



REFERENCES

- Aronson, J.K. 1980. Clinical Pharmacokinetics of Digoxin 1980. Clin. Pharmacokinet. 5 : 137-149.
- Captopril Multicenter Research Group. 1983. A placebo controlled trial of captopril in refractory chronic congestive heart failure. J. Am. Coll. Cardiol. 2 : 755-763.
- Cleland, J.G.F., Dargie, H.J., Hodsman, G.P., Ball, S.G., et al. 1984. Captopril in heart failure ; a double-blind controlled trial. Br. Heart J. 52 : 530-535.
- _____, Dargie, H.J., Hodsman, G.P., Robertson, I.S., and Ball, B.G. 1984. Interaction of digoxin and captopril. Br. J. Clin. Pharmac. 17 : 214 P.
- _____, Dargie, H.J., Pettigrew, A., Gillen, G., and Robertson, J.I.S. 1986. The effects of captopril on serum digoxin and urinary urea and digoxin clearances in patients with congestive heart failure. Am. Heart J. 112 : 130-135.
- Cohn, J.N., et al. 1986. Effect of vasodilator therapy on mortality in chronic congestive heart failure. N. Engl. J. Med. 314 : 1547-1552.
- _____, et al. 1991. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. N. Engl. J. Med. 325 : 303-310.
- Consensus Trial Study Group. 1987. Effects of enalapril on mortality in severe congestive heart failure. N. Engl. J. Med. 316 : 1429-1435.
- Crozier, I.G., Ikram, H., and Nicholls, M.G. 1993. Angiotensin-converting enzyme inhibitors in the treatment of heart failure. In J.S. Robertson, and M.G. Nicholls (eds.), The Renin-Angiotensin System, pp. 93.1-93.21. London : Gower Medical.
- Doering, W., Maass, L., Irmisch, R., and Konig, E. 1987. Pharmacokinetic interaction study with ramipril and digoxin in healthy volunteers. Am. J. Cardiol. 59:60-64 D.
- Doherty, J.E., Soyza, N., Kanc, J.J., Bissett, J.K., and Murphy, M.L. 1978. Clinical pharmacokinetics of digitalis glycosides. Prog. Cardiovasc. Dis. 21(2) : 141-158.

- Douste-Blazy, P.H., Blanc, M., Montastruc, J.L., Conte, D., Cotonat, J., and Galinier, F. 1986. Is there any interaction between digoxin and enalapril? Br. J. Clin. Pharmac. 22 : 752-753.
- Furberg, C.D., and Yusuf, S. 1985. Effect of vasodilators on survival in chronic congestive heart failure. Am. J. Cardiol. 55 : 1110-1113.
- Garrett, E.R. 1970. The clinical significance of pharmacokinetics. In Pharmacological and clinical significance of pharmacokinetics (Symposia Medica Hoechst), pp 5-21. New York : FK Schattaur.
- Iisalo, E. 1977. Clinical pharmacokinetics of digoxin. Clin. Pharmacokinet. 2 : 1-16.
- Johnson, B.F., Wilson, J., Johnson, J., and Flemming, J. 1991. Digoxin Pharmacokinetics and Spirapril, a new ACE Inhibitor. J. Clin. Pharmacol. 31 : 527-530.
- Johnson, J.A., and Lalonde, R.L. 1992. Congestive Heart Failure. In J.T. Dipiro, R.L. Talbert, P.E. Hayes, G.C. Yee, G.R. Matzke, and L.M. Posey (eds.), Pharmacotherapy : a pathophysiologic approach, pp 160-193. USA : Appleton & Lange.
- Jolley, M.E., et al. 1981. Fluorescence polarization immunoassay. III. An automated system for therapeutic drug determination. Clin. Chem. 27 : 1575-1579.
- Keyes, P.W. 1980. Digoxin. In W.E. Evans, J.J. Schentag, and W.J. Jusko(eds.), Applied therapeutics : Principle of therapeutic drug monitoring, pp. 319-349. San Francisco : Applied therapeutic.
- Koup, J.R., Greenblatt, D.J., Jusko, W.J., Smith, T.W. and Koch-Weser, J. 1975. Pharmacokinetics of digoxin in normal subjects after intravenous bolus and infusion doses. J. Pharmacokinet. Biopharm. 3 : 181-192.
- Koup, J.R., Jusko, W.J., Elwood, C.M., and Kohli, R.K. 1975. Digoxin Pharmacokinetics : role of renal failure in dosage regimen design. Clin. Pharmacol. Ther. 20 : 15-23.
- Lee, W.H. and Packer, M. 1986. Prognostic importance of serum sodium concentration and its modification by converting enzyme inhibition in patients with severe chronic heart failure. Circulation 73(2) 257-267.
- Magelli, C., Bassein, L., Ribani, M.A., Liberatore, S., Ambrosioni, E., and Magnani, B. 1989. Lack of effect of captopril on serum digoxin in congestive heart failure. Eur. J. Clin. Pharmacol. 36 : 99-100.

