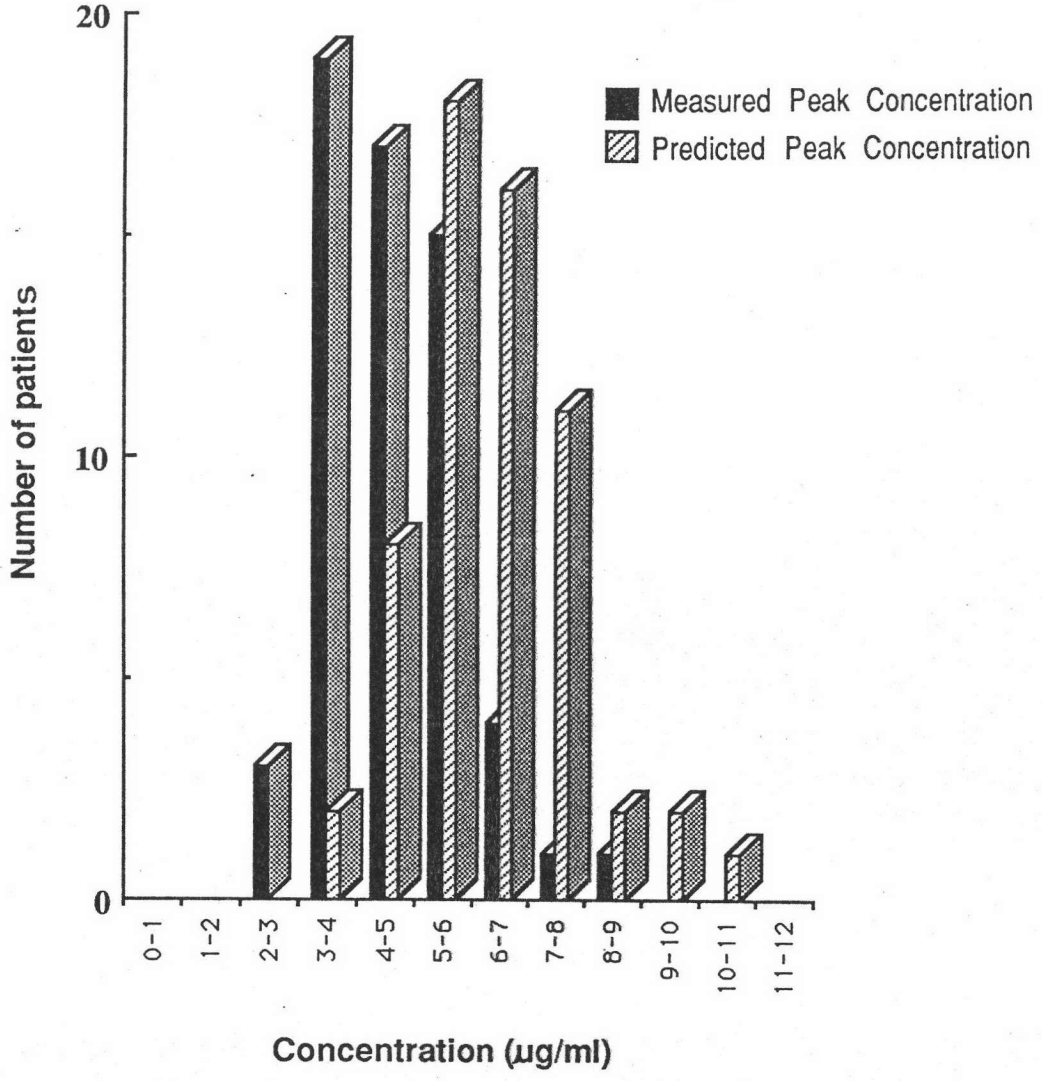

Figure 1 Comparison between the Measured and the Predicted Peak Concentrations

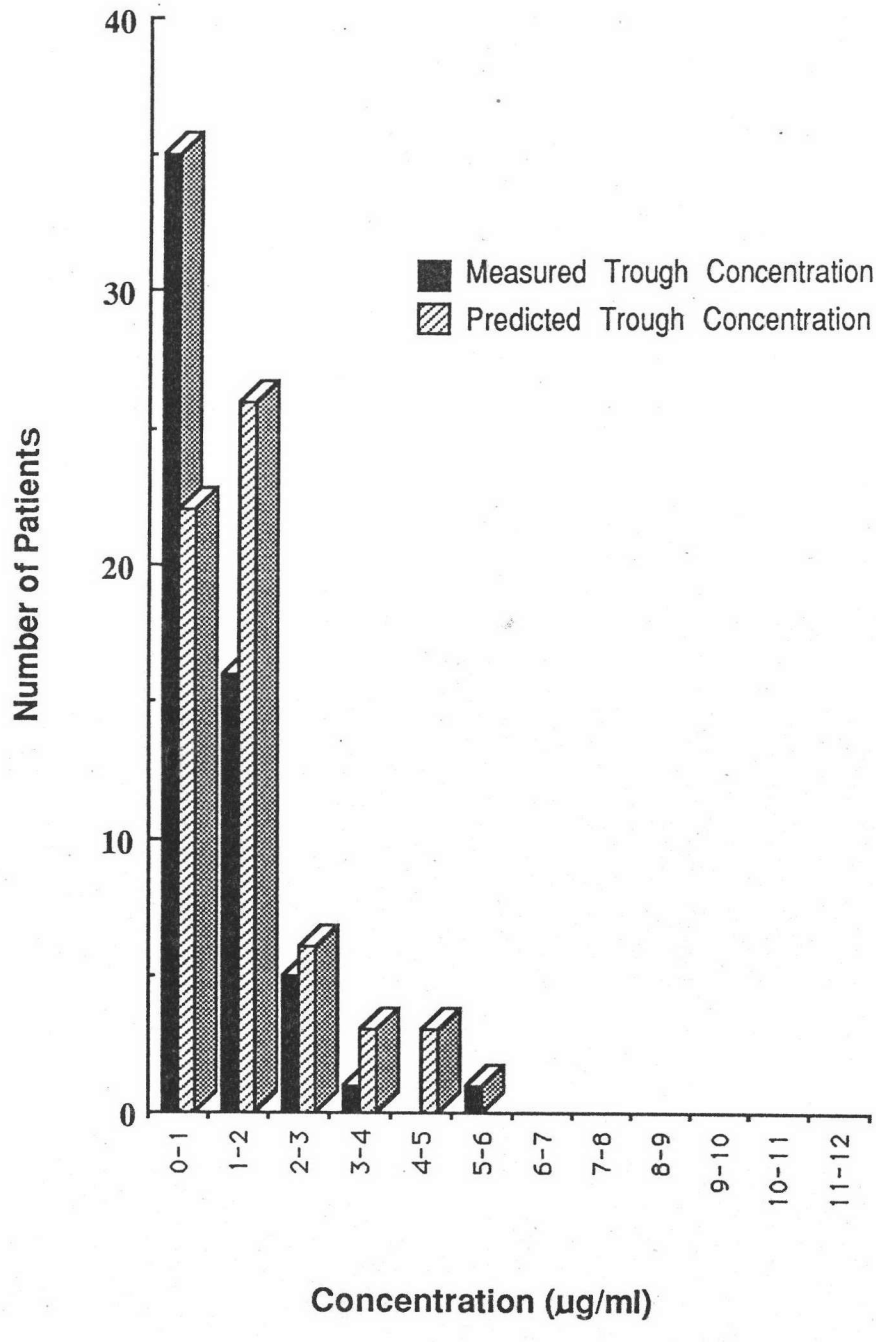

Figure 2 Comparison between the Measured and the Predicted Trough Concentrations

concentrations were 6.279 ± 1.385 µg/ml (means ± SD) and 1.49 ± 1.041 µg/ml respectively. The predicted gentamicin concentrations were calculated by using patient serum creatinine and characteristic. There were differences between the actual (measured) and predicted concentrations in both the peak and the trough concentrations. The differences between actual and predicted peak and trough serum gentamicin concentrations were presented in Table 4A. The mean difference between the measured and the predicted peak concentration was 1.87 ± 1.039 µg/ml. The level of difference was 1 to less than 2 µg/ml for 47% of the 60 cases. The mean difference between the measured and the predicted trough concentrations was 0.754 ± 0.784 µg/ml (mean ± SD). The level of difference was lower than 1 µg/ml for 80% of 60 cases. Percent coefficient of variation (%CV) between the measured and the predicted of peak and trough concentrations were 24.32% and 70.75% respectively (shown in Table 4B). The level of different peak and trough were showed in Tables 4C and 4D.

In this study, Hull and Sarubbi method and equation were used to determine the predicted serum gentamicin concentration after the assigned dosage regimen. The results which showed that gentamicin serum level can not be reliably predicted by Hull and Sarubbi method and equation which relied on serum creatinine value, agree with the finding of Barza, M. and Lauerman (1), Richen, A. and Warrington, S.(20) and Burton, M.E.(54).

Table 4 A : Predicted versus Measured Serum Gentamicin Peak and Trough Concentrations in Studied Patients.

Patient Number	Peak (measured) (µg/ml)	Peak (predicted) (µg/ml)	Difference (µg/ml)	Trough (measured) (µg/ml)	Trough (predicted) (µg/ml)	Difference (µg/ml)
1	4.67000	5.87693	1.20693	1.55000	1.58968	.03968
2	5.28000	7.19376	1.91376	.76000	2.86949	2.10949
3	2.63000	4.06787	1.43787	.63000	1.20622	.57622
4	4.49000	6.13801	1.64801	.90000	1.38680	.48680
5	5.15000	7.50192	2.35192	1.75000	3.90461	2.15461
6	2.77000	6.71104	3.94104	.22000	1.80761	1.58761
7	4.67000	6.10893	1.43893	1.02000	.69437	.32563
8	5.25000	7.04264	1.79264	1.05000	1.55604	.50604
9	3.23000	3.86111	.63111	.26000	.23673	.02327
10	5.26000	5.71898	.45898	.38000	.49765	.11765
11	4.67000	5.35576	.68576	.82000	.94348	.12348
12	3.12000	6.74596	3.62596	1.29000	2.35639	1.06639
13	3.80000	4.20308	.40308	.30000	.26948	.03052
14	3.27000	6.88576	3.61576	1.67000	1.66781	.00219
15	3.37000	4.92098	1.55098	.48000	.90067	.42067
16	3.20000	5.45617	2.25617	1.00000	1.77562	.77562
17	8.23000	6.49320	1.73680	.59000	1.49072	.90072
18	5.46000	9.64569	4.18569	1.02000	3.41874	2.39874
19	5.51000	8.12065	2.61065	2.16000	2.99739	.83739
20	6.89000	5.43675	1.45325	5.01000	1.53693	3.47307
21	5.75000	8.56201	2.81201	2.49000	4.17540	1.68540
22	3.01000	4.67955	1.66955	.36000	.60772	.24772
23	3.94000	5.84865	1.90865	1.40000	2.39664	.99664
24	3.90000	5.64904	1.74904	-	-	-
25	5.51000	5.71828	.20828	.64000	1.19826	.55862

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Patient Number	Peak (measured) (µg/ml)	Peak (predicted) (µg/ml)	Difference (µg/ml)	Trough (measured) (µg/ml)	Trough (predicted) (µg/ml)	Difference (µg/ml)
26	3.70000	6.04189	2.30189	.72000	1.08800	.36800
27	3.58000	7.07231	3.49231	.70000	2.34875	1.64875
28	7.93000	7.06818	.86182	.42000	1.35860	.93860
29	5.49000	7.46789	1.97789	3.16000	3.24362	.08362
30	4.62000	6.99191	2.23191	2.76000	1.50740	1.25260
31	4.91000	7.25704	2.34704	.99000	.97876	.01124
32	3.92000	5.97136	2.05136	1.19000	2.22616	1.03616
33	5.55000	7.27812	1.72812	.25000	1.08429	.83429
34	3.89000	3.80706	.08294	.91000	.19926	.71074
35	3.37000	6.59497	3.22497	-	-	-
36	4.37000	5.04738	.67738	.98000	.79695	.18305
37	2.91000	6.68591	3.77591	.66000	.95302	.29302
38	3.93000	5.17014	1.24014	.69000	.91136	.22136
39	4.80000	6.60183	1.80183	1.61000	1.39267	.21733
40	4.09000	5.65155	1.56155	.23000	.47210	.24210
41	4.04000	5.64448	1.60448	.75000	.91914	.16914
42	4.81000	5.89037	1.08037	.81000	1.56104	.75104
43	3.95000	6.51005	2.56005	.52000	1.15269	.63269
44	5.08000	6.73708	1.65708	.30000	1.06930	.76930
45	4.91000	6.56549	1.65549	1.59000	1.66137	.07137
46	4.38000	7.78128	3.40128	1.07000	1.95434	.88434
47	6.27000	9.87806	3.60806	2.19000	4.14411	1.95411
48	5.97000	10.38682	4.41682	1.19000	4.71299	3.52299
49	3.62000	5.41074	1.79078	.39000	1.05749	.66749
50	4.95000	5.66935	.71935	2.12000	1.57691	.54309

Continued...

