



REFERENCES

- Abbott, TDX FSE Training. Diagnostic Division, Abbott Laboratories, North Chicago, IL 60064
- Barnes, J.P. 1992. Pulmonary disorders. In K.L. Melmon, H.F. Morrelli, B.B. Hoffman (eds.), Melmon and Morrelli's Clinical Pharmacology Basic Principles In Therapeutics. pp. 186 - 218. USA : McGraw - Hill.
- Barnhart, A.G., Hill, M., and Szeffler S.J. 1988. Sustained release theophylline preparations practical recommendations for prescribing and therapeutic drug monitoring. Drugs . 35 : 711 - 726.
- Bennett, D.R. 1994. Drugs used in bronchial disorders. In Drug Evaluations Annual. pp 497 - 536. USA : American Medical Association.
- Berry, R.B., Shinto, R.A., Wong, F. H., etal. 1989. Nebulizer versus spacer for bronchodilator delivery in patients hospitalized for acute exacerbations of COPD. Chest. 96 : 1241 - 1246.
- Bierman, C.W, and Williams, P.V. 1989. Therapeutic monitoring of theophylline rationale and current status. Clinical Pharmacokinetics. 17 (6) : 377 - 384.
- Blackbourn, J., and Sunderland, V.B. 1987. Impact of pharmacist intervention on oral theophylline therapy in adult inpatients. Drug intelligence and Clinical Pharmacy. 21 : 811 - 815.
- Bonham, A., Hendeles, L., Weinberger, etal. 1980. The reliability of serum theophylline determinations from clinical Laboratories. Am Rev Respir Dis. 122 : 829 - 832.
- Edwards, D.J., Zarowitz, B.J., and Slaughter, R.L. 1992. Theophylline, In W.E. Evans, J.J. Schentag, and W.J. Jusko(eds.), Applied Pharmacokinetics Principles of Therapeutic Drug Monitoring. 3 rd ed. pp. 13 - 1 to 13 - 38. Washington : Applied Therapeutics.

- Ellis, E., and Hendeles, L. 1986. Theophylline. In W.J. Taylor, and M.H. DiesCaviness (eds.), A textbook for the Clinical Application of Therapeutic Drug Monitoring. pp. 185 - 205. North Chicago : Abbott Laboratories, Diagnostics Division.
- Frew, J.A., Holgate, T.S. 1993. Clinical Pharmacology of asthma implications for treatment. Drugs. 46(5) : 847 - 862.
- Gibaldi, M. 1991. Individualization and optimization of drug dosing regimens. In Biopharmaceutics and Clinical Pharmacokinetics. pp. 344 - 376. Philadelphia : Lea & Febiger.
- Goldsmith, T.L. 1992. Chronic obstructive pulmonary disease. In E.T. Herfindal, D.R. Grouley, L.L. Hart (eds.), Clinical Pharmacy and Therapeutic. pp. 570 - 580. Maryland : Williams & Wilkins.
- Gotz, V.P. 1993. Chronic obstructive airways disease. In M.A. Koda - Kimble, and L.Y. Young (eds.), Applied Therapeutics : The Clinical use of drugs. pp. 16 - 1 to 16 - 14. Washington : Applied Therapeutics.
- Hendeles, L., lafrate, R.P., and Weinberger, M. 1984. A clinical and pharmacokinetic basis for the selection and use of slow release theophylline products. Clinical Pharmacokinetics. 9 : 95 - 135.
- _____, L., Massanari, M., and Weingerger, M. 1986. Theophylline. In W.E. Evans, J.J. Schentag, W.J Jusko (eds.), Applied Pharmacokinetics : Principles of Therapeutic Drug Monitoring pp. 1105 - 1187 Washington : Applied Therapeutics.
- _____, L., Weinberger, M., Johnson, G. 1978. Monitoring serum theophylline levels. Clinical Pharmacokinetics. 3 : 294 - 312
- _____, L., Weinberger, M., Szeffler, S., Ellis, E. 1992. Safety and efficacy of theophylline in children with asthma. Journal of Pediatrics. 120 (2) : 12 - 18.
- Hepner, G., Vessel, E. 1978. Reduced drug Elimination in congestive heart failure. Am J Med. 65 : 271 - 276.

