

Significance of palpitation among hypertensive patients receiving captopril

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Abstract

Captopril prevent the conversion of angiotensin 1 to II by inhibiting of peptidyl dipeptide carboxy hydrolase enzyme. Captopril is an angiotensin converting enzyme (ACE) inhibitors which is the treatment of hypertension. Hundred & eight hypertensive patients taking captopril as a tablet 25 mg twice daily (47 men & 61 women). Each patient had a complete history detailed, physical examination, all patients were interviewed & full medical history was taken. All patients were questioned about the presence or absence of headache, palpitation, cough, flushing, chest pain, dysgeusia & tachycardia. Blood pressure & heart rate were measured for each patient each visit. In hypertensive men, 29 patients out of 47 (61.7%), hypertensive patients are diagnosed as suffering from palpitation. While in hypertensive women, 39 patients out of 61 women have palpitation after taking captopril for 3 months (64%). In regard to serum potassium, it was estimated in 51 hypertensive patients (27 with palpitation & 24 patients without palpitation). There is no significant difference in regarded to serum potassium between hypertensive patients with palpitation & hypertensive patients without palpitation. In hypertensive patients with palpitation, 9 patients out of 27 patients have hyperkalaemia (33.3%), (serum potassium more than 3 mmol/L). In hypertensive patients without palpitation, only 3 patients out of 24 patients have hyperkalaemia (0.125%). In hypertensive men, there are no significant differences between group with palpitation & patients without palpitation regarding blood pressure in both systolic & diastolic. Also, there is no significant difference regarding heart rate between group of patients with palpitation & group of patients without palpitation. Palpitation can be attributed to one of the three main causes. The first cause is hyperdynamic circulation which includes hypercapnia, pyrexia, thyrotoxicosis, anemia & pregnancy. The second cause is sympathetic overdrive include panic disorders, hypoglycemia, hypoxia, heart failure & mitral valve prolapse. While the third main cause is arrhythmias.

Key words: Captopril, hypertension, palpitation, blood pressure, tachycardia.

Introduction

Captopril is an angiotensin converting enzyme (ACE) inhibitors which is the treatment of hypertension & heart failure. The mechanism of action of captopril has not yet been fully elucidated. It appears that captopril lower blood pressure & be an adjunct in the therapy of congestive heart failure primarily through suppression of renin angiotensin – aldosterone system (1,2).

Captopril prevents the conversion of angiotensin 1 to II by inhibiting of peptidyl dipeptide carboxy hydrolase enzyme. Angioten II stimulate the synthesis & secretion of aldosterone which cause water & sodium retention (1, 3, 4).

ACE inhibitors lower blood pressure by lowering or reducing peripheral vascular resistance without reflexively increasing cardiac output or contractility (6, 7).

Captopril uses may causes side effects such as non productive cough, decrease coronary perfusion, neutropenia, agranulocytosis, anemia, thrombocytopenia, flushing, tachycardia, chest pain & in rare cases palpitation (8).

Palpitations are heart beat sensations that feel like the heart is pounding or simply have unpleasant awareness of your heartbeat. The heart rhythm may be normal or abnormal (9). Palpitations are often not serious. However, it depends on whether or not consists of abnormal rhythm

(arrhythmia). Heart palpitations can be caused by; - exercise, anxiety, stress, fear, fever, caffeine, nicotine, diet pills, overactive thyroid, low level of blood oxygen, heart diseases & anemia (9).

The aim of this study is to explain the presence of some cardiovascular side effects among hypertensive patients taking captopril.

Patients & Methods

Longitudinal prospective study was conducted in Kirkuk governorate from January to end of September 2008. Hundred & eight hypertensive patients taking captopril as a tablet 25 mg twice per day (47 male & 61 women). Each patient had a complete history detailed, physical examination, all patients were interviewed & full medical history was taken. All patients are questioned about the presence or absence of headache, palpitation, cough, flushing, chest pain, dysgeusia & tachycardia.