Patient Number	Peak (measured) (µg/ml)	Peak (predicted) (µg/ml)	Difference (µg/ml)	Trough (measured) (µg/ml)	Trough (predicted) (µg/ml)	Difference (µg/ml)
51	5.74000	7.23662	1.49662	1.84000	.96032	.87968
52	6.87000	4.44674	2.42326	.72000	.17768	.54232
53	5.50000	6.50532	1.00532	1.17000	1.13513	.05487
54	3.33000	4.46712	1.13712	.35000	.42209	.07209
55	4.26000	5.25938	.99938	.55000	.91470	.36470
56	3.37000	4.53162	1.16162	.50000	.34510	.15490
57	5.21000	6.68187	1.47187	.45000	1.01831	.56831
58	4.78000	5.74360	.96360	.50000	1.37639	.87639
59	4.19000	4.76176	.57176	.26000	.39283	.13283
60	6.22000	7.97805	1.75805	.75000	1.37767	.62767
mean±SD	4.626±	6.279±	1.871±	1.053±	1.49±	0.754±
(Range)	1.206	1.385	1.039	0.853	1.041	0.784
	(2.63-8.23)	(3.807-10.387)	(0.083-4.417)	(0.22-5.01)	(0.178-4.713)	(0.002-3.523)
n	n = 60	n = 60	n = 60	n = 58	n = 58	n = 58

B : Comparison between Measured and Predicted Peak and Trough Concentrations.

Serum Concentration Comparison	Percent Coefficient of Variation
Peak (measured) V.S. Peak (predicted)	24.319
Trough (measured) V.S. Trough (predicted)	70.750

C : Level of Difference between Measured and Predicted Peak Concentrations.

Level of Difference	Number (%)
< 1 μg/ml	12 (20%)
1 to < 2 μg/ml	28 (46.666%)
⩾ 2 μg/ml	20 (33.33%)

D : Level of Difference between Measured and Predicted Trough Concentrations .

Level of Difference	Number (%)
< 1 μg/ml	48 (80%)
1 to < 2 μg/ml	7 (11.666%)
⩾ 2 μg/ml	5 (9.33%)

Analysis of the serum concentration data also revealed that the observed volumes of distribution for this group of patients were significantly greater than the Hull and Sarubbi's volume of distribution value (0.26 L/kg).

I. 3 The effect of the number of sample and the sampling time on the calculation of some pharmacokinetic parameters

To determine individualized pharmacokinetic variable value, the Sawchuk and Zaske method which used a minimum of three serum drug concentrations (43) from a subsequent dose to calculate elimination rate constant (Kel) from linear least-squares regression analysis was applied. This elimination rate constant and other pharmacokinetic parameters which obtained by using this elimination rate constant i.e. volume of distribution (Vd) and half-life ($t_{1/2}$) were chosen to be the reference values.

Different elimination rate constants were obtained when the sampling time and number of sample points used were different. The result was presented in Table 5. Three serum samples had been collected in each patients. The first sample was collected just prior to the studied dose, the concentration obtatined from the analysis of this sample was taken as the trough concentration and would be called C_{trough} or $Cpmin_{ss}$. The second sample was

Table 5 Calculated Elimination Rate Constant Values Using Different Number and Sampling Time of Serum Gentamicin Samples.

Patient Number	$Kel_{(scr)}$ ($hour^{-1}$)	$Kel_{(pe.t.po)}$ ($hour^{-1}$)	$Kel_{(pe.po)}$ ($hour^{-1}$)	$Kel_{(pe.t)}$ ($hour^{-1}$)	$Kel_{(po.t)}$ ($hour^{-1}$)	$Kel_{(t)}$ ($hour^{-1}$)
1	.17433	.15542	.18657	.15756	.14964	.17259
2	.12254	.25140	.35717	.25845	.23768	.24496
3	.16208	.18840	.21878	.19054	.18084	.22153
4	.19833	.20929	.27897	.21430	.19078	.23773
5	.08707	.13830	.21651	.14392	.11752	.14531
6	.17490	.36539	.31382	.36185	.37495	.40234
7	.28993	.21265	.28544	.21764	.19912	.23964
8	.20131	.23038	.43512	.23731	.22082	.23667
9	.37224	.35828	.38234	.35994	.35380	.35002
10	.32555	.33747	.51710	.35036	.28973	.34737
11	.23151	.23692	.40600	.24852	.20557	.24019
12	.09146	.08441	.01961	.08029	.09377	.12653
13	.36628	.35539	.46210	.36271	.33560	.34053
14	.18906	.09446	.02669	.08960	.11247	.18431
15	.22642	.27330	.34784	.27841	.25947	.28871
16	.14968	.16529	.17804	.16616	.16293	.19996
17	.19620	.36916	.41601	.37649	.34935	.28968
18	.09019	.15289	.22171	.15568	.14873	.16673
19	.13289	.13238	.13351	.13246	.13210	.13815
20	.16845	.04477	.05968	.04552	.04166	.07605
21	.09575	.12061	.10528	.11956	.12345	.13242
22	.27217	.30338	.30322	.30337	.30341	.32373
23	.11895	.14645	.16634	.14782	.14276	.16155
24	.31128	-	.51177	-	-	-
25	.20833	.30003	.40976	.30755	.27967	.26942
26	.22858	.21787	.24309	.21968	.21117	.26683

Continued...

Patient Number	$Kel_{(Scr)}$ ($hour^{-1}$)	$Kel_{(pe.t.po)}$ ($hour^{-1}$)	$Kel_{(pe.po)}$ ($hour^{-1}$)	$Kel_{(pe.t)}$ ($hour^{-1}$)	$Kel_{(po.t)}$ ($hour^{-1}$)	$Kel_{(t)}$ ($hour^{-1}$)
27	.14697	.23536	.30458	.23315	.24135	.26371
28	.21989	.38919	.42491	.39175	.37970	.34429
29	.11119	.07273	.16288	.07891	.05601	.11106
30	.20458	.06691	.16446	.07359	.04881	.14328
31	.26713	.22761	.22758	.22761	.22762	.25846
32	.13156	.17101	.16077	.17031	.17290	.18449
33	.25386	.44294	.44198	.44287	.44311	.41622
34	.39333	.17369	.66716	.20753	.08218	.21138
35	.27243	-	.57617	-	-	-
36	.24611	.19332	.48855	.21357	.13857	.21777
37	.25975	.19404	.45526	.21195	.14560	.29333
38	.23143	.24200	.33717	.24853	.22435	.25497
39	.20748	.13207	.48183	.15605	.06721	.18790
40	.33100	.40458	.50068	.41117	.38676	.40617
41	.24200	.24063	.23967	.24056	.24080	.25737
42	.17706	.24396	.39742	.21449	.21551	.23880
43	.23083	.28653	.33216	.28966	.27807	.31231
44	.24542	.37693	.77438	.40418	.30322	.38358
45	.18322	.16441	.11772	.16108	.17842	.18301
46	.18422	.19992	.08604	.19335	.21286	.24087
47	.11582	.15299	.11331	.15027	.16035	.16702
48	.10536	.22646	.28385	.23040	.21582	.22610
49	.21761	.30606	.48572	.31831	.27275	.32135
50	.17061	.12315	.09385	.12114	.12585	.14051
51	.26929	.16582	.11784	.16253	.17471	.19387
52	.42933	.27354	.40183	.30076	.27549	.25420

Continued...

Patient Number	$Kel_{(Scr)}$ ($hour^{-1}$)	$Kel_{(pe.t.po)}$ ($hour^{-1}$)	$Kel_{(pe.po)}$ ($hour^{-1}$)	$Kel_{(pe.t)}$ ($hour^{-1}$)	$Kel_{(po.t)}$ ($hour^{-1}$)	$Kel_{(t)}$ ($hour^{-1}$)
53	.23278	.21816	.22577	.21868	.21675	.22169
54	.31457	.30671	.52724	.32183	.26581	.32699
55	.23322	.29306	.33221	.29532	.28861	.28224
56	.34333	.27251	.26407	.27202	.27347	.29067
57	.25083	.35680	.25575	.34987	.37554	.33577
58	.19048	.30189	.28869	.30101	.33174	.29196
59	.33267	.39517	.42346	.39711	.38992	.37124
60	.23417	.29214	.43893	.30221	.266492	.29441
mean $\pm$ SD	0.219 $\pm$ 0.08	0.235 $\pm$ 0.095	0.314 $\pm$ 0.162	0.239 $\pm$ 0.097	0.222 $\pm$ 0.096	0.219 $\pm$ 0.08
(Range)	(0.087 - 0.428)	(0.045 - 0.443)	(0.02 - 0.744)	(0.046 - 0.443)	(0.042 - 0.443)	(0.087 - 0.428)
n	n = 60	n = 58	n = 60	n = 58	n = 58	n = 58

collected thirty minutes after a thirty minutes infusion of the dose, the concentration obtained from the analysis of this sample was admitted as the peak concentration and would be called C_{peak} or $Cpmax_{ss}$. The third sample was collected two hours after the infusion was finished, the concentration obtained from the analysis of this sample would be called C_{post} or $C_{t2.5}$.

When neither concentration was used and the elimination rate constant was calculated by using the individual patient's characteristic and his or her serum creatinine, this elimination rate constant was named $\underline{Kel}_{(Scr)}$.

When all three serum drug concentrations (C_{peak}, C_{trough} and C_{post}) were used in the calculation of the elimination rate constant, that elimination rate constant was named $\underline{Kel}_{(pe.t.po)}$.

When two serum drug concentrations were used for elimination rate constant calculation, three different pairs could be used. If C_{peak} and C_{trough} were used, the elimination rate constant was named $Kel_{(pe.t)}$. If C_{peak} and C_{post} were used, the elimination rate constant was called $\underline{Kel}_{(pe.po)}$. If C_{post} and C_{trough} were used, the elimination rate constant was called $\underline{Kel}_{(po.t)}$.

When one sample concentration only was used for elimination rate constant calculation, the trough

concentration or C_{trough} was used and the elimination rate constant was called $\underline{Kel_{(t)}}$.

