Chapter VI
Conclusion

Fifty patients were monitored for their once-daily gentamicin treatment , the results from this study were concluded as follows :

1. Optimum serum sampling time of once-daily gentamicin dosage regimen and its relatively reference concentration for monitoring nephrotoxicity.

1.1 Once daily gentamicin doses were prescribed by physicisians ranged from 120 to 240 mg/day (2.5- 5.6 mg/kg/day) , 48 % of the patients were prescribed the doses according to the nomogram , 30 % of the patients were prescribed with doses higher than 10 % of the recommended doses according to the nomogram . The nephrotoxicity was developed in 8 % of the patients. All nephrotoxic patients met the criteria after the last day of gentamicin treatment. The electrolytes imbalance was developed in all of them. However , one patient could not determine to be hypokalemia and another one could not determine to be hypomagnesemia due to the treatment since their initial values were below the normal range.

1.2 Measurement of trough concentration was not appropriate for once-daily dosing. The 24-hr serum gentamicin levels of less than 0.3 mg/L , 0.4 mg/L , 0.6 mg/L and 1.4 mg/L of the four nephrotoxic patients determined in this study indicated that the upper limit trough concentration of 2 mg/L and 1 mg/L usually recommended for clinical practice were both too high.The majority of the patients had trough levels at 24-hr of less than 0.3 mg/L which were too low to be detected by the normally used clinical analytical instrument , therefore the actual value could not be evaluated and the reference concentration could not be determined.

1.3 The optimum serum sampling time of once-daily gentamicin dosing for monitoring nephrotoxicity was at 6 or 8 hours after starting the 30-min intravenous infusion. The 6-hr serum gentamicin levels of less than 3.0 mg/L or the 8-hr serum gentamicin levels of less than 2.0 mg/L which provided a significantly lesser chance of developing nephrotoxicity may be the relatively reference concentration for monitoring nephrotoxicity of once-daily gentamicin dosage regimen.

1.4 The influence of other clinical factors on nephrotoxicity was also examined by univariate analysis. The only other significantly clinical factor besides serum gentamicin levels that showed statistically significantly different between the patients in nephrotoxic and non-nephrotoxic groups was the duration of gentamicin treatment.

2. Optimum serum sampling time of once-daily gentamicin dosage regimen and its relatively reference concentration for monitoring efficacy

2.1 Favourable efficacy was recorded in 73 % of the bacterial infected patients in this study.

2.2 The optimum serum sampling time of once-daily gentamicin dosing for monitoring efficacy was at 1 hour after starting the 30-min intravenous infusion. The 1-hr serum gentamicin levels of more than or equal to 11.0 mg/L which provided a significantly greater chance of having a favourable efficacy may be the relatively reference concentration for monitoring efficacy of once-daily gentamicin dosage regimen.

2.3 Univariate analysis showed that the patients who responded with favourable efficacy were more likely to have a lower mean initial temparature , and lower mean initial leukocyte count compared with those who did not respond favourably. A lower respiratory tract infection and infection with *Pseudomonas* species were also associated with unfavourable efficacy.

3. Pharmacokinetic data of the patients

The elimination rate constant of the patients was 0.26 ± 0.09 per hour , the half-life of gentamicin was 3.04 ± 1.25 hours , the volume of distribution was 0.32 ± 0.08 L/kg. and the clearance was 73.25 ± 28.50 ml/min.

The results got here suggested that the optimum serum sampling time points for therapeutic monitoring of once-daily gentamicin dosage regimen were at 1 hour after starting intravenous infusion with relatively reference concentration of more than or equal to 11.0 mg/L to provide a greater chance of having favourable efficacy , and at 6 or 8 hours after starting the drug administration with relatively reference concentrations of less than 3.0 mg/L and 2.0 mg/L respectively to reduce the risk of nephrotoxicity. These conclusions could be used as a guideline for therapeutic drug monitoring of once-daily gentamicin dosage regimen in Thai patients. Although a further prospective study in a large number of patients would be necessary in order to determine whether or not this guideline could result in a higher percentage of efficacy with a lower percentage of nephrotoxicity.