Blood pressure & heart rate were measured for each patient each visit. Blood sample was taken from only 51 hypertensive patients from the total 108 hypertensive patients, 27 patients with palpitation & 24 hypertensive patients without palpitation. Serum potassium was measured by using flameless atomic absorption spectrometry (Spectroil M analysis Spectrometer) in duplicate estimation for each serum sample. A standard sample for potassium is prepared & used for calibration.

All data were arranged & tabulated as a mean & standard deviation. T test was used to compare between different variables & P value of less than 0.05

Results

One hundred eight hypertensive patients taking captopril participating in this study (47 men & 61 women), (table1). In hypertensive men, 29 patients out of 47 (61.7%), hypertensive patients are diagnosed as suffering from

palpitation, (table 2). While in hypertensive women, 39 patients out of 61 women have palpitation after taking captopril for 3 months (64%), (Table 2).

In hypertensive men, there are no significant differences between group with palpitation & patients without palpitation regarding blood pressure in both systolic & diastolic. Also, there is no significant difference regarding heart rate between group of patients with palpitation & group of patients without palpitation (Table 3 & 4).

According to the presence or absence of palpitation & sex, hypertensive patients were divided into 4 subgroups. See table 3 & 4.

Forty five patients (male & females) from the 68 hypertensive patients with palpitation are smokers (66.2%). 30 patients out of 47 men are smokers (63.8%), (Table 5).

Regarding presence of tachycardia (heart rate above 100 beat / minute at rest), 14 men out of 29 hypertensive patients have tachycardia (50%), while only 3 hypertensive women have a tachycardia.

After diagnosing the presence of palpitation & tachycardia, 7 women discontinued the use of captopril without consulting their doctors & only 4 hypertensive men discontinued the use of captopril after having palpitation (18%).

In men, systolic blood pressure in patients with palpitation is lower than that systolic pressure of patients without palpitation (table 3). The same finding is true for hypertensive women (table 4).

Distribution of hypertensive patients with palpitation according to age groups. The highest age group of patients with palpitation is 30 to 39 years. It was found that 33 hypertensive patients have palpitation (48.5%) in this age group (table 6). While the lowest is group of patients less than 30 years (4 patients only, (table 6).

Seven patients developed ischemic heart diseases from all

hypertensive patients (5 men & 2 women) during the period of the study (3 months).

In the present study 5 patients taking captopril develop cough (3 women & 2 men).

In regard to serum potassium, it was estimated in 51 hypertensive patients (27 with palpitation & 24 patients without palpitation). There is no significant difference in regard to serum potassium between hypertensive patients with palpitation & hypertensive patients without palpitation, (Table 7).

In hypertensive patients with palpitation, 9 patients out of 27 patients have hyperkalaemia (33.3%), (serum potassium more than 3 mmol/L). In hypertensive patients without palpitation, only 3 patients out of 24 patients have hyperkalaemia (0.125%), (Table 8).

Discussion

Captopril is an angiotensin-converting enzyme (ACE) inhibitor, a family of drugs used to treat high blood pressure and some types of heart failure. Captopril is also used to slow the progression of kidney disease in people with diabetes. The renin-angiotensin system is a major regulatory system of cardiovascular and renal function. Basic research has revealed exciting new aspects, which could lead to novel or modified therapeutic approaches.

Renin-angiotensin system blockade exerts potent antiatherosclerotic effects, which are mediated by their antihypertensive, anti-inflammatory, antiproliferative, and oxidative stress lowering properties. Inhibitors of the system-i.e., angiotensin converting enzyme inhibitors and angiotensin receptor blockers, are now first-line treatments for hypertensive target organ damage and progressive renal disease.

Their effects are greater than expected by their ability to lower blood pressure alone (1, 2, 3, and 8). In the present study, 108 hypertensive patients

taking captopril participating in this study (47 male & 61 women). 29 men out of 47 hypertensive patients diagnosed as suffering from palpitation. While in hypertensive women, 39 patients out of 61 women have palpitation after taking captopril for 3 months.