- Iafrate, R.P., and Blake, K. 1992. Asthma. In E.T. Herfindal, D.R. Gourley, and L.L Hart (eds.), Clinical Pharmacy and therapeutics. pp. 547 - 569. Maryland : Williams & Wilkins.
- Jolley, M.E., Stroupe, S.D., Schwenzer, K.S., and etal. 1981. Flourescence polarization immunoassay III. an automated system for therapeutic drug determination. Clin. Chem. 21(7) : 1575 - 1579.
- Kelly, H.W.1993. Asthma. In M.A. Koda - Kimble and L.Y. Young (eds.), Applied Therapeutic : The Clinical use of drugs. pp. 15 - 1 to 15 - 21. Washington : Applied Therapeutic.
- _____, and Hill, M.R, 1993. Asthma. In J.T. DiPiro, R.L. Talbert, P.E. Hayes, G.C. Yee, G.R. Matzke, Pharmacotherapy A Pathophysiologic Approach. pp. 408 - 449. Connecticut : Appleton & Lange.
- McEvoy, G.K., Litvak, K., and Welsh, O.H. 1993. Theophylline. In AHFS Drug Information 93. pp. 2278 - 2285. MD : American Society of Hospital Pharmacists.
- Neville, R.G., and McDevitt, D.G. 1991. Clinical audit of theophylline use in general practice. BJCP. Spring 45 : 18 - 20.
- Ogilvie, R., Fernander, P., Winsberg, F. 1977. Cardiovascular response to increasing theophylline concentrations. Eur J Clin Pharmaco. 12 : 409 - 414.
- Oles, K.S. 1990. Therapeutic drug monitoring analysis systems for the physician office laboratory : a review of the literature. DICP, The Annals of Pharmacotherapy. 24 : 1070 - 1077.
- Peck, C.C., Conner, D.P., and Murphy , M.G. 1991. Bedside Clinical Pharmacokinetic (Revised Edition) : simple techniques for individualizing drug therapy. Washington : Applied Therapeutics.
- Rogers, R., Wiener, M.B., Hill, M., and Szeffler, S.J., 1987. Theophylline absorption from two sustained - release products : implications for therapeutic drug monitoring. American Review of Respiratory Disease. 136 : 1168 - 1173.


- Slaughter, R.L., and Lanc, R.A. 1983. Theophylline Clearance in obese patients in relation to smoking and congestive heart failure. Drug Intell Clin Pharm. 17 : 274 - 276.
- Staib, A., Schuppan, D., Lissner, R, etal. 1980. Pharmacokinetics and metabolism of theophylline in patients with liver diseases. Int J clin Pharmacol Ther Toxicol. 18 : 500 - 502
- Stratton, M.A. 1993. Chronic obstructive lung disease. In J.T. DiPiro, R.L. Talbert, P.E. Hayes, G.C. Yee, and G.R. Matzke (eds.), Pharmacotherapy A Pathophysiologic Approach. pp. 450 - 465. Connecticut : Appleton & Lange.
- Vozeh, F., Powell, J., Riegelman, S., etal. 1978. Changes in theophylline clearance during acute illness. JAMA. 240 : 1882 - 1884.
- Wilson, J.F., etal. 1988. Evaluation of Chromatographic and kit immunoassay techniques for the measurement of theophylline in serum : a study based on external quality assurance measurements. Ther Durg Monit. 10 : 438.
- Winter, M.E. 1992. Theophylline. In M.A. Koda - Kimble, and L.Y. Young (eds.), Basic Clinical Pharmacokinetics. pp. 315 - 384. Washington : Applied Therapeutics.
- _____.1993. Clinical pharmacokinetics. In M.A. Koda - Kimble, and L.Y. Young (eds.), Applied Therapeutics : The Clinical use of drugs. pp. 1 - 1 to 1 - 11. Washington : Applied Therapeutics.

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APPENDICES

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จุฬาลงกรณ์มหาวิทยาลัย



Appendix I
Example of Data Record Forms

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Record Form for Patient's Data and Theophylline Serum Concentration Measurement

1 Name..... Surname..... Gender..... Age.....
Weight..... Height..... Ward..... Bed.....

2 Smoking History

- Never Smoking
- Stop Smoking, Used to Smoking — { Number :cigarettes/day,.....tobaccos/day
Space of Time :months, years
Discontinued Smoking Before Blood Sample Collection :days, month
- Smoking — { Number :cigarettes/day,.....tobaccos/day
Space of Time :months, years
Discontinued Smoking Before Blood Sample Collection :days, months, years

3 Respiratory Disorder was treated with Theophylline by Physician's Diagnosis.

- Asthma Allergic Rhinitis
 COPD Others.....

