ORIGINAL ARTICLE

Risk Assessment in Cardiac Failure Patients at High Risk of Hypotension Due to Ace Inhibitor Therapy & Measures to Overcome this Risk

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ABSTRACT

Aim: To find out the proportion of patients of cardiac failure who were at high risk of first dose hypotension due to angiotensin converting enzyme inhibitors and to overcome this effect at their initiation of therapy.

Study Design: It was an observational study

Methods: One hundred adult patients with congestive cardiac failure not taking ACE therapy, who were admitted in Medical Units, Mayo Hospital, Lahore, were registered for this study. Patients were divided into two groups, A and B. Group A had patients who were euvolumic and normonatremic while group B comprised of patients who were hyponatremic & volume depleted due to previous diuretic treatment. Control blood pressure readings were noted. Angiotensin converting enzyme inhibitor (captopril) was administered in smallest dose(6.25mg). Blood pressure was recorded at 30 minutes, 60 minutes and 90 minutes. First dose hypotension was noted by drop in systolic blood pressure > 20 mmHg from the baseline systolic blood pressure after the 90 minutes of captopril administration or decrease in systolic blood pressure below 90 mmHg irrespective of baseline reading.

Results: Out of one hundred patients forty patients (40%) had first dose hypotension at 30minutes, 44 (44%) patients were observed to have first dose hypotension at 60 minutes while fifty (50%) patients suffered first dose hypotension after 90 minutes. Out of fifty patients of group A, 7 patients were observed to have first dose hypotension after ACE therapy while out of 50 patients of group B, 23 patients had first dose hypotension.

Conclusion: ACE inhibitors have an important role in patients with heart failure. First dose hypotension is a common and hazardous side effect of these drugs. However, first dose hypotension can be overcome if the diuretic therapy is stopped approximately 12-24 hours before administering ACE (captopril) or dose of diuretics reduced. Also hyponatremia and hypovolemia corrected before initiation of ACE inhibitor therapy.

Keywords: ACE inhibitor, cardiac failure, first dose hypotension, captopril

INTRODUCTION

The incidence of heart failure increases with advancing age. [(1)] The prognosis of heart failure has improved a lot for the last many years, but the mortality rate remains still high with approximately 50% of patients die after 7-8 years.

Management of heart failure is aimed at relieving the symptoms, retarding disease progression and improving the survival[2]. The management of heart failure depends on the following: Drugs for example diuretics[3]. Angiotensin converting enzyme inhibitors[4], positive inotropic agents[5] and antiarrhythmic drugs while non-pharmacological measures include coronary artery bypass grafting[7] implantable cardioverter defibrillator, insertion of pacemaker etc[8]. The ACE inhibitors are considered standard therapy for heart failure. Their modeof action includes both vasodilation and inhibition of increased neurohormonal activity. They inhibit the renin angiotensin aldosterone system, producing vasodilation by blocking angiotensin-II induced vasoconstriction and decreasing sodium retention by reducing aldosterone secretion. Multiple trials for example consensus, solved, save have proved beneficial role of ACE inhibitors management of heart failure[9,10]. They also increase the production of vasodilating prostaglandins by inhibiting the degradation of bradykinin and thus block the adrenergic nervous system[11,12]. Heart failure patients are particularly prone to risk of first dose hypotensiondue to pre-existent hyperreninemia and hyperaldosteronism. Captopril is considered the preferred agent to start treatment due to its predictable onset and short duration of action

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(approx30-90minutes peak effect). Treatment is usually initiated with smallest dose and the diuretics should be omitted at least 24 hours before start of ACE inhibitor therapy. There is a high risk of first dose hypotension in patients receiving high dose of diuretics and in the presence of hyponatremia (Na < 130mmol/l).

MATERIALANDMETHODS

Study was conducted on one hundred patients of cardiac failure admitted to the medical units of Mayo Hospital, Lahore not taking ACE inhibitors previously. After taking history and doing physical examination, the relevant investigations e.g., blood complete examination, blood urea, serum creatinine, X-ray chest, ECG, Echocardiography and Doppler abdominal ultrasound (to detect bilateral shrunken kidneys and rule out bilateral renal artery stenosis) were ordered and findings entered in a specified proforma. Patients were divided into two groups, A and B. Group A had patients who were euovolumic and normonatremic while group B comprised of patients who were hyponatremic & volume depleted due to previous diuretic treatment. Control blood pressure readings were noted. Angiotensin converting enzyme inhibitor (captopril) was administered in smallest dose (6.25mg). Blood pressure was recorded at 30 minutes, 60 minutes and 90 minutes. First dose hypotension was noted by drop in systolic blood pressure > 20 mmHg from the baseline systolic blood pressure after the 90 minutes of captopril administration or decrease in systolic blood pressure below 90 mmHg irrespective of baseline reading. Blood pressure both systolic and diastolic were recorded before and after giving ACE inhibitor Captopril at the dose of6.25mg at 30,60 and 90 minutes.

