CHAPTER V

CONCLUSION

Following a clinical end-point of pharmacological effect (both efficacious and toxic) is invaluable in guiding drug therapy, but in many circumstances the clinician must place his faith in and entrust his patient's well-being to one or another guideline of drug dosage.

Sixty patients were completely observed in this study, the results obtained were concluded as follow :

1. The percentage of the patients whose peak and trough levels were within the desirable therapeutic range after treatment with traditional dosage regimens was 38.333%.

2. The peak and trough serum gentamicin levels obtained from patients (measured values) were different from the peak and trough serum gentamicin levels calculated from patient pharmacokinetic parameters obtained from patient serum creatinine (predicted values), as shown by the high percentage coefficient of variation (peak : % CV = 24.32, trough : % CV = 70.75).

3. The mean values of pharmacokinetic parameters i.e. elimination rate constant, half-life and volume of distribution of gentamicin obtained from using three measured drug concentrations data were 0.235 $\pm$ 0.095 (mean $\pm$ SD) $hour^{-1}$, 3.733 $\pm$ 2.417 hours, and 0.327 $\pm$ 0.124 L/kg respectively. The predicted values of these pharmacokinetic parameters using Hull and Sarubbi method and equation were different from the forementioned values. The percentage coefficient of variation (% CV) of the predicted values from the measured values of the elimination rate constant, the half-life and the volume of distribution were 54.98, 37.09, and 29.78 respectively.

4. For serum level monitoring and calculation of individualized pharmacokinetic parameters, using two sample points of gentamicin levels (the peak and the trough concentrations) had tendency to represent all of the useful purposes as well as using the three sample points of gentamicin levels (the peak, the trough and the two and a half hours post administration concentrations) required by the Sawchuk and Zaske method since the pharmacokinetic parameters obtained from using these two sample points showed least different values from those obtained from using the three sample points i.e. the % CV of the elimination rate constant was 4.33 and the % CV of the volume of distribution was 0.31 and when the pharmacokinetic parameters obtained from using these two sample points and from using the three sample points were

substituted in the equation for dosage regimen calculation, the same dosage regimens were obtained in 96.55% of the total sixty cases.

5. The clinical outcome as related to the therapeutic drug level range showed that 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 level were in the sub-therapeutic range whether or not the concomitant drug was considered. The same correlation could not be observed when the trough concentration only or when both peak and trough concentrations were considered. Nevertheless, the number of patients in this group were too small to make any conclusion. Further collection of the data in a larger group of patients was required before any conclusion could be made. When possible, toxicity was also needed to observe.

6. In this study, prediction of creatinine clearance from serum creatinine using Cockcroft and Gault method and Bjornsson's Nomogram could provided a quick approximation of the value but was different from the measured creatinine clearance value. The percent coefficient of variation were 36.88% and 36.59% for Cockcroft and Gault method and Bjornsson's Nomogram, respectively.

7. Comparison between the analytical methods, HPLC versus TDx^{R} Analyzer, showed the % CV of the TDx^{R} method was 23.56 using the HPLC method as the standard.

Further studies on the application of pharmacokinetics to serum gentamicin level monitoring should be continued. The pharmacokinetic parameters obtained from the known serum drug concentrations should be used in dosage regimen calculation when the drug levels were not within the therapeutic range. The new dosage regimen should then be started in the patient and the serum drug concentrations should be compared with the predicted drug levels of the new dosage regimen. The reliability of the pharmacokinetic theories and equations could further then be evaluated.