4 Concomitant Disease or Disorder together with Respiratory Disorder.

- Acute Pulmonary Edema Hepatic cirrhosis
 Heart Failure Fever Sustained for > 24 hrs
 Others.....

5 Treatment of Respiratory Disorder

5.1 Theophylline Dosage Forms

- [] 1. IV Infusion for 15 minutes of Aminophylline : Start; Date.....,Time.....,Dose.....mg,Interval.....hrs
- [] 2. Oral Sustained Release Preparations
 - [] 2A. Theo Dur^R : Start; Date.....,Time.....,Dose.....mg,Interval.....hrs
 - [] 2B. Nuelin SR^R : Start; Date.....,Time.....,Dose.....mg,Interval.....hrs
 - [] 2C. Theo 24^R : Start; Date.....,Time.....,Dose.....mg,Interval.....hrs

5.2 Other Drugs (Start; Date.....,Time.....,Dose.....mg,Interval.....hrs)

5.2.1 Beta - Adrenergic Agonists :

.....

5.2.2 Anticholinergic Drugs :

.....

5.2.3 Corticosteroids :

.....

6 Drugs Affecting Theophylline Elimination

- 1. Cimetidine :mg/day
- 2. Norfloxacin (Lexinor^R) :mg/day
- 3. Rifampicin :mg/day
- 4. Ofloxacin (Tarivid^R) :mg/day
- 5. Erythromycin :mg/day
- 6. Allopurinol :mg/day

7. Others :mg/day

Start ; Date.....Time.....

7 Other Factors Affecting Theophylline Elimination :

8 Patient received the last theophylline dosing before blood sample Collection : Date.....,Time.....,Dose.....mg,Interval.....

dosage Form IV infusion for 15 minutes : Aminophylline

Oral Sustained Release Preparations :

Theo Dur^R

Nuelin SR^R

Theo 24^R



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Table : Blood Sample Collection for Theophylline Serum Concentration Measurement

Number	Time for Blood Sample Collection	True Time in Blood Sample Collection	Interval from Administration	Serum Concentration (mcg/ml)
1	<u>IV Infusion for 15 minutes (at Steady State)</u> One hr after finished IV Infusion : Date..... Time.....	Date..... Time..... hrs (Peak)
	2	Immediately before the next dose : Date..... Time.....	Date..... Time..... hrs (Trough)
<u>Oral Sustained Release Preparations (at Steady State)</u>				
3	Six hrs after a dose for Theo Dur ^R or Nuelin SR ^R : Date..... Time.....	Date..... Time..... hrs (Average Serum Concentration or Peak)
	4	Immediately before the next dose : Date..... Time.....	Date..... Time..... hrs (Trough)
5	Twelve hrs after a dose for Theo 24 ^R : Date..... Time.....	Date..... Time..... hrs (Average Serum Concentration or Peak)
	6	Immediately before the next dose : Date..... Time.....	Date..... Time..... hrs (Trough)

** If Patient's Clinical Response were Inappropriate, Therefore the Patient should Receive Theophylline Dosage Regimen Adjustment.

9. Patient received the last theophylline dosing before blood sample collection : Date.....,Time.....,Dose.....mg,Interval.....hrs.

Dosage Form [] IV Infusion for 15 minutes : Aminophylline

[] Oral Sustained Release Preparations :


[] Theo Dur^R

[] Nuelin SR^R

[] Theo 24^R

Table : Blood Sample Collection for Theophylline Serum Concentration Measurement

Number	Time for Blood Sample Collection	True Time in Blood Sample Collection	Interval from Administration	Serum Concentration (mcg/ml)
	<u>IV Infusion for 15 minutes (at Steady State)</u>			
1	One hr after finished IV Infusion : Date..... Time.....	Date..... Time..... hrs (Peak)
2	Immediately before the next dose : Date..... Time.....	Date..... Time..... hrs (Trough)
	<u>Oral Sustained Release Preparations(at Steady State)</u>			
3	Six hrs after a dose for Theo Dur ^R or Nuelin SR ^R : Date..... Time.....	Date..... Time..... hrs (Average Serum Concentration or Peak)
4	Immediately before the next dose : Date..... Time.....	Date..... Time..... hrs (Trough)
5	Twelve hrs after a dose for Theo 24 ^R : Date..... Time.....	Date..... Time..... hrs (Average Serum Concentration or Peak)
6	Immediately before the next dose : Date..... Time.....	Date..... Time..... hrs (Trough)