Operational definitions: First dose hypotension was defined as drop in systolic blood pressure more than 20 mm Hg of the reading noted at the time of administration of captopril after its peak effect (60-90 minutes) or drop in systolic blood pressure below 90 mm Hg irrespective of baseline reading. Patients were given required treatment of heart failure in addition to captopril during the trial. No ACE inhibitor other than captopril was used in this study.

Hponatremia: Mild: 130-134mmol/L. Moderate: 125-129mmol/ L &Profound: <125 mmol/L

Inclusion criteria. Congestive cardiac patients with age> 15 years.

Exclusion criteria

1- Patients taking ACE inhibitor therapy already.
2- Known hypersensitivity to ACE inhibitors.
3- Severe hypotension: systolic BP < 90mmHg
4- Bilateral renal artery stenosis.
5- Renal parenchymal disease.
6- Hyperkalemia (K^+ > 5.6mmol/l)
7- Age < 15 years

It was an observational study, where we administered captopril and observed the proportion of cardiac failure patients who developed hypotension. Data was analyzed with SPSS 17.Comparable values of first dose hypotension in group A and B were evaluated by student T-test and p value calculated (<.05 was significant).

RESULTS

Out of 100 patients, 60 (60%) were male and 45 (45%) were female. Male to female ratio was 1.5:1. Out of 100 patients, 22 patients (22%) were found diabetic and 9 patients (18%) were hypertensive.

Exertional dyspnea was observed in nearly all patients (100%). Ankle edema was present in 68 patients (68%). Jugular venous pressure (JVP) was raised in 66 patients (66%). Apex beat was found shifted in 65 patients (65%). Gallop rhythm was detected in 30 patients (30%). Basal crepitations were present in 36 patients (72%).

Echocardiography showed left ventricular hypertrophy (LVH), abnormal segmental wall motion and global hypokinesia in 80 patients (80%). Valvular heart disease was found in 25 patients (25%).

Systolic blood pressure before captopril administration was observed in the range of 105-170 mm Hg (mean 120.54 ± 18.05). Diastolic blood pressure before captopril administration was noted in the range of 60-100mmHg (mean 75.5±9.01) after captopril administration.

First dose hypotension was observed at 30 minutes in 38 patients (38%). p=.003was obtained from standard T- Test, 2 tailed and 2 sample equal variance

Systolic blood pressure at 30 minutes was observed in the range of 80-160 mm Hg (mean 113.60±19.0).Diastolic blood pressure at 30 minutes was observed in the range of 65-95mmHg (mean 73±7.6).

First dose hypotension recorded at 60 minutes was in 42 patients (42%). p= .07 was obtained from standard T-s test, 2 tailed and 2 sample equal variance. Systolic blood pressure at 60 minutes was in the range of 70-140 mm Hg. (mean 105.70 ± 18.73).Diastolic BP at 60 minutes was in the range of 60-90mmHg (mean 71.90±7.13).

Table.1 :Correlation between serum electrolyte levels and first dose hypotension (n=100)

		SBP Before Captopril Administration	**Serum Electrolytes**	**Drop in SBP at 30 minutes**	**Drop in SBP at 60 minutes**	**Drop in SBP at 90 minutes**
SBP before captopril administration	Pearson correlation Sig. (2 tailed)	1.005 NA***	-.319* .020	-.129 .300	.079 .499	-.312* .016
Serum electrolytes	Pearson correlation Sig. (2 tailed)	-.331* .025	1.001 NA***	**.351**** **.006**	**.212** **.088**	**.500**** **.009**
Drop in SBP at 30 minutes	Pearson correlation Sig. (2 tailed)	-.129 .344	**.360**** **.007**	1.011 NA***	.500** .001	.511** .008
Drop in SBP at 60 minutes	Pearson correlation Sig. (2 tailed)	NA*** .534	NA*** **.089**	.578** .000	1.024 NA***	.524** .003
Drop in SBP at 90 minutes	Pearson correlation Sig. (2 tailed)	-.324* .014	**.512**** **.000**	.500** .001	.543** .002	1.003 NA***

*Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed)
*** NA means not applicable

First dose hypotension was noted at 90 minutes in 50 patients (50%). (p= .000055) was obtained from standard T- Test, 2 tailed and 2 sample equal variance. Systolic BP at 90 minutes was noted in the range of 75-150 mm Hg (mean 104.00 ±19.58). Diastolic Blood Pressure at 90 minutes was observed in the range of 50-90 mm Hg (mean 70 ± 7.95).