- Miyakawa, T., Kobayashi, K., and Shionoiri, H. 1987. The effect of captopril on serum digoxin concentration in patients with mild congestive heart failure. Circulation 76 (suppl IV) : 86.
- Mooradian, A.D. 1988. Digitalis : An update of clinical pharmacokinetics, therapeutic monitoring techniques and treatment recommendations. Clin. Pharmacokinet. 15 : 165-179.
- Morris, F.P., Tamrazian, S., Marks, C., Kelly, J., Stephens, J.D., and Vandenberg, M.J. 1985. An acute pharmacokinetic study of the potential interaction of lisinopril and digoxin in normal volunteers. Br. J. Clin. Pharmac. 20 : 281-282 P.
- Mujais, S.K., et al. 1984. Transient renal dysfunction during initial inhibition of converting enzyme in congestive heart failure. Br. Heart J. 52 : 63-71.
- Newman, T.J., Maskin, C.S., Dennick, L.G., Meyer, J. H., Hallows, B.G., and Cooper, W.H. 1988. Effects of captopril on survival in patients with heart failure. Am. J. Med. 84 (suppl 3A) : 140-144.
- Oeltgen, P.R., Shank, W.A., Blouin, R.A., and Clark, T. 1984. Clinical evaluation of the Abbott TDx fluorescence polarization immunoassay analyzer. Ther. Drug Monit. 6 : 360-367.
- Opie, L.H., Chatterjee, K., Poole-Wilson, P.A., and Sonnenblick, E. 1991 Angiotensin Converting Enzyme Inhibitors and Conventional Vasodilators. In L.H. Opie (ed.), Drugs for the heart, pp 100-128. Philadelphia : W.B. Saunders.
- Packer, M., et al. 1993. Withdrawal of digoxin from patients with chronic heart failure treated with angiotensin-converting enzyme inhibitors. N. Engl. J. Med. 329(2):1-7.
- Raia, J.J., Barone, J.A., Byerly, W.G., and Lacy, C.R. 1990. Angiotensin-converting enzyme inhibitors : a comparative review. DICP Ann. Pharmacother. 24 : 506-525.
- Reuning, R.H., Sams, R.A., and Notari, R.E. 1973. Role of pharmacokinetics in drug dosage adjustment I. Pharmacologic effect kinetics and apparent volume of distribution of digoxin. J. Clin. Pharmacol. 13 : 127-141.
- Reynolds, J.E.F., ed. 1989. Martindale The Extra Pharmacopoeia. 29 th ed. London : The Pharmaceutical Press.
- Romankiewicz, J.A., Brogden, R.N., Heel, R.C., Speight, T.m., and Avery, G.S. 1983. Captopril : an update review of its pharmacological properties and therapeutic efficacy in congestive heart failure. Drugs 25 : 6-40.

- Rosenbloom, D., Craven, M.A. 1983. Postulated effects of alterations in Na: K-ATPase on the pharmacokinetics and pharmacodynamics of digoxin. Clin. Pharm. 2 : 168-173.
- SOLVD Investigators. 1991. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N. Engl. J. Med. 325 : 293-302.
- Swedburg, K., Enerothe, P., Kjekshus, J., and Snapinn, S. 1990. Effects of enalapril and neuroendocrine activation on prognosis in severe congestive heart failure (follow-up of the CONSENSUS trial). Am. J. Cardiol. 66 : 40 -45 D.
- Todd, P.A., and Heel, R.C. 1986. Enalapril : a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in hypertension and congestive heart failure. Drugs 31 : 198-248.
- Vandenburg, M.J., Kelly, J.G., Wiseman, H.T., Mannerling, D., Long, C., and Glover, D.R. 1988. The effect of lisinopril on digoxin pharmacokinetics in patients with congestive heart failure. Br. J. Clin. Pharmac. 21 : 657P.
- Williamson, J., and Chopin, J.M. 1980. Adverse reactions to prescribed drugs in the elderly : a multicentre investigation. Age and Ageing 9 : 73-80.
- Withering, W. 1941. An account of foxglove (1785). In Willius, and Keyes (eds.), Classic in Cardiology , pp. 227. New York : Dover.

