CHAPTER V

CONCLUSION

Sixty one patients were completely followed up for their respiratory disorder treatment with theophylline, the results from this study were concluded as follows :

1. Theophylline was given according to the physician traditional dosage regimen, the number of patients treated with theophylline alone and theophylline together with other drugs (beta - adrenergic agonists, corticosteroids, and anticholinergic drugs) were 18 (29.51%) and 43 (70.49%), respectively. If the therapeutic range was indicated as within 10 - 20 mcg/ml, the majority of patients had peak theophylline serum concentrations within subtherapeutic range (45.76%) and therapeutic range (40.68%) while their majority trough theophylline serum concentrations were within subtherapeutic range (64.41%). In addition, 10.17% of these patients showed no clinical beneficial effect from theophylline therapy and incidence of theophylline adverse reactions observed in these patients were 25.42%.

2. Correlation between theophylline serum concentrations and clinical responses to theophylline therapy could be concluded as follows :

2.1 The usually accepted therapeutic of 10 to 20 mcg/ml is not an absoluted but a statistical concept because this study indicated that the beneficial effect on respiratory disorder was observed at trough theophylline serum concentrations as low as 3.85 ± 0.78 mcg/ml (mean $\pm$ SD) in some patients with mild respiratory disorder, and in the patients treated theophylline together with beta - adrenergic agonists and corticosteroids.

2.2 The adverse reactions of theophylline which occured most often while the theophylline serum concentrations were within therapeutic range such as pulse rate $\geq$ 100/min palpitation, and gastrointestinal effects.

2.3 Theophylline adverse reactions occured more often in patients with higher theophylline serum concentrations than those with low serum levels indicated a good correlation between theophylline serum level and adverse reaction or toxicity.

2.4 When theophylline dosage regimen adjustment are required, the calculation should be based on peak theophylline serum concentration since determination from trough theophylline serum concentration might associate with the increased risk for theophylline adverse reactions.

2.5 There were no difference in the incidence of theophylline adverse reactions whether the patients were treated with theophylline alone or they were treated with theophylline together with other drugs. However, the incidence of adverse reactions from other drugs were observed 19.% in the patients of the later group.

3. In this study, the percentage of patients requiring theophylline dosage regimen adjustment were 29.51 (18 of 61), 88.89% (16 of 18) of these patients had at least one factor which affected theophylline elimination. Seventeen of these 18 patients (94.44%) showed improvement in clinical response after dosage regimen adjustments, ie. adverse reactions were decreased (66.67%), respiratory disorder was improved (22.22%) and theophylline toxicity was decreased (5.56%)

4. The results obtained from comparison between the measured and predicted theophylline serum concentrations after administration of oral sustained release dosage form showed that the mean percentage of difference between the measured and predicted values was 19.40 ± 15.21 (mean ± SD) and the percent coefficient of variation (%CV) was 24.96.

Only three patients were initially received theophylline by intravenous infusion 15 minutes every 6 hours. The mean percentage of difference between the measured and predicted peak serum concentrations was 11.05 ± 9.78 (mean ± SD) and the percent coeffieient of variation was 10.97% while the mean percentage of difference between the measured and predicted trough serum concentrations was 17.00 ± 7.56 (mean ± SD) and the percent coefficient of variation was 15.35.

5. Pharmacokinetic parameters of theophylline in Thai patients obtained from this study show that :

5.1 Theophylline clearance in Thai patients varied in different groups of patients depend on various factors. The values were ranged from 16.52 to 60.63 ml/hr/kg of IBW (mean). Half - lives of theophylline in Thai patients were also varied among different groups of patients. The values were range from 5.93 to 21.30 hours (mean).

5.2 There was some reduction in theophylline clearance with advanced age. Statistical comparison of theophylline clearance between the values of adult patients (mean of age $\pm$ SD = 53.33 $\pm$ 9.00 years) and elderly patients (mean of age = 70.67 $\pm$ 7.46 years) showed no significant at α = 0.10 but significant was determined at α = 0.20. The reason that this difference could not be obtained at a higher confident level might be due to the age of the patients in the adult group was mostly higher than 50 years which is very closely to the age of the elderly group (60 years or older).

5.3 Liver dysfunction and cardiac disorder status were the major causes of altered theophylline metabolism, therefore the patients with these two factors had low clearance and long half - life. Whereas smoking increased theophylline clearance and some drugs such as cimetidine decreased theophylline clearance.

5.4 The values of theophylline clearance and half - life along with the factors which altered these pharmacokinetic parameters obtained from this study were corresponded well with those reported in foreign literatures. However, the number of patients observed in each group was too few for any confident conclusion to be mede. Further study in larger number of patients are highly recommended.

Application of pharmacokinetic theories to adjust for the individual appropriate drug dosage regimen that based on the assessment from serum drug level and clinical responses have improved clinical outcome of the patient as shown from the results of this study. This is shown that therapeutic drug monitoring done by clinical pharmacist in the real situation clinical setting could help in improving the patient's care. Thus, I recommend that the therapeutic drug monitoring should be set up in the hospital when it is applicable. To acheive this, the pharmacist also needs to have the good collaborations between himself and other health professions such as physicians, nurses, etc. This could lead to the recognition of the pharmacy profession that every pharacist wishes for.