The different elimination rate constant values obtained were presented in detail in Table 5. Their corresponding for each individual half-life ($t_{1/2}$) and volume of distribution (Vd) were calculated and presented in Table 6, and Table 7 respectively. Table 8 showed summary of the mean standard deviation and range of these pharmacokinetic parameters obtained.

Elimination rate constants using different sample points were compared with the elimination rate constant obtained from Sawchuk and Zaske method ($Kel_{pe.t.po}$). The result was presented in Table 9. The percent coefficient of variation for $Kel_{(pe.t)}$, $Kel_{(po.t)}$, $Kel_{(pe.po)}$, $Kel_{(t)}$ and $Kel_{(Scr)}$ when compared to $Kel_{(pe.t.po)}$ were 4.38, 13.21, 49.23, 21.33, and 54.98 respectively. It was therefore quite evidence that the elimination rate constant obtained from peak and trough concentrations (two sample points : $Kel_{(pe.t)}$) was least different from that obtained from three sample points while the elimination rate constant obtained from serum creatinine (without any serum gentamicin level data) was the most difference. The elimination rate constant obtained from two sample points, C_{post} and C_{trough}, was fairly good and the elimination rate constant obtained from a single serum concentration (C_{trough}) was better than that obtained from two sample

Table 6 Half-life ($t_{1/2}$) Calculated from Elimination Rate Constants Which Obtained from Different Number and Sampling Time of Serum Gentamicin Samples.

Patient Number	Half-life$_{(Ser)}$ (hour)	Half-life$_{(pe.t.po)}$ (hour)	Half-life$_{(pe.t)}$ (hour)	Half-life$_{(pe.po)}$ (hour)	Half-life$_{(po.t)}$ (hour)	Half-life$_{(t)}$ (hour)
1	3.97514	4.45882	4.39839	3.71434	4.63099	4.01537
2	5.65511	2.75661	2.68137	1.94025	2.91570	2.82899
3	4.27558	3.67840	3.63703	3.16757	3.83203	3.12826
4	3.49412	3.31116	3.23378	2.48414	3.63254	2.91512
5	7.95942	5.01076	4.81518	3.20078	5.89692	4.76918
6	3.96226	1.89660	1.91514	2.20829	1.84823	1.72243
7	2.39020	3.25886	3.18413	2.42786	3.48040	2.89189
8	3.44241	3.00813	2.92029	1.59268	3.13829	2.92808
9	1.86172	1.93424	1.92534	1.81210	1.95873	1.97991
10	2.12869	2.05355	1.97797	1.34017	2.09188	1.99500
11	2.99335	2.92501	2.78856	1.70691	3.37118	2.88519
12	7.57693	8.20955	8.63121	35.33847	7.39011	5.47699
13	1.89201	1.94995	1.91062	1.49968	2.06493	2.03505
14	3.66552	7.33638	7.73437	25.96478	6.16171	3.75987
15	3.06073	2.53567	2.48912	1.99228	2.67078	2.40034
16	4.62989	4.19263	4.17057	3.89236	4.25349	3.46566
17	3.53211	1.87723	1.84070	1.45584	1.98371	2.39233
18	7.68338	4.53264	4.45152	3.12570	4.65958	4.15641
19	5.21488	5.23493	5.23166	5.19056	5.24301	4.38197
20	4.11392	15.48015	15.22431	11.61174	16.63586	9.11245
21	7.23762	5.74577	5.79630	6.58220	5.61348	5.23344
22	2.54623	2.28426	2.28434	2.28544	2.28404	2.14069
23	5.82586	4.73192	4.68828	4.16629	4.85416	4.28963
24	2.22631	1.35413	-	1.35413	-	-
25	3.32640	2.30980	2.25329	1.69123	2.47788	2.57216
26	3.03172	3.18083	3.15459	2.85080	3.28178	2.59719

Continued...

Patient Number	Half-life$_{(Scr)}$ (hour)	Half-life$_{(pe.t.po)}$ (hour)	Half-life$_{(pe.t)}$ (hour)	Half-life$_{(pe.po)}$ (hour)	Half-life$_{(po.t)}$ (hour)	Half-life$_{(t)}$ (hour)
27	4.71512	2.94438	2.97236	2.27524	2.87129	2.62790
28	3.15163	1.78063	1.76899	1.63093	1.82514	2.01281
29	6.23259	9.52888	8.78227	4.25478	12.37328	6.24007
30	3.38738	10.35789	9.41643	4.21384	14.19675	4.83664
31	2.59429	3.04464	3.04467	3.04506	3.044457	20.68123
32	5.26757	4.05246	4.36916	4.31051	4.00799	3.75637
33	2.72985	1.56456	1.56479	1.56794	1.56394	1.66499
34	1.76186	3.98978	3.33926	1.03874	8.43281	3.27843
35	2.54377	1.20277	-	1.20277	-	-
36	2.81580	3.58469	3.24490	1.41847	5.00105	3.18228
37	2.66795	3.57143	3.26960	1.52221	4.75978	2.36256
38	2.99444	2.86359	2.78841	2.05537	3.08885	2.71793
39	3.34003	5.24718	4.44077	1.43826	10.31158	3.68818
40	2.09366	1.71287	1.68542	1.38411	1.79181	1.70618
41	2.86364	2.87998	2.88077	2.89145	2.87787	2.69266
42	3.91387	2.84057	2.72311	1.74373	3.21569	2.90206
43	3.00217	2.41856	2.39243	2.08632	2.49216	2.21892
44	2.82377	1.83854	1.71457	0.89490	2.28548	1.80666
45	3.78225	4.21501	4.30229	5.88690	3.88409	3.78671
46	3.76176	3.46644	3.58422	8.05395	3.25571	2.87706
47	5.98356	4.52974	4.61177	6.11621	4.32185	4.114924
48	6.57733	3.06011	3.00783	2.44146	3.21098	3.06496
49	3.18377	2.26429	2.17721	1.42674	2.53894	2.15656
50	4.06180	5.62738	5.72075	7.38426	5.38964	4.93207
51	2.57347	4.17930	4.26389	5.88079	3.96646	3.57451
52	1.61416	2.36087	2.30416	1.72461	2.51555	2.72623

Continued...

Patient Number	Half-life$_{(Scr)}$ (hour)	Half-life$_{(po.t.po)}$ (hour)	Half-life$_{(po.t)}$ (hour)	Half-life$_{(po.po)}$ (hour)	Half-life$_{(po.t)}$ (hour)	Half-life$_{(t)}$ (hour)
53	2.97702	3.17652	3.16894	3.06950	3.19720	3.12600
54	2.20300	2.25950	2.15331	1.31439	2.60717	2.11934
55	2.97141	2.36468	2.34659	2.08600	2.40113	2.45539
56	2.21845	2.54303	2.54758	2.62428	2.53411	2.38411
57	2.76279	1.94227	1.98074	2.70963	1.84536	2.06391
58	3.63811	2.29553	2.30225	2.40050	2.08901	2.36555
59	2.08317	1.75367	1.74511	1.63651	1.77727	1.86669
60	2.95935	2.37213	2.29313	1.57886	2.61588	2.35388
mean ± SD	3.663 ± 1.562	3.733 ± 2.417	3.654 ± 2.356	3.832 ± 5.469	4.12 ± 2.975	3.146 ± 1.306
Rang	(1.614-7.959)	(1.565-15.48)	(1.565-15.23)	(0.895-35.34)	(1.565-16.64)	(1.665-9.112)
n	n = 60	n = 58	n = 58	n = 60	n = 58	n = 58

Table 7 Volume of Distribution Values Estimated from Different Values of Elimination Rate Constants in Calculation.

Patient Number	$Vd_{(pe.t.po)}$ (L/kg)	$Vd_{(pe.t)}$ (L/kg)	$Vd_{(pe.po)}$ (L/kg)	$Vd_{(po.t)}$ (L/kg)	$Vd_{(Scr)}$ (L/kg)	$Vd_{(t)}$ (L/kg)
1	.35680	.35644	.32571	.38798	.26	.26
2	.24560	.24505	.22170	.35182	.26	.26
3	.37123	.37092	.34905	.46273	.26	.26
4	.34406	.34345	.31055	.48849	.26	.26
5	.27473	.27399	.22359	.41615	.26	.26
6	.48496	.48544	.50674	.43858	.26	.26
7	.38890	.38819	.34801	.45926	.26	.26
8	.33722	.33639	.27593	.36586	.26	.26
9	.31734	.31719	.31197	.33273	.26	.26
10	.27799	.27701	.25402	.54278	.26	.26
11	.29745	.29629	.25298	.43478	.26	.26
12	.62163	.62311	1.88874	.48912	.26	.26
13	.29226	.29167	.27458	.36067	.26	.26
14	.85197	.85497	2.31094	.68026	.26	.26
15	.35853	.35795	.33284	.41964	.26	.26
16	.43277	.43260	.41699	.44732	.26	.26
17	.16559	.16526	.15616	.20407	.26	.26
18	.36161	.36125	.32082	.38094	.26	.26
19	.39627	.39625	.39646	.39757	.26	.26
20	.54186	.54126	.43230	.59996	.26	.26
21	.34764	.34785	.37856	.33161	.26	.26
22	.39642	.39642	.39648	.39629	.26	.26
23	.35136	.35112	.32853	.37127	.26	.26
24	.32907	-	.33631	-	.26	.26
25	.23778	.23724	.21851	.29800	.26	.26
26	.42725	.42698	.40994	.52773	.26	.26

Continued...

Patient Number	$Vd_{(pe.t.po)}$ (L/kg)	$Vd_{(pe.t)}$ (L/kg)	$Vd_{(pe.po)}$ (L/kg)	$Vd_{(po.t)}$ (L/kg)	$Vd_{(Scr)}$ (L/kg)	$Vd_{(t)}$ (L/kg)
27	.42061	.42094	.38041	.39171	.26	.26
28	.19248	.19235	.18881	.25922	.26	.26
29	.47276	.47023	.29170	.72295	.26	.26
30	.77648	.77167	.45159	1.27780	.26	.26
31	.41732	.417.2	.41809	.41729	.26	.26
32	.35395	.35406	.36536	.34488	.26	.26
33	.29352	.29353	.29367	.29300	.26	.26
34	.32708	.32289	.22963	1.37367	.26	.26
35	.41939	-	.42503	-	.26	.26
36	.32866	.32619	.25004	.69391	.26	.26
37	.66873	.66425	.51534	1.28711	.26	.26
38	.34057	.33983	.30535	.42020	.26	.26
39	.43006	.42520	.27844	1.41042	.26	.26
40	.34372	.34312	.32812	.41346	.26	.26
41	.37222	.37223	.37280	.37144	.26	.26
42	.27879	.27782	.24076	.39164	.26	.26
43	.40187	.40148	.38388	.44180	.26	.26
44	.30182	.29963	.37327	.66045	.26	.26
45	.38282	.38340	.46341	.32142	.26	.26
46	.45537	.45656	.68844	.40911	.26	.26
47	.36245	.36293	.43248	.32599	.26	.26
48	.30420	.30378	.20987	.34626	.26	.26
49	.34560	.34435	.30845	.49870	.26	.26
50	.37560	.37604	.44719	.34369	.26	.26
51	.42163	.42226	.51256	.37290	.26	.26
52	.18506	.18467	.17081	.26853	.26	.26

Continued...