APPENDICES

APPENDIX A

EQUATIONS

Equation 1

$$\text{IBW(male)} = 50 + (\text{ht. in inches} - 60)(2.3) \quad \dots \text{kg.}$$

Equation 2

$$\text{IBW(female)} = 45.5 + (\text{ht. in inches} - 60)(2.3) \quad \dots \text{kg.}$$

Equation 3

$$\text{CrCl(male)} = 98 - \frac{[0.8(\text{age} - 20)]}{\text{Scr}} \quad \dots \text{ml/min/70 kg}$$

Equation 4

$$\text{CrCl(female)} = 0.9 \left\{ 98 - \frac{[0.8(\text{age} - 20)]}{\text{Scr}} \right\} \quad \dots \text{ml/min/70 kg}$$

Equation 5

$$\text{CrCl(male)} = \frac{(140 - \text{age})(\text{weight})}{(7.2)(\text{Scr})} \quad \dots \text{ml/min.}$$

Equation 6

$$\text{CrCl(female)} = \frac{(0.85)(140 - \text{age})(\text{weight})}{(7.2)(\text{Scr})} \quad \dots \text{ml/min.}$$

Equation 7

$$\text{Cl} = (1.104)(\text{CrCl}^*) + 28.9 \quad \dots \text{ml/min/1.73m}^2$$

Equation 8

$$\begin{aligned} \text{Cl (patient with congestive heart failure)} \\ = (0.33)(\text{weight}) + (0.9)(\text{CrCl}) \end{aligned} \quad \dots \text{ml/min.}$$

Equation 9

$$\text{Vd digoxin} = 226 + \frac{(298)(\text{CrCl})}{29 + \text{CrCl}} \quad \dots \text{L/70 kg}$$

Equation 10

$$\text{Vd digoxin} = (3.8)(\text{weight}) + (3.1)(\text{CrCl}) \quad \dots \text{L}$$

Equation 11

$$\text{Ke} = \frac{\text{Cl}}{\text{Vd}} \quad \dots \text{hr}^{-1}$$

Equation 12

$$\text{t}_{1/2} = (0.693)(\text{Vd}/\text{Cl}) \quad \dots \text{hr.}$$

Equation 13

$$C_{ss,t_1} = \frac{F \cdot S \cdot D}{Vd} \cdot \frac{e^{-Ke t_1}}{1-e^{-Ke T}} \quad \text{.....mcg/L}$$

Equation 14

$$C_{ss \text{ ave}} = \frac{F \cdot S \cdot D}{Cl \cdot T} \quad \text{.....mcg/L}$$

<i>Abbreviation</i>	<i>Parameter</i>	<i>Unit</i>
Cl	Digoxin clearance	ml/min.
CrCl	Creatinine clearance	ml/min
CrCl*	Creatinine clearance	ml/min/1.73m ²
Css	Digoxin concentration at steady state	mcg/L
Css ave	Average Digoxin concentration at steady state	mcg/L
D	Digoxin dose	mcg.
F	Bioavailability	-
IBW	Ideal body weight	kg
Ke	Elimination rate constant	hr ⁻¹
S	Salt form factor	-
Scr	Serum creatinine	mg/dl
T	Dosing interval	hr.
t _{1/2}	Elimination half life	hr.
t ₁	The time since the last dose	hr.
Vd digoxin	Digoxin volume of distribution	L

APPENDIX B

NEW YORK HEART ASSOCIATION FUNCTIONAL CLASSIFICATION.

<i>Functional class 1</i>
Patients with cardiac disease but without limitation of physical activity . Ordinary physical activity does not cause undue fatigue, dyspnea, or palpitation
<i>Functional class 2</i>
Patients with cardiac disease that results in slight limitation of physical activity . Ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
<i>Functional class 3</i>
Patients with cardiac disease that results in marked limitation of physical activity. Although patients are comfortable at rest, less than ordinary activity will lead to symptoms.
<i>Functional class 4</i>
Patients with cardiac disease that results in an inability to carry on physical activity without discomfort. Symptoms of congestive heart failure are present even at rest. With any physical activity, increased discomfort is experienced.



VITAE

Miss Somratai Ratisoontorn was born on March 23, 1970, in Bangkok, Thailand. She graduated with a Bachelor Degree of Pharmacy with honour in 1991 from the Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand.