ONE - OR MULTICOMPARTMENT GENTAMICIN PHARMACOKINETICS : CLINICAL RELEVANCE?

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The report by Schentag et al (1977) that gentamicin (G) disposition is most appropriately described by a two-compartment (2-cpt) model, raised the question whether these findings invalidate the commonly used one-compartment (1-cpt) model in the management of patients. To examine this question the mean 2-cpt G parameters of the 4 patient groups by Schentag, exhibiting mean creatinine clearances (CLcr) of 15, 38, 60 and 98 ml/min, were utilised in a computer-oriented theoretical investigation. Initially the simulated serum levels following a single G dose were subjected to 1-cpt analysis as reported by R.J.Sawchuk and D.E.Zaske (1976). Thereafter a G dosing regimen to achieve desired steady-state maximum (Cmax) and minimum (Cmin) serum G levels was designed for an average patient in each of the 4 groups.

Comparisons of the 1-cpt projections with the simulated G levels based upon the 2-cpt parameters indicate that(Table 1) 1) the 1-cpt method predicts the Cmax and Cmin levels with clinically acceptable accuracy for patients with CLcr >25ml/min 2) after 7-10 days the 1-cpt method noticeably underestimates Cmax and Cmin levels and accumulation of G in the body in patients with poor renal function (CLcr >25ml/min , and 3) changes in apparent G half-life may occur during multiple dosing independent of changes in renal function.

This evaluation provides theoretical confirmation for the clinical impression that most patients receiving a routine course of G therapy may be adequately managed using simple 1-cpt pharmacokinetics.

Table 1. Comparison of 1 and 2 compartment results.

	$Cmax_{ss}$ (μg/ml)		$Cmin_{ss}$ (μg/ml)		Elim. rate constant (h^{-1})	
Mean CLcr(ml/min)	2-cpt	1-cpt	2-cpt	1-cpt	1st dose	last dose
15	12.3	7.6	7.3	2.6	0.045	0.023
38	8.9	8.5	1.6	1.2	0.116	0.102
60	9.9	9.1	2.2	1.4	0.169	0.145
98	8.7	8.3	1.5	1.0	0.188	0.161

Schentag, J.J. et al (1977) J. Pharmacokin Biopharm 5 : 559-577
Sawchuk, R.J., Zaske, D.E. (1976) Ibid. 4 : 183-195

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