CHAPTER I

INTRODUCTION

Background and Rational

In Thailand, as in other countries, gentamicin is one of the primary antibiotic drugs used for the treatment of infections caused by gram-negative bacteria (1). Gentamicin is among the most frequently selected agents which pharmacokinetic monitoring required since its therapeutic index is narrow and wide variation in blood levels is found when an equal amount of this drug was administered into different individual. The drug must therefore be administered with caution to ensure the safety and therapeutic effect of the patients. Toxic effect on the auditory-vestibular apparatus and the kidney can result in hearing loss, the loss of equilibrium, and acute renal tubular necrosis.

The incidence of toxic effect can be related to the dosage of drug, the length of treatment, individual variability in drug absorption, elimination and distribution of patient (2)

Even though several methods have been purposed to calculate the optimal gentamicin dosage regimen, including the nomograms described by Hull and Sarubbi (3), Chan, *et al* (4), and Dettli (5), individualized pharmacokinetic

method has been reported to have an advantage over the nomogram techniques (6). An application of pharmacokinetic method for calculation of dosage regimen requires the information of drug levels in serum at appropriate time (7,8).

Many hospitals in the United States have developed methods for establishing gentamicin dosage regimens for routine care of individual patient based on measured parameters of renal function and/or individual patient's pharmacokinetic parameters. However, in Thailand the application of pharmacokinetic method for the routine care of individual patient has not yet been established. The clinicians in Thailand generally use nomogram techniques to assess gentamicin dosage regimen.

This study was designed : to investigate drug level in Thai patients after they were treated by traditional clinicians prescribing dosage regimen, to evaluate some pharmacokinetic equations and parameters from literature used to calculate drug levels (Predicted values), to compare the calculated drug levels with the measured drug levels in blood (Measured values), and to determine the appropriate method which would be useful for applied gentamicin therapeutic drug monitoring (Individualizing dosage regimen) for Thai patients.

Objective

1. To determine the percentage of patients whose serum gentamicin levels were within the therapeutic range after treatment with traditional dosage regimens.
2. To compare the serum gentamicin levels obtained from patients (measured values) with the serum gentamicin levels calculated from patients pharmacokinetic parameters obtained from serum creatinine (predicted values).
3. To determine the effect of sampling time and the number of samples on the pharmacokinetic parameters obtained.
4. To create some basic pharmacokinetic parameters data of Thai patients.
5. To establish a practical method for calculating dosage regimen which is convenient and suitable for each individual patient.

Significance of the study

1. From this study, it shall be able to justify whether the dosage regimen obtained from table or nomogram that are currently and widely used by physicians will provide a suitable serum therapeutic level.
2. From this study, it shall be able to justify the relationship between clinical results and the serum levels of patients during the treatment with gentamicin.

3. This study will enable to determine whether the pharmacokinetic parameters and equations that are currently and widely used in foreign countries can be used to predict gentamicin levels accurately. If so, this method shall be recommended for calculating dosage regimens of gentamicin for Thai patients.
4. This study will provide some information about the significant of sampling time.
5. This study will provide a few pharmacokinetic parameters of Thai patients which can be used as the data for calculating the appropriate dosage regimens for each individual patients either manually or when computer program is applied.
6. This study will provide an appropriate method for calculation of creatinine clearance from serum creatinine of Thai patients.