Palpitations can be attributed to one of the three main causes. First cause is hyperdynamic circulation which includes hypercapnia, pyrexia, thyrotoxicosis, anemia & pregnancy. The second cause is sympathetic overdrive include panic disorders, hypoglycemia, hypoxia, heart failure & mitral valve prolapse. While the third main cause is arrhythmias (9,11). Most of patients in this study who suffer from palpitation are feel some how of anxiety or panic & terrified from the future course of the disease & response to the treatment.

Also, in the present study, palpitation may occurred as a side effects of captopril uses & to some extent most of male patients are tea drinker & smokers & both of these two reasons with drug affecting cardiovascular system (3,12). Palpitation is not mentioned in previous literatures as a side effect for captopril. It may be due to hypotension (9, 10,12).

In the present study the systolic blood pressure of patients with palpitation is lower than that of patients without palpitation. An uncommon yet potentially serious side effect of taking ACE inhibitors is increased blood potassium levels. This problem is more likely to occur in people with advanced kidney disease (13,14). Large amounts of high-potassium foods at the same time as ACE inhibitors could cause life-threatening problems.

Therefore, individuals should consult their health care practitioner before supplementing additional potassium and should have their blood levels of potassium checked periodically while taking ACE inhibitors (15,16, 17). In the present study ECG of patients with

palpitation show no change from the previous findings as indicators of hyperkalemia.

In the present study 5 patients taking captopril develop cough (3 women & 2 men). In a double-blind study of patients who had developed a cough attributed to an ACE inhibitor, supplementation with iron (in the form of 256 mg of ferrous sulfate per day) for four weeks reduced the severity of the cough by a statistically significant 45%, compared with a non significant 8% improvement in the placebo group (18).

References

1-Smith CG., Vane JR. The discovery of captopril. *FASEB Journal*. 2003; 17: 788-9.
 2-Atkinson AB., Robertson JIS. Captopril in the treatment of hypertension & cardiac failure. *Lancet*. 1979; 2:836-9.
 3-Marketou, ME., Zacharis, EA., Koukouraki, S. et al. Effect of angiotensin converting enzyme inhibitors on myocardial sympathetic innervations in normotensive patients with type 2 DM. *J. Human Hypertension*. 2007;21:619-26.
 4-Beared K. Management of elderly patients with sustained hypertension. *BMJ*. 1992; 304:412-16.
 5-Calhoun. DA. Treatment of HT crisis. *N. Engl. J. Med*. 1990; 323: 1177-81.
 6-Goodfriend TL., Elliott, ME., Catt, K. Angiotensin receptors & their antagonists. *N. Engl. J. Med*. 1996; 334:1649-54.
 7-Swales, JD. Pharmacological treatment of HT. *Lancet*. 1994; 34:380-85.
 8-Weir MR., Dzan., VJ. The rennin angiotensin system. A specific target for HT management. *Am. J. Hypertension*. 1999; 12:205-10.

9-Mayou R., Sprigings, D., Birkhead J. et al. Characteristics of patients presenting in Clinic with palpitation. *QJM*. 2003; 96(2):115-123.

10- Rush JE, Merrill DD. The Safety and tolerability of lisinopril in clinical trials. *J Cardiovasc Pharmacol* 1987;9 (Suppl 3):S99-107.

11- Sifton DW, ed. Physicians' Desk Reference. Montvale, NJ: Medical Economics Company, Inc., 2000, 1965-8.

12-Strauss, MH., Hall, AS. Angiotensin receptor blockers may increase risk of myocardial infarction: unraveling the ARB-MI paradox. *Circulation*. 2006; 8(114):

13- Good CB, McDermott L, McCloskey B. Diet and serum potassium in patients on ACE inhibitors. *JAMA* 1995;274:538.

14-Burnakis TG, Mioduch HJ. Combined therapy with captopril and potassium supplementation. A potential for hyperkalemia. *Arch Intern Med* 1984;144:2371-2.

15- Burnakis TG. Captopril and increased serum potassium levels. *JAMA*. 1984; 252:1682-3.

16- Ray K, Dorman S, Watson R. Severe hyperkalemia due to the concomitant use of salt substitutes and ACE inhibitors in hypertension: a potentially life threatening interaction. *J Hum Hypertens* 1999;13:717-20.

