

Effect of Indomethacin on Blood Pressure Managed by Captopril and Losartan in Hypertensive Patients

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ABSTRACT

Objective: Determine the role of indomethacin on blood pressure lowering by captopril and losartan in hypertension patients.

Study design: Randomized study design.

Methodology: 200 patients with known hypertension problems including women and men were treated in this study. The complete protocol for the study was approved by the research center and committee of the hospital. Patients were randomly treated with losartan 50mg/day, and captopril 25mg two times/day. Indomethacin 65 mg /day was given to patients in week six.

Results: Among the 200 patients 68 (50%) females received losartan and 68 (50%) females received captopril. Captopril was given to a total of 100 patients including 68 females and 32 males. Their first-week follow-up systolic BP Mean \pm S.E measured value was 152.02 ± 0.9 , Diastolic BP measured value was 94.5 ± 0.5 , Pulse, bpm = 86.6 ± 2.0 with a significant p-value. The fifth week measured reading was 141.04 ± 0.7 = systolic BP, 86.05 ± 1.2 = Diastolic BP, Pulse, bpm = 86.6 ± 2.0 . A significant reduction in BP was observed with a p-value of 0.001. At sixth-week captopril and indomethacin combination results show a lesser reduction in BP systolic/ diastolic = $146.06 \pm 0.2/89.01 \pm 2.0$ mm Hg, pulse rate measured 81.7 ± 1.0 with significant p-value 0.05.

Losartan first week follow-up shows a BP of $153.01 \pm 0.3/92.6 \pm 0.6$, pulse reading was 79.3 ± 2.0 with a p-value of 0.001. In the fifth week, BP was $139.5 \pm 0.1/ 84.03 \pm 0.3$, pulse = 77.6 ± 3.0 showing a significant reduction in BP. The sixth week Losartan + indomethacin results show a lesser decrease in BP with $145.4 \pm 0.1/ 91.02 \pm 0.4$ mm Hg, and 79.01 ± 3.1 value was measured for Pulse, bpm.

Conclusion: The results of this study show that losartan and captopril are more effective in controlling BP than in combination with indomethacin. So, indomethacin reduced the antihypertensive effect of losartan and captopril.

Keywords: captopril, losartan, indomethacin, antihypertensive, blood pressure

INTRODUCTION

Globally, more than one billion are affected with hypertension and it can reach up to 1.56 billion by 2025. It is becoming the leading cause of death and disabilities of lives every year worldwide.⁶ To control the existing situation drug therapy is needed, in case patients fail to change their lifestyle to bring BP to the target goal.⁷ Although, continually drugs invent bring beneficial effects in lowering the blood pressure of hypertension patients.¹ However, the main aim of antihypertensive drug therapy is to lower the occurrence rate of blood pressure relevant to cardiovascular events, still hypertension fatal and non-fatal cardiovascular problems found in patients treated with antihypertensive drugs.² Moreover, 40% stroke reduction is associated with a 5-6 mmHg reduction in diastolic blood pressure in clinical trials while epidemiological data of hypertension patient treatment predict lesser coronary events.³ The underlying mechanism of the antihypertensive effect of the drug captopril is the inhibition of the angiotensin-converting enzyme. A few years back many studies reported that other physiological actions of captopril also have blood pressure-lowering effects.^{4,5}

Although, nonsteroidal anti-inflammatory drugs (NSAIDs) are the most preferable medications in the United States. The ease of access to counter formulation has enhanced their uses, especially among the old. Hypertension high prevalence brings the alteration with concomitant use of (NSAIDs) and antihypertensive medication in the same patient.¹⁸ Various studies have reported the adverse effects of NSAID medication on blood pressure and increase in BP up to 6 mm Hg in treated hypertensive patients.¹⁶⁻¹⁸ While many antihypertensive drugs are proven to be effective such as angiotensin-converting enzyme inhibitors (ACEIs), diuretics, and β -blockers.¹⁵⁻¹⁷ In this study we will see the response of indomethacin on hypertensive patients treated with captopril and losartan to lowering BP.

METHODOLOGY

This is a randomized study designed to include 200 patients with known hypertension problems including women and men. The complete protocol for the study was approved by the research center and committee of the hospital. Written consent was signed by each individual or guardian of patients before enrollment. Before the start of treatment Medical history, physical examination, basic laboratory tests of all types, and necessary data were collected to meet the study criteria.

Exclusion criteria: Patients with a history of cardiovascular problems, renal disease, secondary hypertension, myocardial infarction, issue of intolerance, history of allergic reactions from captopril, losartan, and drugs from the class of NSAIDs.

Procedure: All the trained persons (through a certified and standardized training program) were measuring their blood pressure by using American Heart Association guidelines. A sphygmomanometer was used to calculate the BP in the sitting position of patients. Three reading was taken of each patient and the dose of medication for the study were not given to patients until clinical visits were completed.

An ambulatory blood pressure monitoring technique was applied with the use of the space labs 90217A device. This device was set and auto-monitor the diastolic/systolic blood pressure. To keep the uncertainty minimum, standard measured readings by mercury sphygmomanometer were also noted on the initiated day of Ambulatory blood pressure monitoring that was followed by the day when the monitor was removed. Moreover, patients were randomly treated with losartan 50mg/day, and captopril 25mg two times/day. Indomethacin 65 mg /day was given to patients in week six.

Statistical Analysis: The collected data were analyzed using statistical software 8.1. Analyzed data was presented in percentage, and mean standard error. A P-value less than 0.05 shows significance and above 0.05 shows non-significance.