**Assessment of Clinical Response in Patient
Treated with Theophylline**

ศูนย์วิทยุทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Assessment of Clinical Response in Patient Treated with Theophylline

1. Respiratory Disorder

1.1 Pulmonary Function Test

Assessment	Before Treatment with Theophylline	After Treatment with Theophylline											
		Date	Date	Date	Date	Date	Date	Date	Date	Conclusion			
									(Discharge)	Improved	Unchanged	Worsen	
Peak Expiratory Flow Rate By Peak Flow Meter (L/min)													

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1.2 Assessment of Respiratory Disorder Symptoms

* Note : please write ✓ in assessment 1. - 6. when the patient had respiratory disorder symptoms.

Assessment	Before Treatment with Theophylline	After Treatment with Theophylline											
		Date	Date	Date	Date	Date	Date	Date	Date	Conclusion			
									(Discharge)	Improved	Unchanged	Worsen	
1. Wheeze													
2. Cough													
3. Rales													
4. Dyspnea													
5. Mucus													
6. Others.....													

** Conclusion : Respiratory Disorder Symptoms in this patient

Improved

Not Improved

2. Theophylline Adverse Reactions

2.1 Gastrointestinal System and Nervous System Effects

* Note : Please write ✓ in assessment 1. - 10. when the patient had symptoms.

Symptoms	Before Treatment with Theophylline	After Treatment with Theophylline						Date (Discharge)
		Date	Date	Date	Date	Date	Date	
1. Headache								
2. Dizziness								
3. Nervousness								
4. Insomnia								
5. Seizures								
6. Nausea								
7. Vomiting								
8. Epigastric Pain or Abdominal Pain								
9. Diarrhea								
10. Others.....								

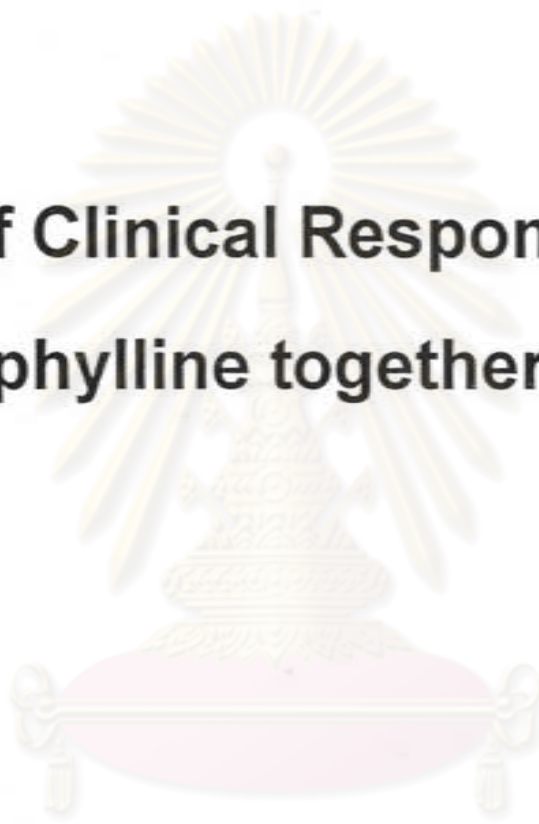
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2.2 Cardiovascular System Effects

* Note : Please write ✓ in symptoms 1. - 6. when the patient had symptoms.

Symptoms	Before Treatment with Theophylline	After Treatment with Theophylline						Date (Discharge)
		Date	Date	Date	Date	Date	Date	
1. Pulse Rate \geq 100/min 2. Muscle Tremor 3. Ventricular Arrhythmias 4. Hypotension 5. Sinus Tachycardia 6. Others.....								

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**Assessment of Clinical Response in Patient
Treated with Theophylline together with other Drugs.**

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Assessment of Clinical Responses in Patient Treated with Theophylline together with Other Drugs (Beta Adrenergic Agonists, Corticosteroids and Anticholinergic Drugs).

1. Respiratory Disorder

1.1 Pulmonary Function Test

Assessment	Before Treatment with Theophylline together with Other Drugs	After Treatment with Theophylline together with Other Drugs									
		Date	Date	Date	Date	Date	Date	Date	Conclusion		
								(Discharge)	Improved	Unchanged	Worsen
Peak Expiratory Flow Rate by Peak Flow Meter (L/min)											

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1.2 Assessment of Respiratory Disorder Symptoms

* Note : Please write ✓ in assessment 1. - 6. when the patient had respiratory disorder symptoms .

