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ORIGINAL ARTICLE

Effect of Celecoxib and Diclofenac on Blood Pressure, Renal Function and Vasoactive Prostanoids in Young Early Subjects

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ABSTRACT

Objective: Determination of celecoxib and diclofenac effects in early young subjects.
Study design: Randomized study designed
Methodology: All the participants received celecoxib 225 mg two times/day and diclofenac 80mg two times/day. First 21 days all participants received celecoxib treatment, before the start of the following medicine diclofenac 3.5 weeks gap was given. The blood pressure (BP) of patients was measured using the ambulatory blood pressure monitoring device (space labs model 90217A).
Results: Group one consisted of young participants had a mean ± SD age 29 ± 3.4 while group 2 elderly had a mean ± SD age 55 ± 5.5. The mean body mass index was (group 1) 21.7 ± 1.8 kg/m^2 and for group 2 = 27.3 ± 1.0 kg/m^2. Group one had 5 (38.46%) females and 8 (61.53%) males while group 2 had 4 (30.76%) females and 9 (69.23%) males. The celecoxib medication baseline BP shows that there was no significant difference found in systolic blood pressure. Similar results for diastolic (mm Hg) for day and night time. Mean arterial pressure was higher in the elderly group -2 than in young group 1, Plasma renin activity was less in group 2 on day one compared to group 1. Plasma renin activity and concentration were decreased after 7 days of celecoxib and diclofenac treatment. A non-significant result was obtained. Group 1 Aldosterone serum (ng/l) for celecoxib received patients 11 ± 2.2 (ng/l) value for day one, day 7 = 13.2 ± 3.2, day 14 = 14.2 ± 3.4. Similarly in the case of diclofenac, the Aldosterone serum (ng/l) value for day one = 11.3 ± 21, day 7= 12.2 ± 2.3, and day 14 = 12.3 ± 2.1. A decrease in values was observed in both groups for aldosterone serum. For group-2 celecoxib, day one=15 ± 2.2, day 7= 14 ± 2.4*. day14= 14 ± 1.4. For diclofenac day one 15 ± 2.2, 7day= 15 ± 1.5, and 14 days = 14 ± 5.1. The comparison of both groups shows that the sodium and potassium decrease in both treatments in both groups.
Conclusion: Overall, we got a non-significant response of both drugs on renal function and blood pressure.
Keywords: blood pressure, renin angiotensin aldosterone system, non-steroidal anti-inflammatory drugs (NSAIDs)

INTRODUCTION

Millions of people have developed hypertension in United State and billions of people across the world treated with non-steroidal anti-inflammatory drugs (NSAIDs).[1-2] The association between hypertension and NSAIDs have reported in several studies. Currently, 50 million individuals are at risk to develop heart disease and stroke because of hypertension in United State. [2-5]

Prostaglandins play a role in the regulation of sodium and water reabsorption by balancing the process of homeostasis.[6] Moreover, prostaglandins may impede the production of renal endothelin-1 in the vasculature, and as a result of this reduction in sodium and water reabsorption occurs. NSAIDs escalate the retention of sodium and water by enhancing tubular reabsorption of water.[7] Prostaglandins help in the regulation of renal function and hemodynamics through their effects on the renin-angiotensin system.[8] In this process synthesis of angiotensin II increase and aldosterone thereby increasing sodium and water reabsorption. Renin causes an increase in blood pressure with the effect of vasoconstriction by angiotensin II. Therefore, NSAIDs lower blood pressure and inhibit the renin-angiotensin system.[9-10] The inhibition of cyclooxygenase COX activity of isoform COX-2 inhibitors have designed to overcome pain and inflammation with less toxic effects.[11] Clinical studies about the COX-2 inhibitor reported the less prevalence of gastrointestinal complications noticed with nonspecific-NSAIDs.[12]

METHODOLOGY

This is a randomized study designed to consist of 36 participants that were divided into two groups, each group had 13 members. All the participants were enrolled with their willingness of which 13 were healthy volunteers of 25-33 (group-1) and 13 were elderly healthy volunteers of age 50- 63 (group-2). The study protocols were approved by the research center and the committee of the hospital. At the initial stage all the necessary information, including medical history, laboratory tests, and electrocardiogram were collected from participants. Written consent was taken from each volunteer member of this study.

Exclusion criteria: People with any kind of disease, heart issue, stroke, cardiovascular, and facing other health issues were excluded from the study.

Procedure: Before giving the medicine doses, it was assured that no medicine was taken before 3 weeks of this study trial. All the participants received celecoxib 225 mg two times/day and diclofenac 80mg two times/day. First 21 days all participants received celecoxib treatment, before the start of the next medicine diclofenac 3.5 weeks gap was given. To meet the treatment we provided the sodium intake detail food chart and ensured the salt intake was less than 5g/day before the beginning of the study.

The blood pressure (BP) of patients was measured using the ambulatory blood pressure monitoring device (space labs model 90217A). Thought out the study period all the readings were measured. Three readings were taken at one time to minimize the error or to keep the uncertainty low. Day one readings were measured using the sphygmomanometer by trained staff of the hospital. The urine sample was collected on day first, day 7, and day 14 to measure the electrolytes. The blood sample was taken in the early daytime on the 1st day, 7th day, and 14 days to determine the plasma renin activity and its concentration, aldosterone, and electrolytes.