Patient Number	$Vd_{(pe.t.po)}$ (L/kg)	$Vd_{(pe.t)}$ (L/kg)	$Vd_{(pe.po)}$ (L/kg)	$Vd_{(po.t)}$ (L/kg)	$Vd_{(scr)}$ (L/kg)	$Vd_{(t)}$ (L/kg)
53	.32344	.32338	.31885	.32910	.26	.26
54	.35307	.35151	.31054	.55599	.26	.26
55	.30093	.30072	.28976	.31059	.26	.26
56	.38240	.38246	.38649	.37956	.26	.26
57	.30317	.30377	.33791	.24883	.26	.26
58	.26127	.26134	.26484	.24134	.26	.26
59	.28523	.28508	.28058	.30121	.26	.26
60	.31066	.30972	.27895	.42149	.26	.26
mean ± SD	0.37 ± 0.124	0.371 ± 0.123	0.397 ± 0.335	0.473 ± 0.262	0.26 ± 0.0	0.26 ± 0.0
(Range)	(0.166- 0.852)	(0.165 - 0.855)	(0.156 - 2.311)	(0.204 - 1.41)	(0.26 - 0.26)	(0.26 - 0.26)
n	n = 60	n = 58	n = 60	n = 58	n = 60	n = 60

Table 8 Summarized Different Pharmacokinetic Parameters Obtained in This Study.

	Kel means ± SD (Range) n	Vd means ± SD (Range) n	Half-life means ± SD (Range) n
3P : Peak-Trough-Post	0.235 ± 0.095 (0.045 - 0.443) n = 58	0.372 ± 0.124 (0.166 - 0.852) n = 58	3.733 ± 2.417 (1.565 - 15.48 n = 58
2P : Peak-Trough	0.239 ± 0.097 (0.046 - 0.443) n = 58	0.371 ± 0.123 (0.165 - 0.855) n = 58	3.654 ± 2.356 (1.565 - 15.224) n = 58
: Post-Trough	0.222 ± 0.096 (0.042 - 0.443) n = 58	0.473 ± 0.262 (0.204 - 1.41) n = 58	4.12 ± 2.975 (1.565 - 16.638) n = 58
: Peak-Post	0.314 ± 0.162 (0.02 - 0.744) n = 60	0.397 ± 0.335 (0.156 - 2.311) n = 60	3.832 ± 5.469 (0.895 - 35.338) n = 60
1P : Trough	0.249 ± 0.08 (0.076 - 0.416) n = 58	0.26 ± 0.00 (0.26 - 0.26) n = 58	0.26 ± 0.00 (0.26 - 0.26) n = 58
0P : Prediction with Hull and Sarubbi	0.219 ± 0.08 (0.087 - 0.428) n = 60	0.26 ± 0.00 (0.26 - 0.26) n = 60	3.663 ± 1.562 (1.614 - 7.959) n = 60

Table 9 Comparison between Elimination Rate Constant (Kel) Values Estimated from Different Number and Sampling Time of Serum Gentamicin Samples.

Comparison between different Kel	Percent coefficent of variation
1. $Kel_{(pe.t.po)}$ (n = 58) V.S. $Kel_{(pe.t)}$ (n = 58)	% CV = 4.382
2. $Kel_{(pe.t.po)}$ (n = 58) V.S. $Kel_{(po.t)}$ (n = 58)	% CV = 13.207
3. $Kel_{(pe.t.po)}$ (n = 58) V.S. $Kel_{(pe.po)}$ (n = 58)	% CV = 49.230
4. $Kel_{(pe.t.po)}$ (n = 58) V.S. $Kel_{(t)}$ (n = 58)	% CV = 21.333
5. $Kel_{(pe.t.po)}$ (n = 58) V.S. $Kel_{(Scr)}$ (n = 58)	% CV = 54.980

n = Number of Sample

% CV = Percent Coefficient of Variation

points, C_{peak} and C_{post}. The correlation between $Kel_{(Scr)}$ and $Kel_{(pe.t.po)}$, $Kel_{(pe.t.po)}$ and $Kel_{(t)}$, $Kel_{(pe.t.po)}$ and $Kel_{(po.t)}$, $Kel_{(pe.t.po)}$ and $Kel_{(pe.po)}$ and $Kel_{(pe.t.po)}$ and $Kel_{(pe.t)}$ were presented in Figures 3, 4, 5, 6, and 7 respectively and the correlation coefficients were 0.555, 0.957, 0.972, 0.676, and 0.996 respectively.

Table 10 showed the comparison between $t_{1/2}$ obtained from $Kel_{(pe.t.po)}$ and those obtained form other Kel and Table 11 showed the comparison between Vd obtained from $Kel_{(pe.t.po)}$ and those obtained from other Kel. The percent coefficient of variation for $Half\text{-}life_{(pe.t)}$, $Half\text{-}life_{(po.t)}$, $Half\text{-}life_{(pe.po)}$, $Half\text{-}life_{(t)}$ and $Half\text{-}life_{(Scr)}$ when compared to $Half\text{-}life_{(pe.t.po)}$ were 4.08, 19.48, 68.77, 16.04, and 37.09 respectively, and for $Vd_{(pe.t)}$, $Vd_{(po.t)}$, $Vd_{(pe.po)}$, $Vd_{(t)}$ and $Vd_{(Scr)}$ when compared to $Vd_{(pe.t.po)}$ were 0.31, 44.34, 38.11, 29.78, and 29.78 respectively.

From the results of comparison, pharmacokinetic parameters obtained from peak and trough concentrations gave least different from those obtained from three sample points (peak, trough and post concentrations).

Correlation coefficient	=	0.55587
$t_{95\%,\ calc}$	=	5.00419
$t_{95\%,\ table}$	≈	2.00400

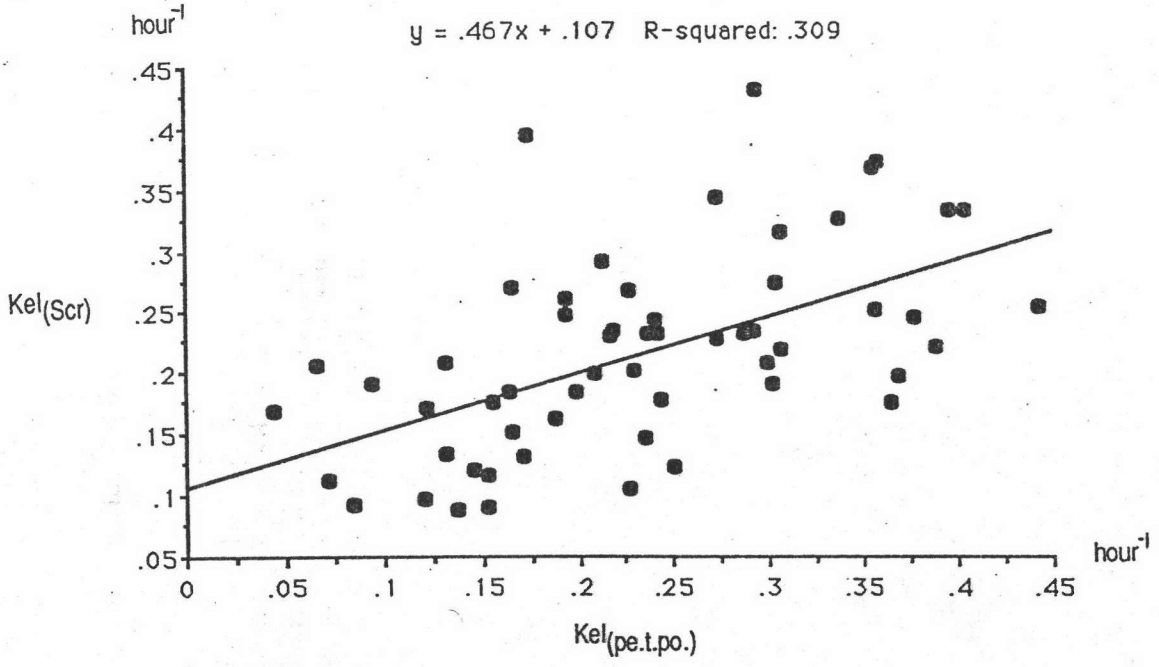

Figure 3 Correlation between $Kel_{(pe.t.po)}$ and $Kel_{(Scr)}$

Correlation coefficient	=	0.95707
$t_{95\%,\ calc}$	=	24.71167
$t_{95\%,\ table}$	≃	2.00400