Assessment	Before Treatment with Theophylline together with Other Drugs	After Treatment with Theophylline together with Other Drugs									
		Date	Date	Date	Date	Date	Date	Date	Conclusion		
								(Discharge)	Improved	Unchanged	Worsen
1. Wheeze											
2. Cough											
3. Rales											
4. Dyspnea											
5. Mucus											
6. Others.....											

** Conclusion : Respiratory Disorder Symptoms in this patient Improved
 Not Improved

2. Adverse Drug Reactions

2.1 Gastrointestinal System and Nervous System Effects

* Note : Please write ✓ in assessment 1. - 10. when the patient had symptoms.

Symptoms	Before Treatment with Theophylline together with Other Drugs	After Treatment with Theophylline together with Other Drugs						
		Date	Date	Date	Date	Date	Date	Date (Discharge)
1. Headache								
2. Dizziness								
3. Nervousness								
4. Insomnia								
5. Seizures								
6. Nausea								
7. Vomiting								
8. Epigastric Pain or Abdominal Pain								
9. Diarrhea								
10. Others.....								

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2.2 Cardiovascular System Effects

* Note : Please write ✓ in Symptoms 1. - 6. when the patient had symptoms.

Symptoms	Before Treatment with Theophylline together with Other Drugs	After Treatment with Theophylline together with Other Drugs						
		Date	Date	Date	Date	Date	Date	Date (Discharge)
1. Pulse Rate \geq 100/min 2. Muscle Tremor 3. Ventricular Arrhythmias 4. Hypotension 5. Sinus Tachycardia 6. Others.....								

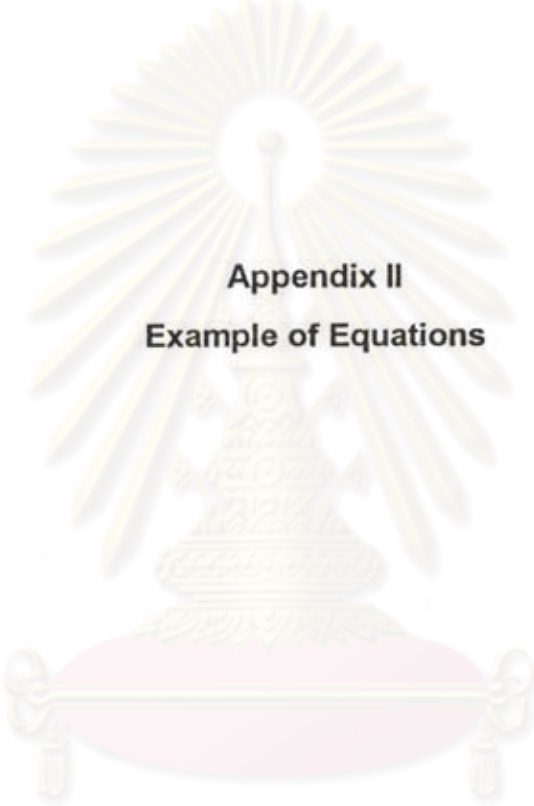
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2.3 Other Effects

* Note : Please write ✓ in symptoms 1. - 5. when the patient had symptoms.

Symptoms	Before Treatment with Theophylline together with Other Drugs	After Treatment with Theophylline together with Other Drugs						
		Date	Date	Date	Date	Date	Date	Date (Discharge)
1. Thrush 2. Dysphonia 3. Cough 4. Dry Mouth 5. Others.....								

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Appendix II
Example of Equations

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จุฬาลงกรณ์มหาวิทยาลัย

Equations used for calculation of theophylline pharmacokinetic parameters and serum concentrations

$$\text{Equation 1 : IBW (male) = } \frac{106 + 6 (\text{height in inches} - 60)}{2.2} \text{ kg}$$

$$\text{Equation 2 : IBW (female) = } \frac{100 + 5 (\text{height in inches} - 60)}{2.2} \text{ kg}$$

$$\text{Equation 3 : Vd theophylline = } (0.5) (\text{IBW}) + 0.25 (\text{TBW} - \text{IBW}) \text{ L}$$

$$\text{Equation 4 : Cl theophylline = (Factor) (0.04) (IBW) L/hr}$$

* Factor refers to any of the following Disease or Concurrent Therapy Factors which are relevant in a particular patient :

