Chapter I

Introduction

Background and Rationale

Digoxin is the widely prescribed cardiac glycoside despite the continuing controversy about its indications and its value as using for maintenance or long term treatment. (Brodie and Feely, 1986). Digoxin is used for the treatment of heart failure, atrial fibrillation, atrial arrhythmia and also for controlling the symptoms from rheumatic heart disease, with or without other drugs. Digoxin has wide factors which should be considered before using or prescribing to the patients. Because it has a narrow therapeutic ratio. The dose which acheives therapeutic benefit is almost the same causing the toxic effect. Signs and Symptoms of digoxin toxicity are nausea, vomitting and other effects relating to the abnormal function of the heart. The toxic effects are frequent and can be severe or lethal. So the prescribing of digoxin should be seriously concentrated. The serum concentration must be within the optimum therapeutic range. Furthermore, the risks or side effects should be reduced or supposed to be none. (Lee and Smith, 1983; Aronson, 1983).

There is the predictable relationship between serum concentrations and clinical or other effects of the drug - digoxin better than the relationship with the dose. The signs and symptoms of digoxin toxicity may be difficult to distinguish from which of the underlying disease. And now the method used for determination of digoxin in serum is sufficiently sensitive, specific and

accurate. So the digoxin monitoring in patients is useful and fruitful to be done. (Koren and Parker, 1985).

Numerous studies were reviewed, finding that the results of drug monitoring can reduce total toxic drug reactions. Furthermore, therapeutic drug monitoring services are effective in keeping patients' serum drug concentrations within an acceptable therapeutic ranges, providing the key to reducing the occurence of toxic drug reactions. The occurence of toxic drug reactions was much lower in patients monitored by a therapeutic drug monitoring service than in nonmonitored patients. (Ried, Horn and Mckenna, 1990)

Since digoxin therapeutic monitoring has been advantage for the patients, but there are still little studies or researches about this in Thai patients. This study was designed to create some information about the pharmacokinetic parameters, observe the measured serum digoxin concentrations in Thai patients with heart failure at Chulalongkorn Hospital. And also monitoring is done for individual patients, who use digoxin with or without other drugs, aiming their good clinical states throughout their treatment. Observing the possibility of undertreatment, overdosage and causing digoxin toxicity are concomitantly detected. When the patients digoxin serum are not within therapeutic level, adjusting and calculating the new dosage regimen have been initiated with the co-ordination from the physicians. The clinical states of the patients, the results of the treatment and the monitoring of the drug as above are studied to acheive the excellent point to each patients.

Objective

1. To study whether the recently and widely dose of digoxin used by physicians will provide a suitable serum therapeutic level.

2.   To study the relationship between the serum digoxin levels and the clinical results, side effects of toxicities or the patients during the treatment with digoxin.

3.   To calculate and adjust the appropriate dose and dosage regimen of digoxin for individual Thai patient with heart failure, including combination with or without other drugs by the pharmacokinetic method, aiming the serum digoxin level within the assigned therapeutic range.

4.   To compare the serum digoxin levels (measured values) obtained from the patients with the calculated levels (predicted values) from patients pharmacokinetic parameters obtained from serum creatinine.

5.   To initiate the possible method for monitoring the therapeutic drug level of digoxin used in Thai hospitals as the model drug .

The Significance of the Study

1.   This study will provide the answer whether the basis data of the serum digoxin level in Thai patients with heart failure will be within the therapeutic ranges.

2.   This study will give the information about the digoxin therapeutic level monitoring by using the pharmacokinetic parameters and equations which may decrease the digoxin toxicities in patients during the treatments.

3.   This study would be the appropriateness method to use the pharmacokinetic parameters and equations that are currently and widely used in foreign countries , which can be used to predict digoxin levels in Thai patients.

4.   This study should initiate the method of digoxin therapeutic level monitoring in hospital in the future.