17- Stoltz ML. Severe hyperkalemia during very-low-calorie diets and angiotensin converting enzyme use. *JAMA* 1990;264:2737-8.

18- Lee SC, Park SW, Kim DK, et al. Iron supplementation inhibits cough associated with ACE inhibitors. *Hypertension*. 2001; 38:166-70. 838-54.

Table (1): Distribution of hypertensive patients according to sex

| Sex | Number of patients | Percentage % |
|--------|--------------------|--------------|
| Male | 47 | 43.5 |
| Female | 61 | 56.5 |
| Total | 108 | 100% |

Table (2): Distribution of palpitation patients according to sex

| Sex | Total number | Number of with palpitation | % | Number of without palpitation | % |
|--------|--------------|----------------------------|------|-------------------------------|------|
| Male | 47 | 29 | 42.6 | 18 | 45 |
| Female | 61 | 39 | 57.4 | 22 | 55 |
| Total | 108 | 68 | 100% | 40 | 100% |

Table (3): Show the characteristics of hypertensive men patients

| | Patients with palpitation. N=14 | Patients without palpitation. N=8 | |
|------------------------------|---------------------------------|-----------------------------------|----|
| Age (years) | 57.36 ± 8.1 | 61.2 ± 5.2 | NS |
| Pulse rate b/min | 81.6 ± 13.3 | 81.8 ± 9.6 | NS |
| Systolic blood pressure mmHg | 145 ± 21.5 | 148.3 ± 18.3 | NS |
| Diastolic Bp mmHg | 84.3 ± 9.4 | 88.3 ± 5.2 | NS |

Table (4): Show the characteristics of hypertensive women patients

| | Patients with palpitation. N=17 | Patients without palpitation. N=18 | |
|--------------------------------|---------------------------------|------------------------------------|----|
| Age (years) | 53.35 ± 7.3 | 56.44 ± 6.4 | NS |
| Pulse rate (b/min) | 87.2 ± 13.4 | 86.12 ± 14.5 | NS |
| Systolic blood pressure (mmHg) | 144.23 ± 24.9 | 146.1 ± 17.5 | NS |
| Diastolic Bp (mmHg) | 86.3 ± 9.4 | 84.22 ± 10.4 | NS |

Table (5): Distribution of hypertensive patients according to palpitation & smoking

| | Number of patients with palpitation | percentage | Number of patients without palpitation | Percentage |
|------------|-------------------------------------|------------|--|------------|
| Smoker | 45 | 66.2 | 22 | 55 |
| Non-smoker | 23 | 33.8 | 18 | 45 |
| Total | 68 | 100% | 40 | 100% |

Table (6): Distribution of hypertensive patients with palpitation according to age groups

| Age groups | Number of patients with palpitation | percentage | Number of patients without Palpitation | % |
|--------------|-------------------------------------|------------|--|------|
| Less than 30 | 4 | 5.9 | 5 | 12.5 |
| 30to 39 | 33 | 48.5 | 14 | 35 |
| 40 to 49 | 18 | 26.5 | 17 | 42.5 |
| 50 | 13 | 19.1 | 4 | 10 |
| Total | 68 | 100 | 40 | 100 |

Table (7): Show the mean & standard deviation (SD) of serum concentration of potassium in hypertensive patients with & without palpitation.

| Potassium concentration | 27 patients with palpitation | 24 patients without palpitation |
|--------------------------------|-------------------------------------|--|
| Mean (mmol/L) | 4.67 | 4.39 NS |
| S. D | 0.79 | 0.53 |
| Range | 3.6 to 5.7 | 3.7 to 5.5 |

Table (8): Distribution of hypertensive patients with & without palpitation in regard to serum potassium

| Hypertensive patients | With palpitation | Without palpitation | Total |
|--------------------------------------|-------------------------|----------------------------|--------------|
| Male patients with hyperkalemia | 3 | 2 | 5 |
| Male patients without hyperkalemia | 11 | 10 | 21 |
| Female patients with hyperkalemia | 6 | 1 | 7 |
| Female patients without hyperkalemia | 7 | 11 | 18 |
| Total | 27 | 24 | 51 |