RESULTS

A total of 200 patients were part of this including 136 (68%) females and males 64 (32%). The age varies from 30 to 40 years 71 (35.5%), age group 41-70 includes 129 (64.5%) patients. Mean \pm SE value was measured for BP, Ambulatory blood pressure monitoring initially measured in mm Hg was Systolic = 150.5 ± 1.0 , Diastolic = 95.01 ± 0.5 . BP measured at clinic was Systolic = 151.5 ± 0.4 , Diastolic = 102.1 ± 0.3 .

Among the 200 patients, 68 (50%) females received losartan and 68 (50%) females received captopril. After medication measured BP reading includes the Losartan received, ABPM, mm Hg (Systolic = 153.5 ± 1.0 , Diastolic = 96.08 ± 0.5), Clinic observation BP mm Hg (Systolic = 152.5 ± 0.3 , Diastolic = 102.1 ± 0.1), captopril received patients BP ABPM, mm Hg (Systolic = 150.3 ± 2.0 , Diastolic = 96.01 ± 0.5), Clinic observation BP mm Hg (Systolic = 151.5 ± 0.5 , Diastolic = 103.1 ± 0.2). we obtained non-significant results for both groups.

Table.2 represents the medication follow-up and treatment results, captopril was given to a total of 100 patients including 68 females and 32 males. Their first-week follow-up systolic BP Mean \pm S.E measured value was 152.02 ± 0.9 , Diastolic BP measured value was 94.5 ± 0.5 , Pulse, bpm = 86.6 ± 2.0 with a significant p-value. The fifth week measured reading was 141.04 ± 0.7 = systolic BP, 86.05 ± 1.2 = Diastolic BP, Pulse, bpm = 86.6 ± 2.0 . A significant reduction in BP was observed with a p-value of 0.001. At sixth-week captopril and indomethacin combination results show

Table 2: Treatment and follow up results

Medication	Number of patients n=200	Follow up	Mean \pm S.E (Systolic BP, mm Hg)	Mean \pm S.E (Diastolic BP, mm Hg)	Mean \pm S.E (Pulse, bpm)	p-value
Captopril	100 (50%)	1 st week	152.02 ± 0.9	94.5 ± 0.5	86.6 ± 2.0	0.001
Captopril		5 th week	141.04 ± 0.7	86.05 ± 1.2	86.6 ± 2.0	0.001
Captopril + indomethacin	100	6 th week	146.06 ± 0.2	89.01 ± 2.0	81.7 ± 1.0	<0.05
Losartan	100 (50%)	1 st week	153.01 ± 0.3	92.6 ± 0.6	79.3 ± 2.0	0.001
Losartan	100	5 th week	139.5 ± 0.1	84.03 ± 0.3	77.6 ± 3.0	0.001
Losartan + indomethacin	100	6 th week	145.4 ± 0.1	91.02 ± 0.4	79.01 ± 3.1	<0.05

DISCUSSION

Globally, hypertension has a high prevalence, especially in non-pregnant women in the United States. Antihypertensive drug therapy is a well-known treatment to prevent hypertension patients from any cardiovascular disorders.⁸ In the current study NSAID indomethacin blunts the antihypertensive effect of captopril and losartan. An ambulatory blood pressure monitoring device was used to measure all values. Indomethacin had no clear effect in lowering blood pressure but it also attenuate the losartan and captopril response in patients. Losartan and captopril had a clear lowering effect in 5th week of follow-up. Various studies results show that NSAID medications had a positive effect on hypertensive patients.⁹⁻¹⁰ Commonly it shows minor effects but is properly visible with β -blockers vasodilators. This shows that mechanism of action of the antihypertensive agent is the non-specific or actual mechanism of NSAIDs to regulate BP is poorly understood.¹¹

Moreover, a study reported that there was no effect of indomethacin significantly on the hypertension patients treated with losartan and measured the BP using ABPM.¹² Another study administered indomethacin in 10 losartan-treated hypertensive patients concluded that patients gained body weight, and a rise in intravascular volume but no reduction in blood pressure.¹³

CONCLUSION

Finally, the present study results indicate the clear lowering effects on BP with losartan and captopril while with indomethacin the BP lowering effect was not prominent.

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Losartan first week follow-up shows a BP of $153.01 \pm 0.3/92.6 \pm 0.6$, pulse reading was 79.3 ± 2.0 with a p-value of 0.001. In the fifth week, BP was $139.5 \pm 0.1/ 84.03 \pm 0.3$, pulse = 77.6 ± 3.0 showing a significant reduction in BP. The sixth week Losartan + indomethacin results show a lesser decrease in BP with $145.4 \pm 0.1/ 91.02 \pm 0.4$ mm Hg, and 79.01 ± 3.1 value was measured for a pulse, bpm.

Table 1: Patients characteristic

Characteristic	Number of patients 200	Losartan	Captopril	P-value
Age year				
30-40	71 (35.5%)	35 (49%)	36 (50.70%)	>0.05
41-70	129 (64.5%)	64 (49.61%)	65 (50.38%)	>0.05
Gender				
Female	136 (68%)	68 (50%)	68 (50%)	>0.05
Male	64 (32%)	32 (50%)	32 (50%)	>0.05
ABPM, mm Hg				
Systolic	150.5 ± 1.0	153.5 ± 1.0	150.3 ± 2.0	>0.05
Diastolic	95.01 ± 0.5	96.08 ± 0.5	96.01 ± 0.5	>0.05
Clinic observation BP mm Hg				
Systolic	151.5 ± 0.4	152.5 ± 0.3	151.5 ± 0.5	>0.05
Diastolic	102.1 ± 0.3	102.1 ± 0.1	103.1 ± 0.2	>0.05

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