In 50 patients (50%)first dose hypotension was observed.40 patients (40%) were of group B and 10 patients (10%) were detected from group A. It means that 20% contribution was from group A (normovolemic, normonatremic) and 80% contribution was from group B (hyponatremic, hypovolemic).

First dose hypotension was noted in 38 patients (38%) at 30 minutes, 44 patients (44%) at 60 minutes and 50 patients (50%) at 90 minutes. It was observed that first dose hypotension was more common in hyponatremic & hypovolemic patients.

DISCUSSION

In this study of100 patients, 60 were male and 40 patients were female with a male to female ratio 1.5:1[13] in Western population studies the ratio was 4:1

In our study, 25 patients (25%) were diabetic. This was slightly more as compared to another study [(14)] in which the incidence of diabetes in CHF patients was 17%.

The dilated cardiomyopathy was present in 45 patients (45%). In other studies the prevalence of dilated cardiomyopathy was low being 21% and 5% in other studies[15].

Hypertension was present in 6 patients (12%) in our study[16]. Hypertensive heart failure was common in a study at Hong Kong, [(17)] which is contrary to our study.

Valvular heart disease was found to be cause of Cardiac failure in 22 patients (22%) while other studies showed valvular heart disease as a cause of Cardiac failure in 15%[8], 13%[19] and 4%[20].

First dose hypotension was observed in 50 patients (50%) at 90 minutes. It was in accordance with another study which showed mean drop in Blood Pressure> 20 mm Hg after captopril administration in about 50% of patients[21. 22].

First dose hypotension was noted in 42 patients (42%) at60 minutes. It was almost similar to another study where BP drop after 1 hour first dose of captopril was (38%)[23,24]. However, some studies showed first dose hypotension with captopril within three hours was only 18%[25, 26].

First dose hypotension was also observed in normotensives, normovolemic patients (10%). It was similar to another study, which showed this incidence about 15%[27].

First dose hypotension was commonly noted in hyponatremic, hypovolemic patients in this study(40%). It was in accordance with another study[28].

First dose hypotension was observed less commonly in hypertensive patients (24%) in our study. It was observed in our study that if hyponatremia corrected before administering captopril (group A), then ACE inhibitors (captopril) was well tolerated[29].

This study with conducted with captopril keeping in mind the view that captopril is equally well tolerated and effective as compared to other ACE inhibitors like Enalapril in treatment of cardiac failure. It was in accordancewith other studies[30], which also showed similar results.

Table 2: Risk factors for first dose hypotension & measures to reduce the risk

Risk factors	Precautions
Initial low blood pressure	Omit the morning dose of diuretic (if mandatory, give later)
Acute heart failure	start with small dose of ACE inhibitor
High doses of diuretics	Administer to a sitting patient who remains sitting for 1-2 hours
Low serum sodium	patient should be monitored
Other vasodilators	if hypotension occurs, put lie him down and elevate the legs

Patients greater than 75years age are at high risk for hypotension, and must be started initially on small doses. ACE inhibitors, captopril (Short-acting) must be monitored at least for 1-2 hours , whereas long-Acting ACE inhibitors(e.g. Enalapril Lisinopril, Quinapril, Fosinopril) must be followed for at least 2-3 hours. If well tolerated, then titration of ACE inhibitor must be done: Captopril 12.5 mg twice or thrice daily or Enalapril 2.5mg two times daily. The dose of ACE inhibitor in the elderly patients needs to be adjusted and a more prolonged period of monitoring is warranted.

CONCLUSION

ACE inhibitors have a very beneficial and key role in patients with chronic heart failure. However, first dose hypotension with these drugs is a very common and hazardous side effect, which usually fears the doctors about the prescription of these drugs. Also due to this common side effect, ACE inhibitors are usually prescribed under dosed. However, first dose hypotension can be avoided/minimized if the diuretics are omitted 12-24 hours before introducing captopril or dose of diuretics reduced as well as hyponatremia and volume depletion corrected before instituting ACE inhibitor therapy especially captopril.

