Pharmacological Management for Chronic Heart Failure

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Angiotensin-converting enzyme inhibitors (ACEI) and beta-blockers are main stream of pharmacological treatment for chronic heart failure. However, the role of angiotensin receptor blockers (ARB) as first line management for chronic heart failure is still not in consensus. Several studies such as Val-HeFT¹, STRETCH² and CHARM-overall³ trials show benefits of ARB in patients of heart failure. The benefits include improving exercise tolerance times, symptoms and signs of congestive heart failure (CHF), cardiothoracic ratio (STRETCH study), and reduced mortality (Val-HeFT and CHARM-overall studies). When comparing with ACEI, HEAVEN⁴ and RESOLVD⁵ show ARBs are similarly efficacious and safe for treating heart failure. ELITE⁶ study even shows ARB was associated with a lower mortality than ACEI in elderly heart failure patients. However, in ELITE study, the primary endpoint is not mortality and the case numbers is small (722 patients). In ELITE II trial with symptomatic CHF patients⁷, in OPTIMAAL⁸ and VALIANT⁹ trials involving high risk and heart failure after acute myocardial infarction, ARB does not prove to be superior to ACEI. According to CHARM-alternative 10 trial, ARB was generally well tolerated and reduced cardiovascular mortality and morbidity in patients with symptomatic chronic heart failure and intolerance to ACE inhibitors.

The role for combination of ARB and ACEI in treatment of CHF patients is still controversial. In Val-HeFT¹ trial, combination of ARB and ACEI is associated with increased mortality. In VALIANT⁹ trials involving patients with heart failure after acute myocardial infarction, combining ARB with ACEI increase the rate of adverse events without improving survival. In CHARM-Added¹¹ trial, the addition of ARB to ACEI and other treatment leads to a further clinically important reduction in relevant cardiovascular events in patients with CHF and reduced left-ventricular ejection fraction. In a quantitative review of data from randomized clinical trials¹², combination ARB plus ACE inhibitor vs control treatment that included ACE inhibitors was associated with significant increases in medication discontinuations because of adverse effects in patients with chronic heart failure (RR, 1.38 [95% CI, 1.22-1.55]) or in patients with acute myocardial infarction with symptomatic left ventricular dysfunction (RR, 1.17 [95% CI, 1.03-1.34]), and for both conditions there were significant increases in worsening renal function (RR, 2.17 [95% CI, 1.59-2.97] and RR, 1.61 [95% CI, 1.31-1.98], respectively), hyperkalemia (RR, 4.87 [95% CI, 2.39-9.94] and RR, 1.33 [95% CI, 0.90-1.98], respectively; the latter was not significant), and symptomatic hypotension (RR, 1.50 [95% CI, 1.09-2.07], and RR,

1.48 [95% CI, 1.33-3.18], respectively).

The compliance of medication is very important in heart failure patients.¹³ The combined home-based intervention with clinical nursing specialists could improve compliance of medication for chronic heart failure. The system is capable of decreasing adverse outcome, most notably hospitalization and length of stay, could trigger significant cost savings in the management of heart failure.¹⁴

References

- 1. Cohn JN, Tognoni G; Valsartan Heart Failure Trial Investigators. A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. N Engl J Med. 2001; 345: 1667-1675
- 2. Riegger GA, Bouzo H, Petr P, Munz J, Spacek R, Pethig H, von Behren V, George M, Arens H. Improvement in exercise tolerance and symptoms of congestive heart failure during treatment with candesartan cilexetil. Symptom, Tolerability, Response to Exercise Trial of Candesartan Cilexetil in Heart Failure (STRETCH) Investigators. Circulation. 1999; 100: 2224-2230.
- 3. Pfeffer MA, Swedberg K, Granger CB, Held P, McMurray JJ, Michelson EL, Olofsson B, Ostergren J, Yusuf S, Pocock S; CHARM Investigators and Committees. Effects of candesartan on mortality and morbidity in patients with chronic heart failure: the CHARM-Overall programme. Lancet. 2003; 362: 759-766.
- 4. Willenheimer R, Helmers C, Pantev E, Rydberg E, Lofdahl P, Gordon A; Heart Failure Valsartan Exercise Capacity Evaluation Study Group. Safety and efficacy of valsartan versus enalapril in heart failure patients. Int J Cardiol. 2002; 85: 261-270.
- 5. McKelvie RS, Yusuf S, Pericak D, Avezum A, Burns RJ, Probstfield J, Tsuyuki RT, White M, Rouleau J, Latini R, Maggioni A, Young J, Pogue J. Comparison of candesartan, enalapril, and their combination in congestive heart failure: randomized evaluation of strategies for left ventricular dysfunction (RESOLVD) pilot study. The RESOLVD Pilot Study Investigators. Circulation. 1999; 100: 1056-1064.
- 6. Pitt B, Segal R, Martinez FA, Meurers G, Cowley AJ, Thomas I, Deedwania PC, Ney DE, Snavely DB, Chang PI. Randomised trial of losartan versus captopril in patients over 65 with heart failure (Evaluation of Losartan in the Elderly Study, ELITE). Lancet. 1997; 349: 747-752.
- 7. Pitt B, Poole-Wilson PA, Segal R, Martinez FA, Dickstein K, Camm AJ, Konstam MA, Riegger G, Klinger GH, Neaton J, Sharma D, Thiyagarajan B. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial--the Losartan Heart Failure Survival Study ELITE II. Lancet. 2000; 355: 1582-1587.

- 8. Dickstein K, Kjekshus J; OPTIMAAL Steering Committee of the OPTIMAAL Study Group. Effects of losartan and captopril on mortality and morbidity in high-risk patients after acute myocardial infarction: the OPTIMAAL randomised trial. Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan. Lancet. 2002; 360: 752-760.
- 9. Pfeffer MA, McMurray JJ, Velazquez EJ, Rouleau JL, Kober L, Maggioni AP, Solomon SD, Swedberg K, Van de Werf F, White H, Leimberger JD, Henis M, Edwards S, Zelenkofske S, Sellers MA, Califf RM; Valsartan in Acute Myocardial Infarction Trial Investigators. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. N Engl J Med. 2003; 349: 1893-1906.
- 10. Granger CB, McMurray JJ, Yusuf S, Held P, Michelson EL, Olofsson B, Ostergren J, Pfeffer MA, Swedberg K; CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-Alternative trial. Lancet. 2003;362:772-776.
- 11. McMurray JJ, Ostergren J, Swedberg K, Granger CB, Held P, Michelson EL, Olofsson B, Yusuf S, Pfeffer MA; CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. Lancet. 2003;362:767-771.
- 12. Phillips CO, Kashani A, Ko DK, Francis G, Krumholz HM. Adverse effects of combination angiotensin II receptor blockers plus angiotensin-converting enzyme inhibitors for left ventricular dysfunction: a quantitative review of data from randomized clinical trials. Arch Intern Med. 2007; 167: 1930-1936.
- 13. Frishman WH. Importance of medication adherence in cardiovascular disease and the value of once-daily treatment regimens. Cardiol Rev. 2007; 15: 257-263.
- 14. Ho YL, Hsu TP, Chen CP, Lee CY, Lin YH, Hsu RB, Wu YW, Chou NK, Lee CM, Wang SS, Ting HT, Chen MF. Improved cost-effectiveness for management of chronic heart failure by combined home-based intervention with clinical nursing specialists. J Formos Med Assoc. 2007; 106: 313-319.