CHAPTER 2

REVIEW OF RELATED LITERATURE

ACE inhibitor now is widely used as an ajunctive treatment in patients with CHF. Enalapril, due to its prolonged action duration and less side effects is recommended for all mild, moderate, and severe congestive heart failure in adult patients. The hemodynamic and clinical effects on improving the heart function by reducing the systemic resistance and increasing the cardiac output, have been confirmed by several well designed randomized controlled trial. Sharpe,[10] in 1984, conducted a randomized, double-blind and placebo-controlled study. 36 patients with NY heart association functional class II-III heart failure who were clinically stable on digoxin and diuretic therapy. After baseline assessment, enalapril group received 10mg every day to compare with placebo group. After 3 months, enalapril group showed a significant improvement as judged by left ventricular shortening fraction, functional class, exercise duration measurements comparing with placebo group. Cleland[11] in 1985 carried a similar controlled study, 20 patients with NY functional class II-IV were randomly assigned in to enalapril and placebo group, all patients were on digoxin and diuretics before the trial started. Results showed that enalapril significantly reduce the LV end-diastolic dimension, and improved functional class and exercise tolerance. In response to enalapril, the plasma concentration of agiotensin II was reduced and that of active renin. In 1986, the United States National Institutes of Health commenced the Studies Of Left Ventricular Dysfunction, in which 23 international medical centers have been participated and 2569 patients were

enroled the trial. The results indicate a 16% reduction in all-cause mortality risk, and a 22% reduction in progressive heart failure mortality risk. There was also a 26% reduction in the total number of death and hospitalizations in the treatment group[1]. For the pediatric population, it might be inappropriate to use the experience in adults as a basis for predicting the outcome of ACE inhibitor in infant and child, this is not only because underlying etiology differences, in addition, there exist age-related differences in myocardial contractile function, circulatory physiology and drug disposition. 1990, Stern reported 12 cases with dilated cardiomyopathy age (4 weeks-15 years), after administered captopril for 3 months, left ventricular volume reduced 20%. In 1989 Frenneaux[12] treated 8 infants with severe CHF, aged (range from 4 days to 12weeks), Enalapril added as an additional medication plus digoxin and diuretics therapy. The starting dose was 0.1 mg/kg/day, increasing to response 0.12-0.43mg/kg/day. These patients can be categorized had congenital heart disease with Left-to- right shunt; left or right outflow tract stenosis and myocarditis. Those with Left-to-Right shunt and coarctation all had clinical improvement by measuring the weight, heart rate, sweaty, gallop rhythm after 2 weeks treatment, and no side effects found in this study. A group of children (8 cases) with CHF caused by dilated cardiomyopathy were chosen for treatment with enalapril while digoxin and diuretics remained[14]. Therapeutic dose was 0.5mg/kg/day. After 12 month follow-up, all cases showed a significantly reduced sizes of heart and liver and hormonal changes indicated alleviation of CHF. Blood pressure slightly decreased after 5 days but was well tolerated. During 1986-1991, Leversha group[13] carried out a study, based on a relatively large sample (63 cases), on efficacy of enalapril in CHF caused by congenital and acquired heart diseases. 72% were on digoxin and diuretics before

enalapril started. The patients included: left-to-right shunt; impaired ventricular function; valve regurgitation; postoperative palliation; post operation repair; systemic hypertension and pulmonary hypertension. Patient's age ranged from 9 days to 17 years. Overall 58% of patients showed improvement in response to enalapril, 30% showed no change in clinical (myocarditis cases). 12% required discontinuance due to side effects (increasing of serum creatinine and hypotension.). Lioyd[16] at University of Iowa, in 1989, conducted an orally administered enalapril dose-finding study for infants with congestive heart failure. 10 patients age from 6 weeks to 8 months with symptomatic congestive heart failure caused by congenital heart disease were enroled. The enalapril dose escalated from 0.02, 0.04, 0.08mg/kg/day within 9 days. No any side effects had been found. The issue of safety of enalapril in infant and child also has been carefully observed in some reports. Leversha[13] and Frenneaux[15] by escalating dosage within 3-10 days, 0.02-0.08mg/kg/day for infant; 0.1-0.5mg/kg/day for child, showed a safe and appropriate response. The favourable hemodynamic effects of ACE inhibitors in adults with CHF have been reported extensively. These effects were strongly associated with clinical improvement.