Disease Factors :

Non - smoker = 1.0	Smoker = 1.6
Heart Failure = 0.4	Pneumonia = 0.4
Cirrhosis = 0.4	Severe Pulmonary Obstruction = 0.8

Concurrent Therapy Factors :

Allopurinol = 0.75	Cimetidine = 0.60
Erythromycin = 0.75	Isoproterenol = 1.2
Phenobarbital = 1.3	Phenytoin = 1.75
Propranolol = 0.6	Troleandomycin = 0.5

$$\text{Equation 5 : } K_d = \frac{\text{Cl}}{\text{Vd}} \text{ hr}^{-1}$$

$$\text{Equation 6 : } t_{1/2} = \frac{(0.693) (\text{Vd})}{\text{Cl}} \text{ hr}$$

$$\text{Equation 7 : } C_{\text{pss ave}} = \frac{(\text{S}) (\text{F}) (\text{Dose}) / \text{T}}{\text{Cl}} \text{ mg/L}$$

$$\text{Equation 8 : Maintenance Dose = } \frac{(\text{Cl}) (C_{\text{pssave}}) (\text{T})}{(\text{S}) (\text{F})} \text{ mg}$$

$$\text{Equation 9 : } C_{\text{pss}} t_1 = \frac{(S) (F) (\text{Dose})}{V_d} \text{ mg/L} \\ \frac{1}{(1 - e^{-k_d T})} \times (e^{-k_d t_1})$$

IBW = Ideal body weight (kg)

TBW = Total body weight (kg)

V_d _{theophylline} = Theophylline Volume of Distribution (L)

Cl _{theophylline} = Theophylline Clearance (L/hr)

K_d = Elimination rate constant (hr^{-1})

$t_{1/2}$ = Half - life (hr)

$C_{\text{pss ave}}$ = Average serum concentration at steady state

C_{pss} = Serum concentration at steady state

S = Salt form factor

F = Bioavailability


t_1 = Time since the last dose (hr)

Oral dosage regimen :

Dose = Theophylline Dose (mg/kg)

T = Dosing interval (hr)

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จุฬาลงกรณ์มหาวิทยาลัย



Appendix III
Details of Clinical Responses in Patients

ศูนย์วิทยุทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Clinical Responses in Patients.

Patient Number ^(a)	Clinical Responses ^(b)							
	Respiratory Disorder Symptoms						Peak Expiratory	Adverse Reactions
	Wheeze	Cough	Rales	Dyspnea	Mucus	Other	Flow Rate	
1	↓	↓	-	↓	-	-	↑	-
2	↓	↓	-	↓	-	-	↑	-
3	-	↓	-	↓	-	Rhonchi ↓	Not measured	-
4	↓	-	-	-	-	-	↑	-
*5	B	↓	↓	-	↓	↓ Rhonchi	↑	palpitation, PR ≥ 100/min, dizziness, and hypotension from theophylline
	A	↓	↓	-	↓	↓ Rhonchi	↑	-
6		-	↓	-	↓	↓	Not measured	-
*7	B	↓	↓	-	↓	↓	Not measured	muscle tremor from theophylline
	A	↓	↓	-	↓	↓	Not measured	-

Continued

Patient Number ^(a)		Clinical Responses ^(b)							
		Respiratory Disorder Symptoms					Peak Expiratory Flow Rate	Adverse Reactions	
		Wheeze	Cough	Rales	Dyspnea	Mucus			Other
*8	B	-	↓	-	↓	↓	-	Not measured	NIV, anorexia and dizziness from theophylline, muscle tremor from Berotec ^R
Discontinued Berotec ^R									
	A	-	↓	-	↓	↓	-	Not measured	-
*9	B	↓	↓	↓	↓	↓	-	↑	-
Discontinued Erythromycin									
	A	↓	↔	↓	↔	↔	-	↔	-
10		↓	↓	-	↓	↓	-	↑	-
*11	B	↓	↓	↓	↓	↓	-	↑	↕
	A	↓	↓	↓	↓	↓	-	↑	-
12		↓	↓	-	↓	-	-	↑	PR ≥ 100/min from Bricanyl ^R (SC)
13		↓	↓	-	↓	-	-	↑	dry mouth and irritated throat from Pulmicort ^R Inhaler

