

INCIDENCE OF COUGH WITH FOSINOPRIL IN PATIENTS HAVING COUGH WITH CAPTOPRIL - A CROSS - OVER STUDY

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SUMMARY

Background: Cough is a group side effect of all angiotensin converting enzyme (ACE) inhibitors. Although it is known to be a group effect, there are claims about different compounds having low incidence of cough compared to others.

Objective: To assess the severity and frequency of cough with ACE inhibitor fosiopril in hypertensive patients with ACE inhibitor captopril associated cough. **Methods:** 10 patients who developed cough while taking captopril (generic preparation) for hypertension were studied. The patients who were taking captoril were crossed over to fosiopril.

Results: There were 10 patients, 3 male and 7 female. The mean age of all patients was 53.69 + 10.40 years. These patients were followed up for a mean period of 7.3 weeks. The mean systolic blood pressure at start of the study was 161.6 + 18.19 mmHg and at the end was 142.4 + 11.94, showing a reduction of 19.2 mmHg (11.88 %). The diastolic blood pressure at the beginning of tile study was 96.2 + 10.02 mmHg and at the end of the study was 84.0 + 9.12 mmHg, showing a reduction of 12.2 mmHg (12.68%). The mean heart rate at the start of the study was 82.6 + 18.05 and at the end of the study was 74.2 + 10.18 beats /minute. The cough profile at the end of the study showed no cough in 6 patients and reduced severity and frequency in 4 patients.

Conclusion: Hypertensive patients with previous ACE inhibitor captopril associated cough reported significantly less frequent cough with fosiopril.

Keywords: Angiotensin converting enzyme inhibitors, Hypertension, Fosiopril, Captopril, Cough

INTRODUCTION

Angiotensin converting enzyme (ACE) inhibitors are used widely in the treatment of hypertension. Guidelines for the management of hypertension issued by the World Health Organization (WHO) and the International Society of Hypertension class ACE inhibitors as suitable agents for first line treatment (1). Long-term use of ACE inhibitors is associated with a side effect profile well tolerated by most patients. However, in some patients ACE inhibitors have been associated with a non-productive persistent (2-8). The frequency of ACE inhibitor associated

cough has been reported to range from 10-20% (9-13). Although it is known to be a group effect, there are claims about different compounds having low incidence of cough compared to others.

Fosiopril is the first ACE inhibitor from a new class of agents with phosphorus. It is a prodrug that is completely de-esterified in the liver and gastrointestinal tract to form the active diacid fosioprilat, which subsequently is metabolized to almost an equal extent by the hepatic and renal pathway (14). Fosiopril has been reported to cause less ACE inhibitor associated cough compared with other ACE inhibitors when given to patients with hypertension (15, 16).

This study was designed to assess the severity and frequency of cough in hypertensive patients with

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ACE inhibitor fosinopril who were already having ACE inhibitor captopril associated cough.

METHODS

Patients fulfilling the following criteria were included in this study:

- Patients of any sex less than 70 years of age.
- Female patients who were not planning for pregnancy and not breast feeding.
- Patients who were having cough with other ACE inhibitors
- Patients who did not have malignant, accelerated or secondary hypertension.
- Patients who did not-suffered M.I. or C.V.A.
- Patients having blood pressure less than 200/115 mmHg.
- Patients who did not have significant hepatic or renal dysfunction.
- Patients who did not suffer from alcohol or drug abuse
- Patients without any other systemic disease.
- Patients who gave informed consent.

These patients were selected from a pool of patients with hypertension having ACE inhibitor captopril (generic preparation) related cough, which was persistent and not responding to usual cough suppressants. The frequency and severity of cough was graded as shown in table-I.

**Table - I
COUGH INDEX**

0-	No cough
1-	Rare
2-	Occasional
3-	Frequent
4-	Almost constant

These patients were given a wash-out period of two weeks. Then ACE inhibitor fosinopril was started in a dose of 10 mg once daily. These patients were regularly followed every week for control of blood pressure and cough profile. Detailed inquiry was done on each visit about the frequency, severity, nature and timing of cough.