REFERENCES

1. Davidsons's principles and practice of Medicne18thedn 1999;192-94.
2. Massie BM. Pathophysiology of heart failure. In Cecil textbook of medicine 21st edition 1999.
3. Grauer K. Heart failure program and abstracts from the American Academy of Family Physicians 52nd Annual Scientific Assembly; 2000; Dallas, Texas Session 352.
4. Barry M, Massie MD, Thomas M, Amidon MD. Functional classification of heart disease.In Current Medical Diagnosis & Treatment 2000; 351-52.
5. Kramer BK, Schweda F, Reiger GA. Diuretic treatment and diuretic resistance in heart failure.Am J Med. 1999; 106:90.
6. Coodley E. Newer drug therapy for congestive heart failure. Arch intern Med 1999;159:1177-83.
7. Pitt B, Zannad F, Remme WJ. Randomized Aldactone Evaluation Study Investigators.The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N Engl J Med 1999; 341: 709-17.
8. Davies MK, Gibbs CR, Lip GY. Management: diuretics, ACE inhibitors and nitrates. BMJ.2000; 320:428-31.
9. MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised intervention Trial in Congestive Heart Failure (MERIT-HF) Lancet 1999;353:2001-07.
10. Abraham WT. Beta-blockers: the new standard of therapy for mild heart failure. Arch Intern Med 2000;160:1237-47.
11. Pepper GS, Lee RW. Sympathetic activation in heart failure and its treatment with beta-blockers. Arch Intern Med 1999;159:225-34.
12. CIBIS-II Investigators: The Cardiac Insufficiency Bisprolol Study II (CIBIS-II: A randomized trial). Lancet 1999; 353.
13. John CL, James M. ACE inhibitors standard treatment for CHF. B M J 2000;321: 1113-16: 1095-96.
14. Leor J, Reicher RH, Goldbourt U. Aspirin and mortality in patients treated with ACE inhibitors: a cohort study of 11,575 patients with coronary artery disease. J Am CollCardiol 1999; 33:1920-25.
15. The SOLVD investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. N Engl J Med 1999;325:293-302.
16. Milton Packer. Higher doses better than lower doses of ACE inhibitors in CHF.The ATLAS Study Group 1999; 100:1-7.
17. Brunner - La RH, Weilenmann D, Kiowski W, Maly E, Candinas R, Follath F. Within-patient comparison of effects of different dosages of enalapril on functional capacity and neurohormone levels in patients with CHF. Am Heart J 1999;138:654-62.
18. Massie GP. Tolerance of ACE inhibitors in CHF. Arch Intern Med 2001;161:165-71.
19. Philip A, Poole-Wilson, Betram P. Evaluation of losartan in The Elderly Study, The Losartan heart failure survival study.ELITE II study.Am Heart J 1999; 138:1005-06:1126-32.
20. Eulalia R. Blood ACE levels predictor. Eur Heart J 2000; 21:14-16:53-57.
21. Hertzel G. The ACE inhibitor ramipril effect on cardiovascular events and kidney disease in diabetic patients. The Heart Outcomes Prevention Evaluation (HOPE) study NEngl J Med 2000;342:145-53:201-02.
22. Salim Y. ACE inhibitor versus vitamin E supplements in patients with cardiac failure. N Eng J Med 2000; 342:145-53: 201-02.
23. Eric V, Robert C, Bertram P. Captopril versus losartan in CHF. Lancet 2000; 355:1568-69:1575-87.
24. Faiez Z, Kwame A. The under dosage and under prescription of ACE inhibitors in CHF with low blood pressure. Am Heart J 2000; 139:624-31.
25. Eryonnai B, Koldas L, Ayan F, Keser N, Siramaci. First dose hypotension with ACE inhibitors. JPN Heart J 2001; 42: 185.
26. Spinar J, Vitovec J, Pluhaek L, Spinarosa L, Thomas J. First dose hypotension after initial doses of ACE inhibitors.Int J, cardiol 2000; 75:197-204.
27. Tovinthran S, Raja Soorya C, Soong WC. Captopril suppression test in normotensives.Department of medicine, Alexandra Hospital, Singapore 2000.
28. Clement DL, Debuyzore M, Tomos M, Vanavermaete G. Captopril in heart insufficient patients study (CHIPS) Actacardiol 2000; 1-7.
29. Haiat R, Piat O, Galloi SH. Blood pressure response to first 36 hours of heart failure therapy with captopril. J Cardiovasc 1999; 33:953-9.
30. Navookarasu NT, Rehman AR, Abdullah I. First dose hypotension with ACE inhibitors.Int J ClinPrac 1999; 25-30