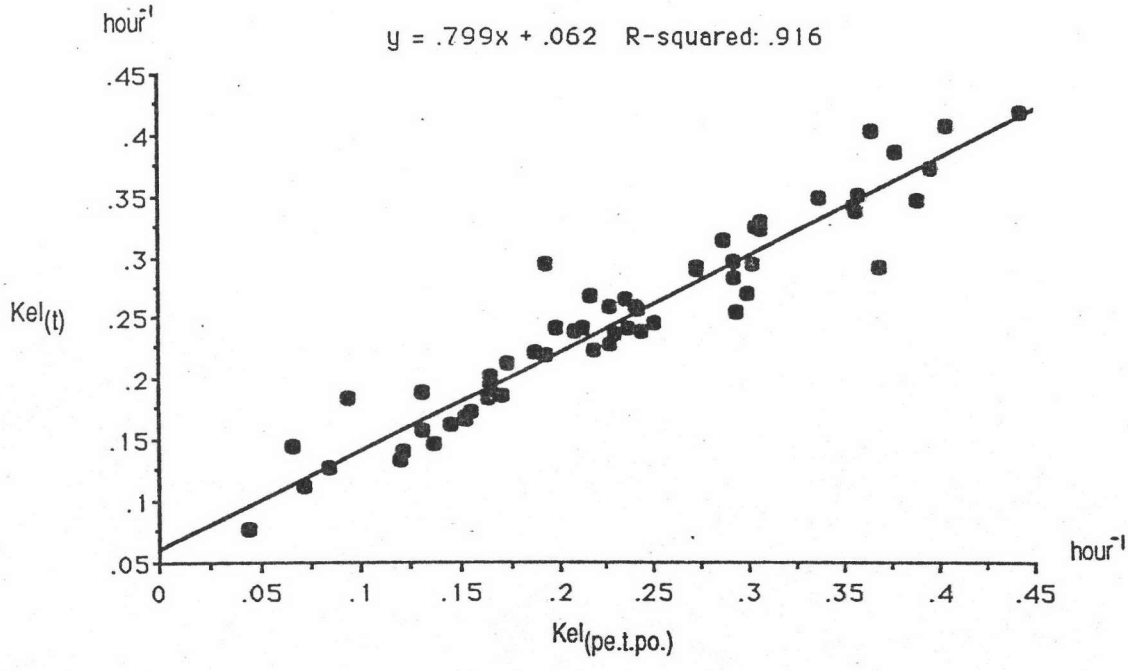

Figure 4 Correlation between $Kel_{(pe.t.po)}$ and $Kel_{(t)}$

Correlation coefficient = 0.97211

$t_{95\%,\ calc}$ = 31.01905

$t_{95\%,\ table}$ ≃ 2.00400

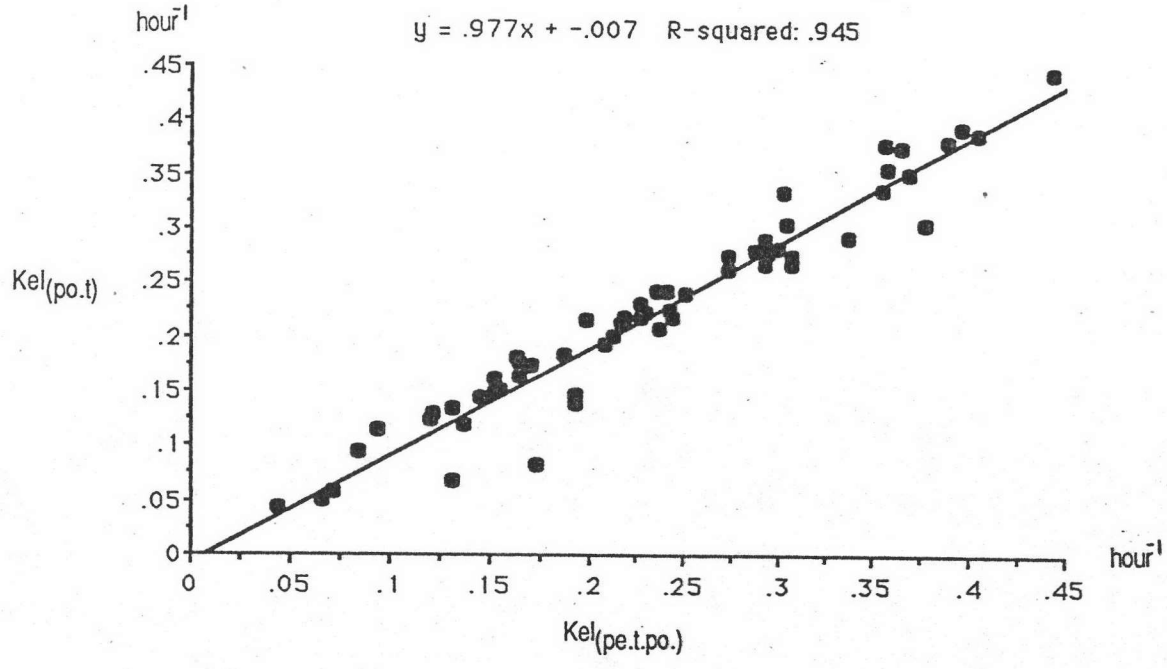

Figure 5 Correlation between $Kel_{(pe.t.po)}$ and $Kel_{(po.t)}$

Correlation coefficient = 0.67601

$t_{95\%,\ calc}$ = 6.86518

$t_{95\%,\ table}$ ≈ 2.00400

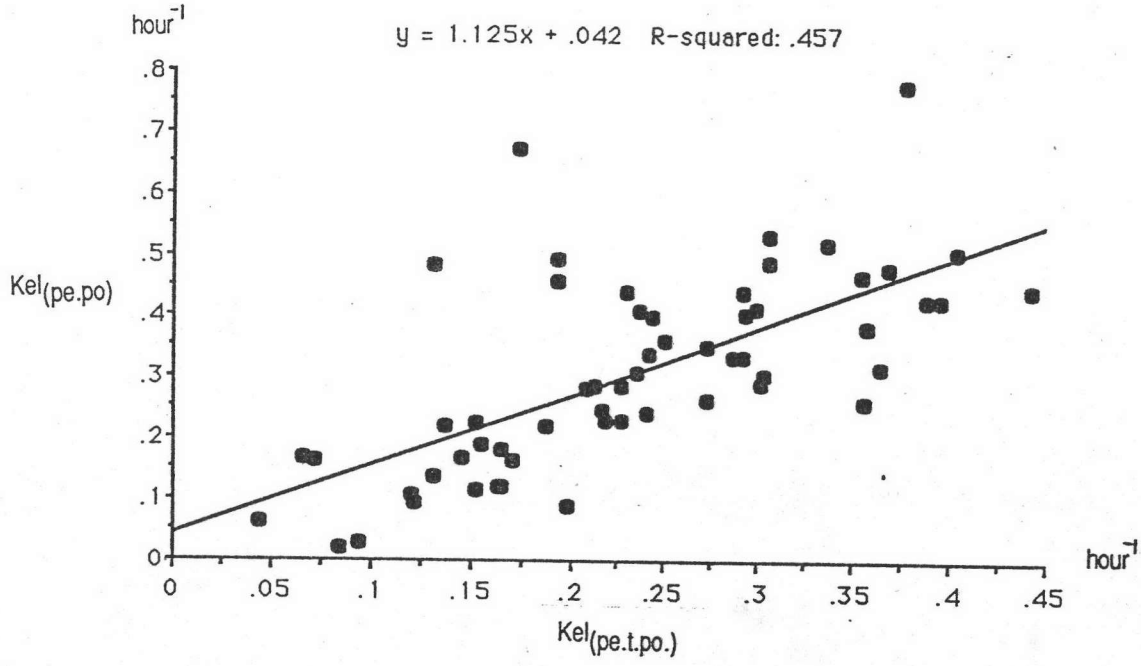

Figure 6 Correlation between $Kel_{(pe.t.po)}$ and $Kel_{(pe.po)}$

Correlation coefficient	=	0.99649
$t_{95\%,\ calc}$	=	89.12912
$t_{95\%,\ table}$	≈	2.00400

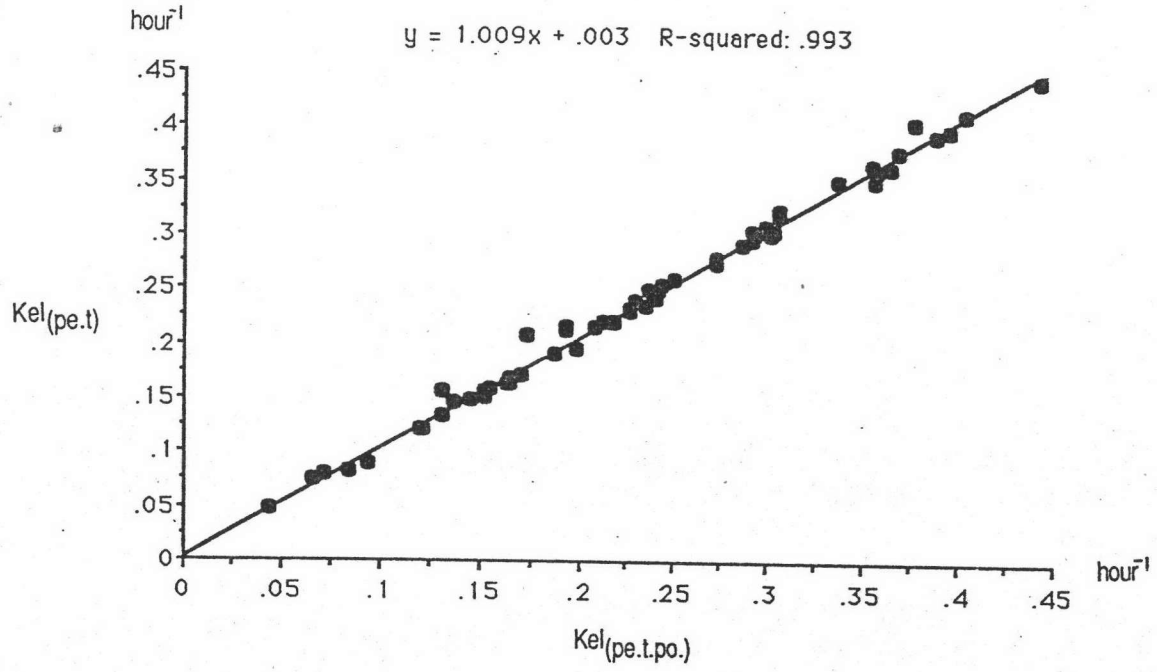

Figure 7 Correlation between $Kel_{(pe.t.po)}$ and $Kel_{(pe.t)}$

Table 10 Comparison between Volume of Distribution (Vd) Values Estimated from Different Values of Elimination Rate Constants in Calculation.

Comparison between different Vd	Percent coefficient of variation
1. $Vd_{(pe.t.po)}$ (n = 58) V.S. $Vd_{(pe.t)}$ (n = 58)	% CV = 0.308
2. $Vd_{(pe.t.po)}$ (n = 58) V.S. $Vd_{(po.t)}$ (n = 58)	% CV = 44.336
3. $Vd_{(pe.t.po)}$ (n = 58) V.S. $Vd_{(pe.po)}$ (n = 58)	% CV = 38.106
4. $Vd_{(pe.t.po)}$ (n = 58) V.S. $Vd_{(t)}$ (n = 58)	% CV = 29.780
5. $Vd_{(pe.t.po)}$ (n = 58) V.S. $Vd_{(scr)}$ (n = 58)	% CV = 29.780

n = Number of Sample

% CV = Percent Coefficient of Variation

Table 11 Comparison between Half-life ($t_{1/2}$) Values Obtained from Elimination Rate Constant Which Estimated from Different Number and Sampling Time of Serum Gentamicin Samples.

Comparison between different Half-life	Percent coefficent of variation
1. $Half\text{-}life_{(pe.t.po)}$ (n = 58) V.S. $Half\text{-}life_{(pe.t)}$ (n = 58)	% CV = 4.080
2. $Half\text{-}life_{(pe.t.po)}$ (n = 58) V.S. $Half\text{-}life_{(po.t)}$ (n = 58)	% CV = 19.481
3. $Half\text{-}life_{(pe.t.po)}$ (n = 58) V.S. $Half\text{-}life_{(pe.po)}$ (n = 58)	% CV = 68.769
4. $Half\text{-}life_{(pe.t.po)}$ (n = 58) V.S. $Half\text{-}life_{(t)}$ (n = 58)	% CV = 16.044
5. $Half\text{-}life_{(pe.t.po)}$ (n = 58) V.S. $Half\text{-}life_{(Ser)}$ (n = 58)	% CV = 37.087

n = Number of Sample

% CV = Percent Coefficient of Variation

I. 4 Calculation of dosage regimen by using individual pharmacokinetic parameters of the patient

Instruction of physicians on gentamicin usage often emphasizes selection of the appropriate agent for specific pathogens and infection, with secondary focus on average dosing practice and toxicity concerns. In the absence of a background in pharmacokinetic and toxicity principles, it may be easy for physicians to presume that the proper choice of a drug given in conventional doses should result in positive outcome for their patients.

Recommended dosage regimens were calculated by using individual pharmacokinetic parameters using different sets of sample as shown in Table 12. The same desired peak (6 μg/ml) and trough (1 μg/ml) concentrations were used in the calculation. The difference between the dosage regimen (DR) that calculated by using pharmacokinetic parameters obtained from three sample points ($DR_{(pe.t.po)}$) and the dosage regimen that calculated by using pharmacokinetic parameters obtained from other sets of sample points ($DR_{(pe.t)}$, $DR_{(po.t)}$, $DR_{(pe.po)}$, $DR_{(t)}$) were summarized in Table 13. The difference between $DR_{(pe.t.po)}$ and the dosage regimens that calculated by using the pharmacokinetic parameters obtained from Hull and Sarubbi method and equation ($DR_{(Scr)}$) were also presented in Table 13. $DR_{(pe.t)}$ was least different from $DR_{(pe.t.po)}$.

Table 12 Summarized Different Recommended Dosage Regimen Obtained from Different Pharmacokinetic Parameters.