The data collected were analysed. Values are mentioned in mean ± standard deviation.

RESULTS

10 patients were included in the final analysis. 3 were male and 7 were female patients. The patients' characteristics before and after the study are shown in table II and III. The mean age of these patients was 53.69 ± 10.40 years. Mean age of male patients was

**Table - II
PATIENTS' CHARACTERISTICS AT THE BEGINNING OF STUDY**

Pt. No.	Age	Sex	SBP	DBP	Heart Rate	Cough Index
1	65	M	150	90	80	3
2	45	F	160	100	96	3
3	50	F	160	90	104	4
4	60	M	160	100	76	4
5	60	F	170	100	76	4
6	72	M	150	90	92	3
7	40	F	160	90	70	3
8	40	F	160	90	70	3
9	50	F	170	100	74	3
10	55	F	160	102	78	3

**Table - III
PATIENTS' PROFILE AT THE END OF STUDY**

Pt. No.	SBP	DBP	Heart Rate	Cough Index
1	140	86	70	0
2	140	90	80	0
3	140	90	90	2
4	145	90	70	0
5	145	85	74	3
6	140	85	74	2
7	150	90	72	0
8	155	90	76	0
9	140	90	70	2
10	130	90	70	0

65.66 ± 3 .29 and female patients was 48.57 ± 8.18 years (Table-IV). These patients were followed up for a mean period of 7.3 weeks (range: 6 to 11 weeks). The mean systolic, blood pressure at start of the study was 161.6 ± 18.19 mmHg and at the end was 142.4± 011.94, showing a reduction of 19.2 mmHg (11.88%) (Table-V and VI). The mean systolic blood pressure

Table - IV
MEAN AGE OF PATIENTS

Sex	No. of Pts.	Age (Years)
Male	3	65.66+3.29
Female	7	48.57+8.18
Total	10	53.69+10.40

Table - V
BLOOD PRESURE AT THE BEGINNING
OF STUDY

Sex	SBP	DBP	Heart Index
Male	153.3	93.3	82.6
Female	165.1	97.4	82.5
Total	161.6	96.2	82.6

Table - VI
BLOOD PRESURE AT THE END
OF STUDY

Sex	SBP	DBP	Heart Index
Male	141.3	87.0	71.3
Female	142.9	88.5	75.4
Total	142.4	88.6	74.2

in male patients at start of the study was 153.3 mmHg and at the end was 141.3 mmHg, showing a reduction of 12.0 mmHg (7.8%). The mean systolic blood pressure in female patients at start of the study was 165.1 mmHg and at the end was 142.9 mmHg showing a reduction of 22.2 mmHg (13.5%). The mean diastolic blood pressure of all patients at the beginning of the study was 97.4 mmHg and at the end of the study was 88.6 mmHg, showing a reduction of 8.8 mmHg (9.1 %). The mean diastolic, blood pressure in male patients at start of the study was 93.3 mmHg and at tile end was 73.3 mmHg, showing a reduction of 20.0 mm (21.5%). The mean diastolic blood pressure in female patients at start of the study was 97.4 mmHg and at the end was 88.6 mmHg, showing a reduction of 8.8 mmHg (9.1 %). The mean heart rate at the start of the study was 82.6 ± 18.05 and at the end of the study was 74.2 ± 10.18 beats /minute. The cough profile at the end of the study showed no cough in 6 patients and reduced severity and frequency in 4 patients.

DISCUSSION

In this prospective study, hypertensive patient receiving ACE inhibitors for treatment of hypertension and has developed persistent dry cough has been included. From a pool of over a hundred and fifty patient with hyper tension receiving ACE inhibitors, 15 patient had ACE inhibitor associated cough. All these patient were receiving captopril for control of there blood pressure. These patients were switched over to fosinopril according to the study protocol.10 patients who had at least six week of follow-up or heaving less then six-week follow-up.