Continued

Patient Number ^(a)	Clinical Responses ^(b)							
	Respiratory Disorder Symptoms						Peak Expiratory Flow Rate	Adverse Reactions
	Wheeze	Cough	Rales	Dyspnea	Mucus	Other		
14 ^(c)	↔	↔	-	↔	↔	-	Not measured	-
15	↓	↓	-	↓	↓	-	↑	-
16	↓	↓	↓	↓	↓	-	↑	-
*17 B	↔	↓	-	↑	↔	-	↓	Nervousness from theophylline
C ^(d)	↓	↓	-	↓	↓	-	Not measured	-
C	↓	↓	-	↓	↓	-	Not measured	-
*18 B	↔	↓	↓	↔	↓	-	↔	-
A	↓	↓	↓	↓	↓	-	↑	-
19	↓	↓	-	↓	↓	-	↑	-
20	↓	↓	-	↓	↓	-	↑	-
21	↓	↓	-	↓	↓	-	↑	-
22	↓	-	-	↓	↓	-	↑	-

Continued

Patient Number ^(a)	Clinical Responses ^(b)							
	Respiratory Disorder Symptoms						Peak Expiratory Flow Rate	Adverse Reactions
	Wheeze	Cough	Rales	Dyspnea	Mucus	Other		
23	↓	↓	-	↓	↓	-	↑	-
24	↓	-	-	↓	↓	-	Not measured	-
25	↓	↓	-	↓	↓	-	↑	-
26	↓	↓	-	↓	↓	-	↑	-
27	↓	↓	-	↓	↓	-	↑	-
28	-	↓	↓	↓	↓	-	↑	-
29	↓	-	-	↓	↓	-	↑	palpitation and PR \geq 100/min from theophylline muscle tremor, palpitation and PR \geq 100/min from Meptin ^R and Ipradol ^R
30	-	↓	↓	↓	↔	-	↑	palpitation, PR \geq 100/min muscle tremor, dizziness and anorexia from theophylline muscle tremor, palpitation and PR \geq 100/min from Berotec ^R



continued

Patient Number ^(a)	Clinical Responses ^(b)							
	Respiratory Disorder Symptoms						Peak Expiratory Flow Rate	Adverse Reactions
	Wheeze	Cough	Rales	Dyspnea	Mucus	Other		
(e)	-	↓	↓	↓	↔	-	↑	muscle tremor, palpitation and PR ≥ 100/min from Berotec ^R
31 ^(f)	↓	↔	-	↑	↔	-		-
32	↓	↓	↓	↓	↓	-	↑	-
Discontinue Rifampicin	↓	↓	↓	↓	↓	-	↑	-
*33 B	↓	↓	-	↓	-	-	↑	N/V, palpitation, PR ≥ 100/min anorexia, and insomnia from theophylline
C	↓	↓	-	↓	-	-	↑	-
*34 B	↓	↓	↓	↓	↓	-	↑	PR ≥ 100/min, palpitation and nausea from theophylline
A } R }	↓	↓	↓	↓	↓	-	↑	PR ≥ 100/min, palpitation from Bricanyl ^R , dry mouth from Bricanyl ^R Inhaler
Discontinued Bricanyl								dry mouth from Bricanyl ^R Inhaler

Continued

Patient Number ^(a)		Clinical Responses ^(b)							
		Respiratory Disorder Symptoms						Peak Expiratory Flow Rate	Adverse Reactions
		Wheeze	Cough	Rales	Dyspnea	Mucus	Other		
*35	B	↓	↓	↓	↓	↓	-	Not measured	-
	A	↓	↓	↓	↓	↓	-	Not measured	-
	A ^(f)	↔	↔	↔	↑	↔	-	Not measured	-
*36	B	↓	↓	↓	↓	↓	-	Not measured	PR ≥ 100/min, palpitation, and sinus tachycardia from theophylline
	A	↓	↓	↓	↓	↓	-	Not measured	-
37		↓	↓	-	↓	↓	-	↑	N/V from prednisolone (oral) and dexamethasone injection
*38	B	↔	↓	-	↔	↓	-	Not measured	-
	A	↓	↓	-	↓	↓	-	Not measured	-
39		↓	↓	-	↓	↓	-	↑	-
40		↓	↓	-	↓	↓	-	↑	PR ≥ 100/min, palpitation from Bricanyl ^R (SC) epigastric pain from prednisolone (oral)