Patient Number	Initial Dosage Regimen		Recommended Dosage Regimen											
			Samples Used for the Calculation											
			Serum Creatinine		3 Points Peak-Trough-Post		2 Points Peak-Trough		2 Points Peak-Post		2 Points Post-Trough		1 Point Trough	
	MD (mg)	Interval (hour)	MD1 (mg)	Interval.1 (hour)	MD2 (mg)	Interval.2 (hour)	MD3 (mg)	Interval.3 (hour)	MD4 (mg)	Interval.4 (hour)	MD5 (mg)	Interval.5 (hour)	MD6 (mg)	Interval.6 (hour)
1	60	8	70	12	100	12	100	12	90	12	100	12	70	12
2	50	8	50	12	60	8	60	8	60	6	80	8	60	8
3	40	8	70	12	100	12	100	8	90	8	130	12	70	8
4	60	8	60	8	80	8	80	8	70	6	110	8	60	8
5	40	8	60	24	60	12	60	12	50	8	80	12	50	12
6	70	8	70	12	140	6	140	6	140	6	120	6	80	6
7	80	8	70	6	100	8	100	8	90	6	110	8	70	8
8	80	8	70	8	100	8	100	8	90	6	100	8	70	8
9	60	8	90	6	100	6	100	6	100	6	110	6	90	6
10	100	8	100	6	100	6	100	6	110	6	190	6	100	6
11	60	8	70	8	80	8	80	8	70	6	110	8	70	8
12	50	12	60	24	140	24	140	24	400	90	110	24	50	12
13	60	8	80	6	80	6	80	6	90	6	110	6	80	6
14	80	8	70	8	240	24	240	24	600	64	170	12	80	12
15	60	8	70	8	100	8	100	6	100	6	120	8	70	6
16	60	8	80	12	140	12	140	12	130	12	140	12	80	8
17	80	8	70	8	60	6	60	6	60	6	70	6	80	6
18	60	12	50	24	70	12	70	12	60	8	70	12	50	12
19	80	8	70	12	100	12	100	12	100	12	110	12	80	12

Continued..

Patient Number	Initial Dosage Regimen		Recommended Dosage Regimen											
			Samples Used for the Calculation											
			Serum Creatinine		3 Points Peak-Trough-Post		2 Points Peak-Trough		2 Points Peak-Post		2 Points Post-Trough		1 Point Trough	
	MD (mg)	Interval (hour)	MD1 (mg)	Interval.1 (hour)	MD2 (mg)	Interval.2 (hour)	MD3 (mg)	Interval.3 (hour)	MD4 (mg)	Interval.4 (hour)	MD5 (mg)	Interval.5 (hour)	MD6 (mg)	Interval.6 (hour)
20	60	8	80	12	140	36	140	36	120	36	180	48	70	24
21	60	8	70	24	80	12	80	12	80	12	80	12	60	12
22	60	8	80	8	110	6	110	6	110	6	110	6	80	6
23	50	8	60	12	100	12	100	12	90	12	100	12	70	12
24	80	8	80	6	-	-	-	-	120	6	-	-	-	-
25	80	8	80	8	80	6	80	6	80	6	100	6	90	8
26	60	8	60	8	100	8	100	8	100	8	120	8	60	8
27	60	8	60	12	100	8	100	8	90	6	100	8	70	8
28	80	8	70	8	60	6	60	6	60	6	80	6	70	6
29	60	8	60	12	120	24	120	24	80	12	190	36	60	12
30	80	8	70	8	200	24	200	24	120	12	330	36	70	12
31	80	8	70	8	100	8	100	8	100	8	100	8	70	8
32	60	8	70	12	110	12	110	12	110	12	110	12	80	12
33	80	8	70	8	80	6	80	6	80	6	80	6	70	6
34	60	8	90	6	100	12	100	8	90	6	420	24	80	8
35	80	8	70	8	-	-	-	-	130	6	-	-	-	-
36	60	8	70	8	80	8	80	8	80	6	160	12	70	8
37	60	8	50	8	120	8	120	8	120	6	240	12	50	6
38	60	8	70	8	100	8	100	8	80	6	110	8	70	8

Continued...

Patient Number	Initial Dosage Regimen		Recommended Dosage Regimen											
			Samples Used for the Calculation											
			Serum Creatinine		3 Points Peak-Trough-Post		2 Points Peak-Trough		2 Points Peak-Post		2 Points Post-Trough		1 Point Trough	
	MD (mg)	Interval (hour)	MD1 (mg)	Interval.1 (hour)	MD2 (mg)	Interval.2 (hour)	MD3 (mg)	Interval.3 (hour)	MD4 (mg)	Interval.4 (hour)	MD5 (mg)	Interval.5 (hour)	MD6 (mg)	Interval.6 (hour)
39	60	8	50	8	90	12	90	12	80	6	280	24	60	12
40	80	8	80	6	110	6	110	6	110	6	130	6	80	6
41	80	8	90	8	120	8	120	8	120	8	120	8	90	8
42	60	8	70	12	80	8	80	8	70	6	100	8	70	8
43	80	8	70	8	110	6	110	6	120	6	120	6	80	6
44	80	8	70	8	90	6	90	6	130	6	180	6	80	6
45	60	8	60	12	90	12	90	12	90	12	80	12	60	12
46	80	8	70	12	110	8	110	8	180	24	100	8	70	8
47	80	8	60	12	100	12	90	12	100	12	90	12	70	12
48	60	8	40	12	60	8	60	8	60	6	70	8	50	8
49	60	8	70	8	90	6	90	6	100	6	140	8	70	6
50	60	8	70	12	90	12	90	12	120	24	90	12	70	12
51	80	8	70	8	100	12	100	12	100	12	90	12	60	8
52	60	8	80	6	50	6	50	6	50	6	70	8	70	8
53	80	8	70	8	90	8	90	8	90	8	90	8	70	8
54	60	8	70	6	100	6	100	6	100	6	160	8	80	6
55	60	8	70	8	80	6	80	6	80	6	80	6	70	6
56	60	8	70	6	110	8	110	8	100	8	110	8	70	6
57	80	8	70	8	90	6	90	6	100	8	70	6	70	6

Continued...

Patient Number	Initial Dosage Regimen		Recommended Dosage Regimen											
			Samples Used for the Calculation											
			Serum Creatinine		3 Points Peak-Trough-Post		2 Points Peak-Trough		2 Points Peak-Post		2 Points Post-Trough		1 Point Trough	
	MD (mg)	Interval (hour)	MD1 (mg)	Interval.1 (hour)	MD2 (mg)	Interval.2 (hour)	MD3 (mg)	Interval.3 (hour)	MD4 (mg)	Interval.4 (hour)	MD5 (mg)	Interval.5 (hour)	MD6 (mg)	Interval.6 (hour)
58	60	8	60	8	70	6	70	6	70	6	70	6	70	6
59	60	8	70	6	80	6	80	6	80	6	90	6	70	6
60	80	8	60	8	70	6	70	6	70	6	100	6	60	6

The predictive methods (algorithms or dosing chart) appear superior to physician intuition but are still subject to consider error and should only be used as starting point in therapy as seen from the result here. Only 2 out of the 58 cases studied showed the same dosage regimen when the pharmacokinetic parameters obtained from using serum creatinine (without any data of serum drug concentration) were used for dosage regimen calculation as compared to the dosage regimen obtained when three samples of serum drug concentrations were involved. Therapy can be best improved to the individual patient using measured serum gentamicin concentrations.

In clinical practice, the three sample point (peak, trough and post) pharmacokinetic parameters and two sample point (peak and trough) pharmacokinetic parameters provided the same dosage regimens 56 out of the 58 cases studied when these pharmacokinetic parameters were used to calculate dosage regimens. When two sample points were used, the sampling time relative to the time after the dose administered was improved (61, 7, 8). The proper sampling time can reduce much of the error. When one serum drug concentration sample was used to provide the pharmacokinetic parameters necessary for drug dosage regimen calculation, 4 out of 60 cases resulted in the same dosage regimen as $DR_{(pe.t.po)}$. The percentage of accuracy was not high since the less number of sample points which could provide the same accuracy was considered

Table 13 Comparison between Dosage Regimen Calculated from Different Elimination Rate Constants.

	$DR_{(pe.t.po)}$ V.S. $DR_{(Scr)}$	$DR_{(pe.t.po)}$ V.S. $DR_{(pe.t)}$	$DR_{(pe.t.po)}$ V.S. $DR_{(pe.po)}$	$DR_{(pe.t.po)}$ V.S. $DR_{(po.t)}$	$DR_{(pe.t.po)}$ V.S. $DR_{(t)}$
1. Same Dosage Regimen	2(3.45%)	56(96.55%)	22(37.93%)	17(29.31%)	4(6.90%)
2. Different Dosage Regimen	56(96.55%)	2(3.45%)	36(62.07%)	41(70.69%)	54(93.10%)
: Only Interval	2(3.57%)	1(50%)	5(13.89%)	-	36(66.66%)
: Only MD	26(46.43%)	1(50%)	12(33.33%)	29(70.70%)	-
: Both MD and Interval	28(50%)	-	19(52.78%)	12(29.27%)	18(33.33%)

$DR_{(Scr)}$ = Dosage Regimen Calculated by Using $Kel_{(Scr)}$ (MD1 and Interval 1)

$DR_{(pe.t.po)}$ = Dosage Regimen Calculated by Using $Kel_{(pe.t.po)}$ (MD2 and Interval 2)

$DR_{(pe.t)}$ = Dosage Regimen Calculated by Using $Kel_{(pe.t)}$ (MD3 and Interval 3)

$DR_{(pe.po)}$ = Dosage Regimen Calculated by Using $Kel_{(pe.po)}$ (MD4 and Interval 4)

$DR_{(po.t)}$ = Dosage Regimen Calculated by Using $Kel_{(po.t)}$ (MD5 and Interval 5)

$DR_{(t)}$ = Dosage Regimen Calculated by Using $Kel_{(t)}$ (MD6 and Interval 6)

MD = Maintenance Dose

In = Time of Dosing Interval or τ

to be more economic and convenient to the patient. Therefore, two sample points sampling at the peak and trough concentrations was recommended for clinical practice of drug level monitoring.

II Prediction of Creatinine Clearance from Serum Creatinine

The creatinine clearance of eighteen patients were obtained from their urinary creatinine excretion rate using the standard formula for calculation of creatinine clearance (Equation 15, Appendix C). The creatinine clearance value obtained from this method which was called measured method, was compared with Cockcroft and Gault method (Equation 3 and 4, Appendix C) and Bjornsson's Nomogram (Figure A; Appendix D) which both of them required the serum creatinine data of the patient instead of the urinary creatinine excretion rate. The creatinine clearance values obtained from different methods were presented in Table 14.

There were difference in the creatinine clearance values between measured method and Cockcroft and Gault method (Percent coefficient of variation; %CV = 36.88) and between measured method and Bjornsson's Nomogram (% CV = 36.60) as shown in Table 15 A. In addition, the correlation coefficient (r) of the creatinine clearance values between measured method and Cockcroft and Gault method was = 0.715, between measured method and

Table 14 Characteristic of the Patients and their Creatinine Clearance Values Obtained from Different Methods of Estimation.

Patient Number	Sex	Age (year)	TBW (kg)	IBW (kg)	Height (cm)	Scr (mg/dl)	UCr (ml/min)	Total Volume (ml)	CrCl(Urine) (ml/min)	CrCl(Cockcroft) (ml/min)	CrCl(Nomogram) (ml/min)
1	M	34	56.50	61.96	163.00	1.54	72.00	1180	38.30	54.01330	54.11
2	M	24	60.00	63.80	165.00	1.15	53.00	1300	41.60	84.05790	81.16
3	M	27	49.00	64.72	166.00	0.85	70.00	1800	105.80	90.47386	90.92
4	M	65	47.00	46.32	146.00	1.08	45.00	1500	43.40	44.67490	47.00
5	F	46	53.50	45.50	150.00	0.92	75.00	1440	81.50	54.88300	58.10
6	F	38	47.50	52.36	158.00	1.34	43.00	1800	40.10	42.68000	43.70
7	F	31	48.00	50.52	156.00	1.05	56.00	1100	40.70	58.82539	60.00
8	M	65	63.00	64.72	166.00	1.30	65.00	1500	52.10	50.48077	51.50
9	M	52	48.00	59.66	160.50	0.67	129.00	1040	139.10	87.56219	91.00
10	F	37	66.50	51.62	156.00	1.21	46.10	1700	45.00	51.27182	52.50
11	F	20	49.50	52.82	158.50	0.49	55.00	1700	132.50	143.11224	145.00
12	F	21	54.50	56.50	162.50	0.97	48.40	2000	69.30	78.93290	80.10
13	F	22	64.00	54.70	160.00	0.79	37.40	1300	42.70	96.45587	100.00
14	M	29	44.00	60.12	161.00	1.10	26.40	3500	58.33	61.66666	59.50
15	M	60	68.00	63.80	165.00	6.04	37.80	2300	10.00	11.73657	14.70
16	M	37	66.00	73.00	175.00	1.26	50.80	3800	106.40	74.93386	73.00
17	F	36	59.00	51.94	157.00	0.80	27.50	3800	90.71	79.17632	80.50
18	M	27	49.00	64.72	166.00	0.80	37.00	2200	72.68	96.12847	92.00

Table 15 A : Comparison between Creatinine Clearance Calculated from Different Methods.