As the result have shown, fosinopril effective control hypertension. The mean systolic blood pressure before treatment was 161.6 mmHg, which dropped to 142.4 mmHg. There was 12% reduction in the mean systolic blood pressure. Similarly the mean diastolic blood pressure before the start of foinopril therapy was 97.4 mmHg and 88.6mmHg at the end of study. This shows a 9% reduction in the diastolic blood pressure. Other studies have also shown that fosinopril effectively controls blood pressure (16).

Out of 10 patients with captopril induced cough, six patient s had no cough at the end of study after a mean follow-up of 7.3 weeks (range 6-11 weeks). The remaining four patients had reduced severity and frequency of cough. This shows an improvement in cough profile in all 10 patients. Other investigators have also reported similar result with fasinopril. David et al compared the cough profile in the hypertensive patient with enalapril and fasinopril in a cross-over study, and reported a significantly lower cumulative cough cross in patient receiving fosinopril in comparison to enalapril. In another study hypertensive patient reporting cough associated with quinapril, experienced resolution when switched to fasoinopril, and had cough reappeared when rechanged with quinapril (17). This proves that patients who experience cough on one ACE inhibitors, particularly if switched over to fosinopril, therefore can drive substantial benefits from an ACE inhibitor for hypertension or other clinical indication, rather then avoiding the uses of ACE inhibitors altogether.

CONCLUSION

In this study, hypertensive patient with ACE inhibitor associated cough with captopril reported significantly less frequent cough with fosinopril. This study also suggests patient who experience cough on one ACE inhibitor, may not develop cough with another ACE inhibitor like fosinopril.

REFERENCES

1. Zanchetti A, Chalmers J, Arakawa K, et al. The 1993 guidelines for the management of mild hypertension: memorandum from a WHO/ISH meeting. *Blood Press* 1993;2:86.
2. Sesoko S, Kaneko Y. Cough associated with the use of captopril. *Arch Intern Med* 1985;45:1524.
3. Inman WHW. Enalapril induced cough. *Lancet* 1986;4:1218.
4. Reisin L, Schneeweiss A. Spontaneous disappearance of cough induced by angiotensin converting inhibitors (captopril or enalapril). *Am J Cardiol* 1992;70:398.
5. Poole MD, Postma DS. Characterization of cough associated with angiotensin converting enzyme inhibition. *Otolaryngeal Head Neck Surg* 1991; 105; 714.
6. Coulter DM, Edwards R. Cough associated with captopril and enalapril. *BMJ* 1987;194:1521.
7. Israel-Blet D, Delaume C, Christien J. Enalapril induced cough. *Lancet* 1986;4:918.
8. Goldszer GRC, Lilly LS, Solomon HS. Prevalence of cough during angiotensin enzyme inhibition therapy. *Am J Med* 1988;85:887.
9. Gibson GR. Enalapril induced cough. *Arch Intern Med* 1989; 149:270 1.
10. Stoller JK, Mehta A, Vidt D. Captopril induced cough. *Chest* 1988;93:659.
11. Just PM. The positive association of cough with angiotensin enzyme inhibitors. *Pharmacotherapy* 1989;9:82.
12. Sebastain JL, McKinney WP, Kaufman J, Young MJ. Angiotensin enzyme inhibitors and cough. Prevalence in an out patient medical clinic population. *Chest* 1991;99:36.
13. Simon SR, Black HR, Moser M, Berland WE. Cough and ACE inhibitor. *Arch Intern Med* 1992;52:1698.
14. Sahn DJ, de Maria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 1978;58:1072.
15. Germino FW, Lastra J, Pool P, et al. Evaluation of the cough profile of fosinopril in hypertensive patients with ACE inhibitor associated cough - a pilot study. *Current Therap Res* 1993;54:5.
16. David D, Jallad N, Germino FW, et al. A comparison of the cough profile of fosinopril and enalapril in hypertensive patients with a history of ACE inhibitor associated cough. *Am J Therap* 1995;2:806.
17. Sharif MN, Evans BL, Pylypchuk GB: Cough induced by quinapred with resolution after changing to fosinopril. *Ann Pharmacother* 1994;28:720.