Continued

Patient Number ^(a)		Clinical Responses ^(b)								
		Respiratory Disorder Symptoms					Peak Expiratory Flow Rate	Adverse Reactions		
		Wheeze	Cough	Rales	Dyspnea	Mucus			Other	
*41	B	↓	↓	-	↔	↓	-	↔	PR ≥ 100/min, palpitation anorexia and insomnia from theophylline	-
	A	↓	↓	-	↓	↓	-	↑		-
42		↓	↓	↓	↓	-	Rhonchi ↓	Not measured	-	
*43	B	-	-	-	↓	↓	-	Not measured	dizziness, N, insomnia, and anorexia from theophylline (toxicity)	-
Discontinued Theo Dur ^R Continued Tedral ^R		-	-	-	↓	↓	-	Not measured	-	
44		-	↓	-	-	-	-	↑	-	
45		↓	↓	-	↓	-	-	Not measured	-	
46		-	↓	-	↓	↓	-	↑	-	

Continued

Patient Number ^(a)		Respiratory Disorder Symptoms						Clinical Responses ^(b)	
		Respiratory Disorder Symptoms						Peak Expiratory Flow Rate	Adverse Reactions
		Wheeze	Cough	Rales	Dyspnea	Mucus	Other		
47		-	↓	↓	↓	↓	-	↑	-
48		-	↓	↓	↓	↓	-	↑	-
49		↓	-	-	-	-	-	↑	-
50		-	↓	-	-	-	-	↑	-
51		-	↓	-	↓	-	-	↑	-
52		-	-	-	↓	-	-	↑	-
53		-	↓	-	↓	-	-	↑	-
*54	B	-	-	-	↓	-	-	↑	N/V anorexia, insomnia
	A	-	-	-	↓	-	-	↑	-
*55	B	-	↓	-	-	↓	-	Not measured	PR ≥ 100/min, sinus tachycardia, palpitation
	A	-	↓	-	-	↓	-	Not measured	-
56		-	↓	-	↓	↓	-	Not measured	PR ≥ 100/min, sinus tachycardia, palpitation

Continued

Patient Number ^(a)	Clinical Responses ^(b)							
	Respiratory Disorder Symptoms						Peak Expiratory	Adverse Reactions
	Wheeze	Cough	Rales	Dyspnea	Mucus	Other	Flow Rate	
Discontinue Cimetidine	-	↓	-	↓	↓	-	Not measured	-
*57 B	-	-	-	↓	-	-	↑	PR ≥ 100/min, N, anorexia, dizziness, sinus tachycardia, palpitation
A	-	-	-	↓	-	-	↑	-
58	↓	↓	↓	↓	↓	-		
59	↓	-	-	-	-	-	Not measured	PR ≥ 100/min, palpitation
60	↓	↓	↓	↓	-	-	↑	-
*61 B	↓	↓	-	-	-	-	↑	PR ≥ 100/min, palpitation, N/V
A	↓	↓	-	-	-	-	↑	-
A ^(b)	↓	↓	-	-	-	-	↑	PR ≥ 100/min, palpitation, N/V, anorexia, insomnia
A ^(b)	↓	↓	-	-	-	-	↑	PR ≥ 100/min, palpitation, N
C	↓	↓	-	-	-	-	Not measured	-

(a) Patient Number 1 - 43 : Patients were treated with theophylline together with other drugs (beta - adrenergic agonists, corticosteroids and anticholinergic drugs).

Patient Number 44 - 61 : Patients were treated with theophylline alone.

* Dosage regimen had been adjusted

B Befor dosage regimen adjustment

A After theophylline dosage regimen adjustment

C Theophylline was discontinued and changed to other drugs.

(b) Clinical Responses

: Respiratory Disorder symptoms

- No Occured ↑ Increased

↔ Unchangeable ↓ Decreased

: Peak Expiratory Flow Rate

↑ peak flow rate value was increased.

↓ peak flow rate value was decreased.

↔ peak flow rate value was unchangeable.

These symbols were comparison of clinical responses between before treatment with theophylline and when patients were discharged from hospital.

: Adverse Reactions

PR : Pulse Rate ↕ : Patient with high risk for adwers reaction

N/V : Nausea and Vomiting N : Nausea



- (c) Patient was referred to private hospital.
- (d) Patient was treated respiratory failure status by Bird's respiration.
- (e) Theophylline serum concentration was decreased after patient had received Moripront^R , Geriatric Pharmaton^R , and Moriamine^R .
- (f) Patient had respiratory failure status, later patient died in CCU.
- (h) Patient had liver dysfunction status

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