Comparison between different methods	Percent coefficient of variation
CrCl(Urine) V.S. CrCl(Cockcroft)	% CV = 36.879
CrCl(Urine) V.S. CrCl(Nomogram)	% CV = 36.591
CrCl(Cockcroft) V.S. CrCl(Nomogram)	% CV = 6.248

B : Correlation of Calculated Creatinine Clearance to Measured Creatinine Clearance.

	CrCl(Cockcroft)	CrCl(Nomogram)
CrCl(Urine)	r = 0.715	r = 0.725
	r^2 = 0.511	r^2 = 0.525
CrCl(Nomogram)	r = 0.997	-
	r^2 = 0.994	-

Correlation coefficient	=	0.71484
$t_{95\%,\ calc}$	=	4.08898
$t_{95\%,\ table}$	=	2.12000

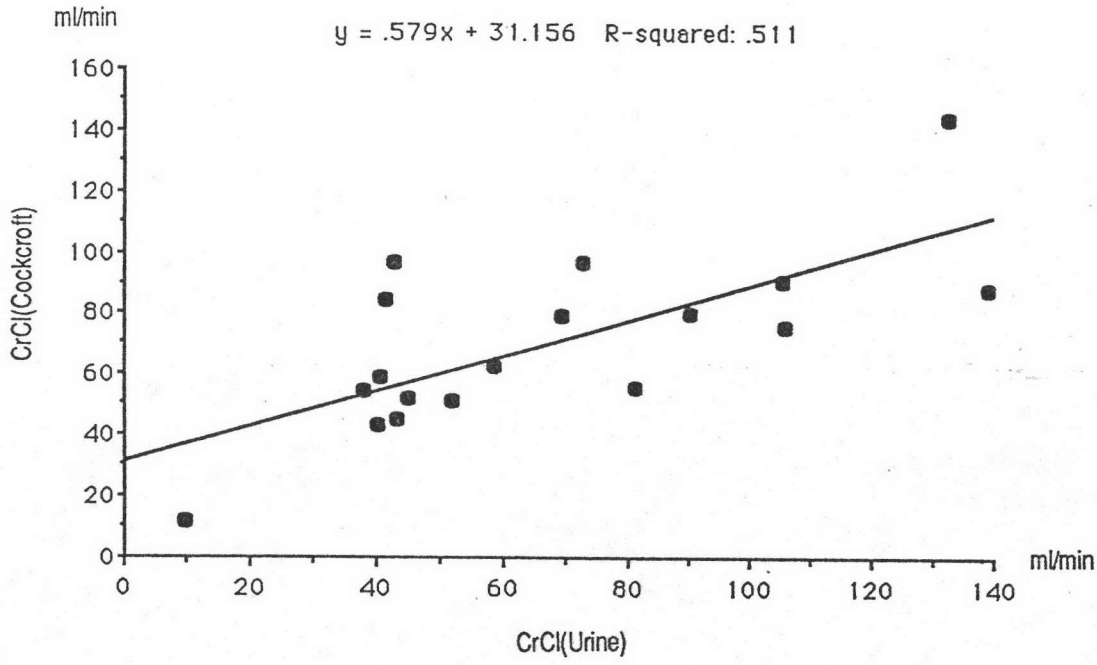

Figure 8 Correlation between CrCl(Urine) and CrCl Obtained from Cockcroft and Gault Method

Correlation coefficient = 0.72457

$t_{95\%,\ calc}$ = 4.20526

$t_{95\%,\ table}$ = 2.12000

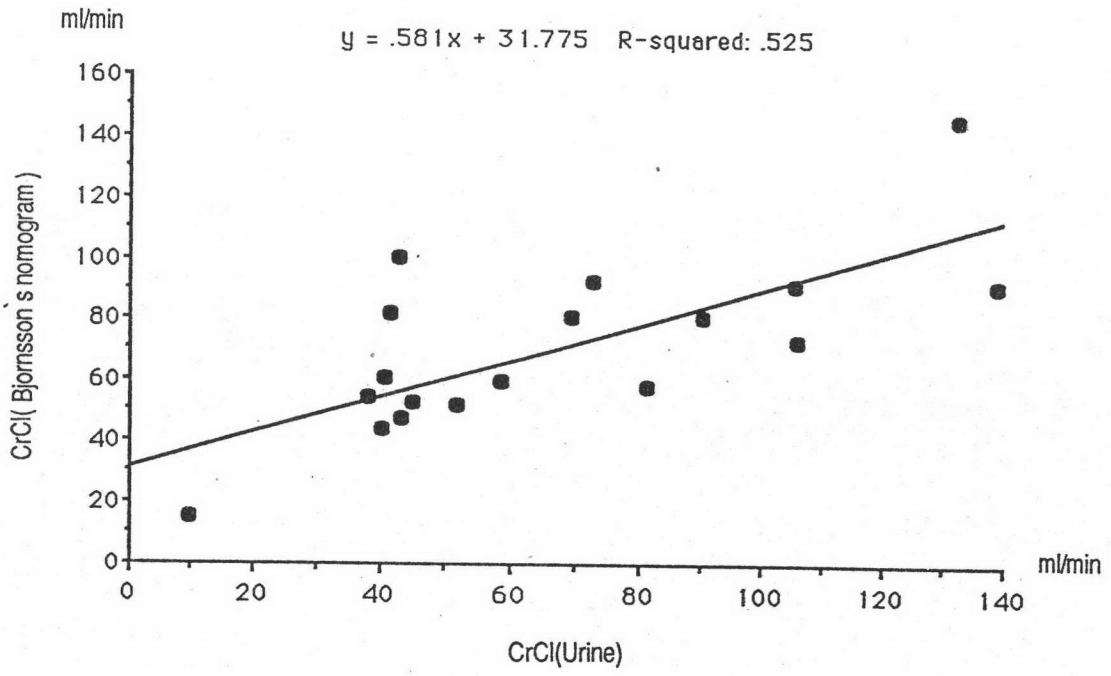

Figure 9 Correlation between CrCl(Urine) and CrCl Obtained from Bjornsson's Nomogram

Correlation coefficient	=	0.99699
$t_{95\%,\ calc}$	=	51.48463
$t_{95\%,\ table}$	=	2.12000

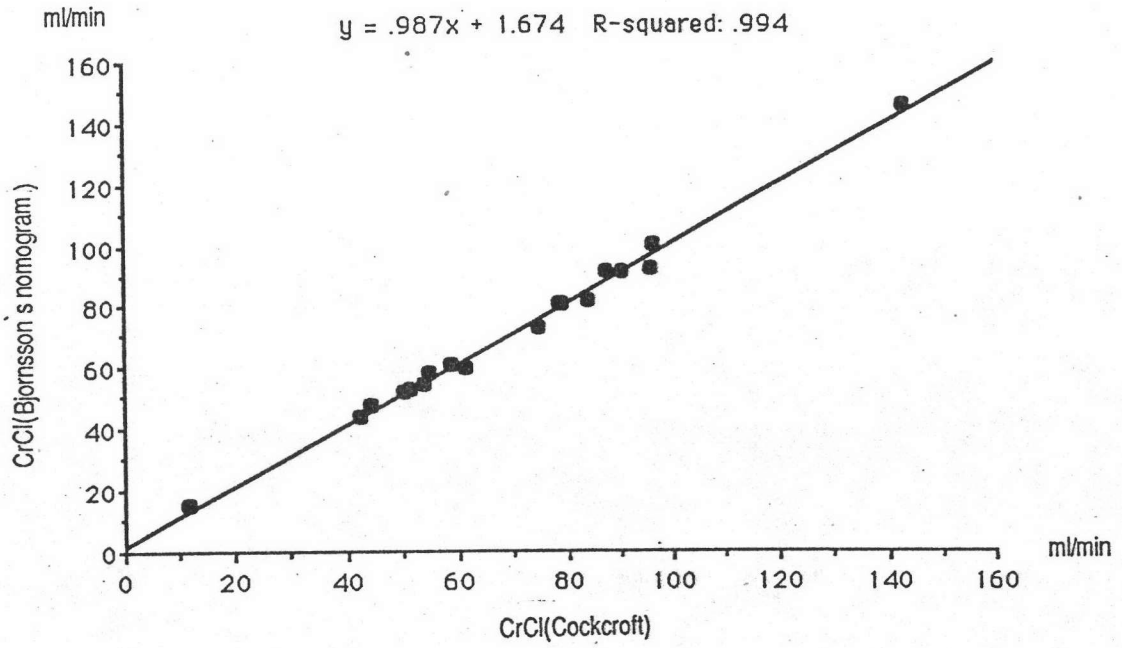

Figure 10 Correlation between CrCl Obtained from Cockcroft and Gault Method and CrCl Obtained from Bjornsson's Nomogram

Bjornsson's Nomogram was 0.725 while the correlation coefficient between Cockcroft and Gault method and Bjornsson's Nomogram was 0.997. These results were presented in Table 15 B and Figures 8, 9, and 10 respectively. The estimation of creatinine clearance (Ccr) from serum creatinine using Cockcroft and Gault method or Bjornsson's Nomogram can only provide a quick approximation of the values. There were no significant difference in the values of creatinine clearance obtained whether the Cockcroft and Gault method or Bjornsson's Nomogram was used.

In this study, the measured values may lose some accuracy since some volume of the urine may be lost during collecting. In addition, the estimation of Ccr from serum creatinine (Scr) may not be accurate if Scr was not at steady-state and/or the laboratory method and worker were varied. A better control in each steps is required for a better correlation of the methods.

III Comparison Between the Fluorescence Polarization Immunoassay Technology (FPIA) and High Performance Liquid Chromatography (HPLC) Method

The result of thirty serum samples which were analyzed by both methods were shown in Table 16. Each serum was analyzed two times by TDx ^{R} Analyzer (FPIA Technique). Serum samples were analyzed the first time in the day that each blood sample was drawn from the patient

Table 16 Drug Concentrations of Thirty Serum Samples Obtained by Two Different Analytical Methods HPLC and TDx® Analyzer (TDx).

Patient Number	Drug Concentration (µg/ml)		
	HPLC	TDx(new)	TDx(old)
1	4.07000	3.91	3.94
2	2.83750	2.88	3.07
3	4.12259	3.99	3.90
4	1.61898	1.96	1.81
5	5.52269	5.55	5.51
6	2.08579	3.04	2.98
7	4.00795	4.70	4.67
8	2.76118	3.34	3.3
9	1.73775	2.10	2.30
10	2.05963	2.08	3.39
11	3.00387	3.96	4.37
12	3.98019	5.46	5.49
13	2.39862	2.61	2.76
14	5.74736	6.91	7.30
15	1.39137	2.30	2.16
16	3.29558	6.03	6.27
17	3.15663	5.36	5.29
18	1.01405	1.49	1.59
19	3.46761	4.93	4.91
20	2.24894	3.77	3.88
21	3.09084	5.01	5.38
22	2.44793	3.80	3.76
23	0.65915	0.98	1.21
24	0.84670	1.31	1.23
25	2.42621	3.78	3.82
26	1.04248	1.00	0.77
27	2.95218	5.26	5.08
28	1.14820	1.58	1.59
29	0.22542	0.55	0.78
30	2.79231	3.95	4.30

Correlation coefficient = 0.88602

$t_{95\%, calc}$ = 10.11101

$t_{95\%, table}$ = 2.04800.

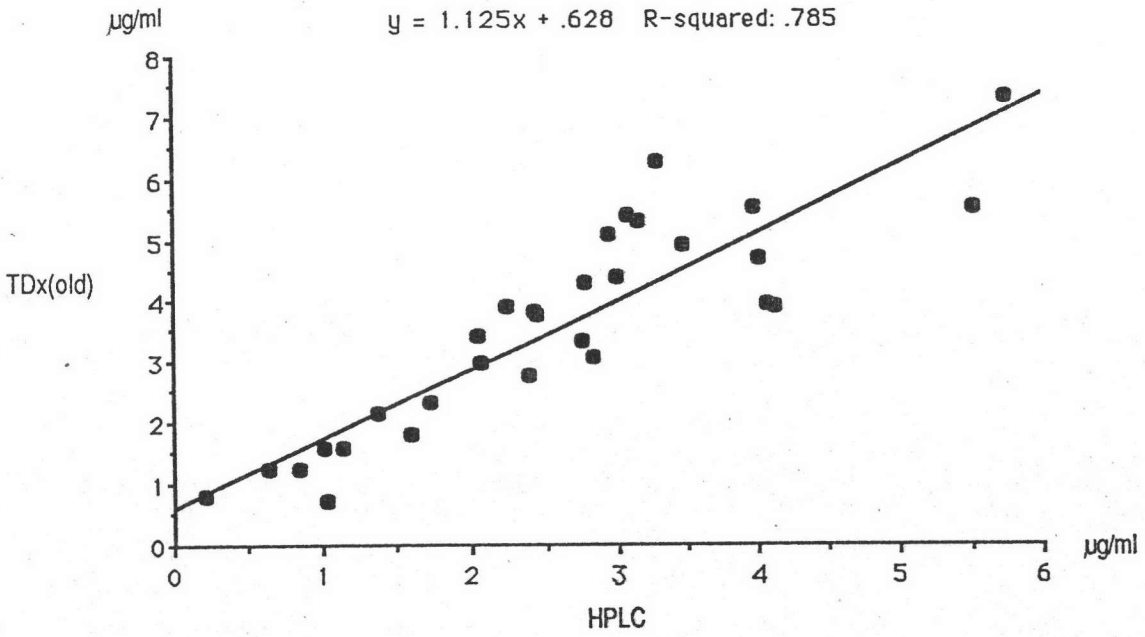

Figure 11 Correlation between Drug Concentration Obtained from Different Analytical Method TDx^R Analyzer and HPLC. (The Samples Were Analyzed by Both Methods in the Same Day)

TDx(new) = Drug concentration obtained when the samples were analyzed by TDx^R Analyzer at the same day of HPLC analyzed (µg/ml).

Correlation coefficient = 0.98539

$t_{95\%, calc}$ = 30.61890

$t_{95\%, table}$ = 2.04800

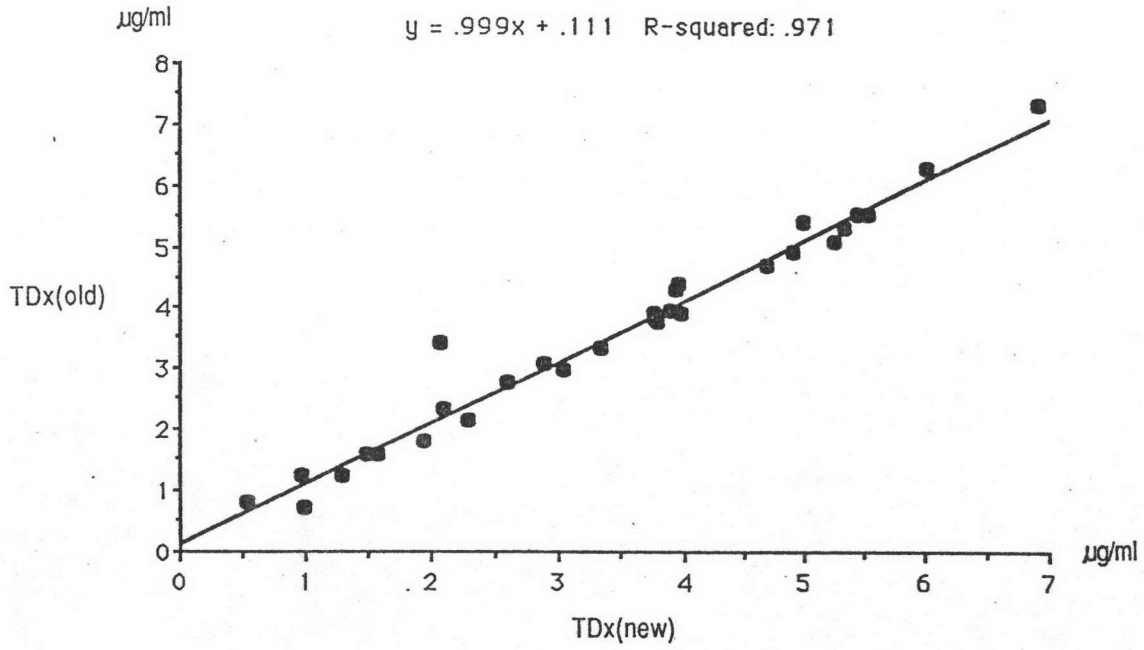

Figure 12 Correlation between Drug Concentration Obtained from Different Analytical Method TDx® Analyzer and HPLC. (The Samples Were Drawn and Were Analyzed by HPLC Method after Blood Samples Were Stored Approximately 1-21 Days) ..

TDx(old) = Drug concentration obtained when the samples were analyzed immediately after the blood samples were drawn (µg/ml).

Correlation coefficient	=	0.89331
$t_{95\%,\ calc}$	=	10.51731
$t_{95\%,\ table}$	=	2.04800

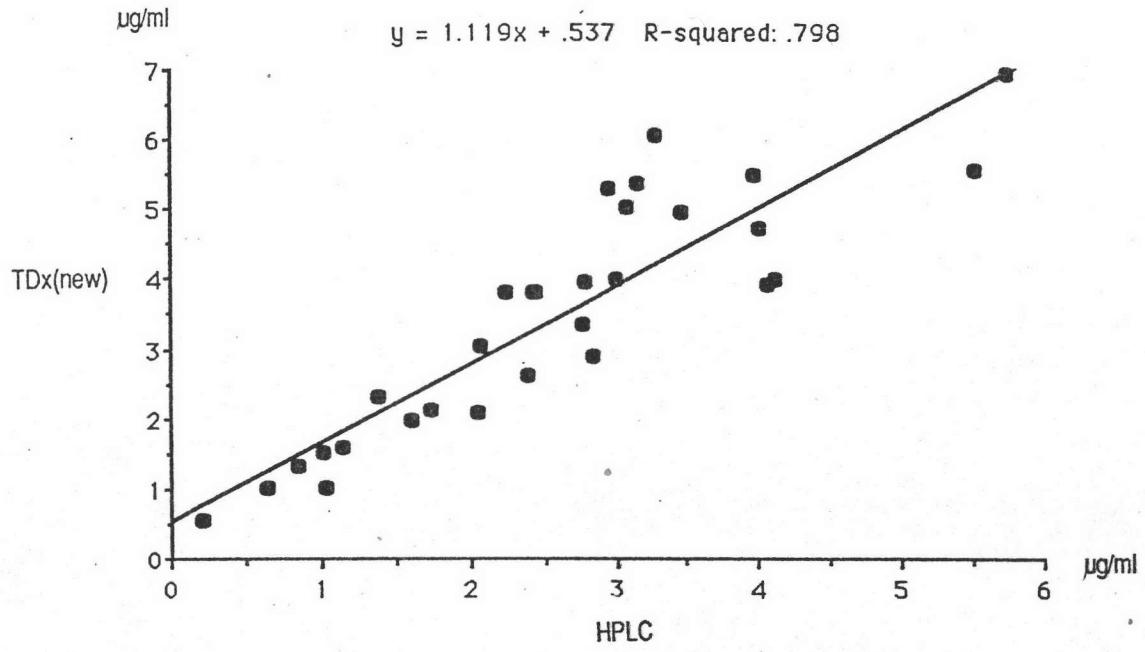

Figure 13 Correlation between Drug Concentration Obtained from the Same Analytical Method at Different Analytical Time

TDx(new) = Same as Figure 11

TDx(old) = Same as Figure 12

(TDx(old)) and the second time, in the day that each blood samples was analyzed by HPLC technique (TDx(new)).

When the serum concentrations obtained from FPIA and HPLC was compared, the percent coefficient of variation between the concentrations obtained from TDx^R Analyzer which analyzed immediately after the drawing (TDx(old)) and the concentrations obtained from HPLC-analyzed was 32.53, and between the concentrations obtained from TDx^R Analyzer which were stored for some times before analyzed (TDx(new)) and the concentrations obtained from HPLC-analyzed (HPLC) was 23.56, as shown in Table 17 A. In addition, the correlation between TDx(new) and HPLC showed $r = 0.839$ and between TDx(old) and HPLC showed $r = 0.866$ and between TDx(old) and TDx(new) showed $r = 0.986$. These results were shown in Table 17 B and Figure 11, 12, and 13 respectively.

The HPLC condition used here was simply chosen for convenience from the method developed by the personal of Chulalongkorn Hospital. The percent recovery and the accuracy of the method have not been absolutely confirmed. However, since the standard curve showed quite a good result ($r^2 = 0.998$), the condition and method used here were considered to be reliable.

The result from this study showed that TDx^R Analyzer (FPIA method) could not give exactly the same

Table 17 A : Comparison between Serum Drug Concentration Values Obtained from HPLC Method and TDx ® Analyzer

Comparison between different methods and analytical time	Percent coefficient of variation
TDx(old) V.S. HPLC	% CV = 32.525
TDx(new) V.S. HPLC	% CV = 23.561
TDx(new) V.S. TDx(old)	% CV = 14.853

B : Correlation between Serum Drug Concentration Values Obtained from HPLC Method and TDx ® Analyzer

	TDx(old)	TDx(new)
HPLC	r = 0.886	r = 0.893
	r^2 = 0.785	r^2 = 0.798
TDx(new)	r = 0.986	-
	r^2 = 0.971	-

TDx(new) = Drug concentrations obtained when the samples were analyzed by TDx® analyzer at the same day of HPLC analyzed (µg/ml).

TDx(old) = Drug concentrations obtained when the samples were analyzed immediatedly after the blood samples were drawn (µg/ml).

gentamicin concentration as compared with HPLC method. However, since the TDx^{R} Analyzer method is more convenient and the result could be obtained in a very short time, the procedure of HPLC analysis is considered to be more economic and not too tedious only if more than 15 serum samples were needed to analyzed at the same time. The correlation coefficient (r) between the two methods was higher than 0.8, the TDx^{R} Analyzer method was considered to be a recommended method for analysis the serum gentamicin concentration for clinical use.