Statistical analysis: Statistical analysis was performed on statistics 8.1 software. A T-test was performed to compare the values of both groups and data presented in mean and standard deviation form. A P-value higher than 0.05 is considered non-significant while less than 0.05 shows significant analysis.

RESULTS

In the present study, Group one consists of young participants had a mean ± SD age 29 ± 3.4 while group 2 elderly had a mean ± SD age 55 ± 5.5. The mean body mass index was (group 1) 21.7 ± 1.8

kg/m^2 and for group 2 = 27.3 ± 1.0 kg/m^2. Group one had 5 (38.46%) females and 8 (61.53%) males while group 2 had 4 (30.76%) females and 9 (69.23%) males. The celecoxib medication baseline BP shows that there was no significant difference found in systolic blood pressure during the day time 115 ± 7.0 mm Hg and 115 ± 6.0 mmHg at night time, Similar results for diastolic (mm Hg) for day and night time, (85 ± 3.0 and 84 ± 5.1). Mean arterial pressure was higher in the elderly group -2 than in young group 1, that was 118/83 ± 1.6 day time and 119/84 ±1.8 at night for the first group, and for the elderly mean arterial pressure in the daytime was 134/94 ± 2.1 and for night time 137/ 93 ± 3.1.

The diclofenac medication results shows the baseline day time systolic BP = 118 ± 5.2, night time = 116 ± 3.2, diastolic BP day time = 83 ± 4.2, night time = 82 ± 3.2, pulse day time = 91 ± 1.3, pulse night = 91 ±1.2, mean arterial pressure day = 122/ 84 ± 2.4 , night = 123/83 ± 1.3 for group-1. While for the group-2 elderly, systolic BP day time = 125 ± 2.3, night time = 123 ± 2.1, diastolic day time = 91 ± 0.2, night time = 90 ± 2.1, pulse day time reading = 92 ± 4.2, pulse night time = 92 ± 2.3, mean arterial pressure day time reading = 130/91 ± 0.1, and night time reading = 131/92 ± 1.3. There was no significant difference found in the case of diclofenac except the mean arterial pressure was higher in the 2nd group as compared to the first one. Table.1.

Table 2 represents that plasma renin activity was less in group 2 on day one as compared to group 1. Plasma renin activity and concentration were decreased after 7 days of celecoxib and diclofenac treatment. A non-significant result was obtained. Group 1 Aldosterone serum (ng/l) for celecoxib received patients 11 ± 2.2 (ng/l) value for day one, day 7 = 13.2 ± 3.2, day 14 = 14.2 ± 3.4. Similarly in the case of diclofenac, the Aldosterone serum (ng/l) value for day one = 11.3 ± 21, day 7= 12.2 ± 2.3, and day 14 = 12.3 ± 2.1.

A decrease in values was observed in both groups for aldosterone serum. For group-2 celecoxib, day one=15 ± 2.2, day 7= 14 ± 2.4*. day14= 14 ± 1.4. For diclofenac day one 15 ± 2.2, 7day= 15 ± 1.5, and 14 days = 14 ± 5.1. The comparison of both groups shows that the sodium and potassium decrease in both treatments in both groups.

Table 1: General Characteristics of study

	Group-1, n=13		Group-2, n=13	
Age , mean ± SD	29 ± 3.4		55 ± 5.5	
Body mass index (kg/m^2), mean ± SD	21.7 ± 1.8		27.3 ± 1.0	
Gender				
Female	5 (38.46%)		4 (30.76%)	
Male	8 (61.53%)		9 (69.23%)	
Celecoxib medication				
	Day	Night	Day	Night
Systolic BP mmHg	115 ± 7.0	115 ± 6.0	121 ± 2.8	120 ± 6.8
Diastolic BP mmHg	85 ± 3.0	84 ± 5.1	85 ± 5.8	86 ± 6.5
Pulse	91 ± 1.3	91 ± 1.2	92 ± 3.1	93 ± 4.1
Mean Arterial pressure	118/83 ± 1.6	119/84 ±1.8	134/94 ± 2.1	137/ 93 ± 3.1
Diclofenac medication				
Systolic BP	118 ± 5.2	116 ± 3.2	125 ± 2.3	123 ± 2.1
Diastolic BP	83 ± 4.2	82 ± 3.2	91 ± 0.2	90 ± 2.1
Pulse	92 ± 2.3	91 ±1.2	92 ± 4.2	92 ± 2.3
Mean arterial pressure	122/ 84 ± 2.4	123/83 ± 1.3	130/91 ± 0.1	131/92 ± 1.3

There was no statically difference was found, so, p-value for each parameter was higher than 0.05.

Table 2: renin angiotensin aldosterone system effect

Celecoxib results				Diclofenac results		
Factors	Day one	7 days	14 days	Day one	7 day	14 day
Group-1						
Plasma renin activity	2.1 ± 0.12	2.1 ± 0.23	2.3 ± 1.3	2.01±0.83	1.9 ± 1.2	2.0 ± 1.2
Plasma renin concentration	5.21 ± 1.2	5.12 ± 2.3	4.31 ± 1.2	5.31 ± 2.1	4.21 ± 1.2	3.71 ± 0.3
Aldosterone	11 ± 2.2	13.2 ± 3.2	14.2 ± 3.4	11.3 ± 21	12.2 ± 2.3	12.3 ± 2.1
Fe Sodium percentage	0.56 ± 0.31	0.43 ± 0.2	0.51 ± 0.4	0.56 ± 0.2	0.42 ± 0.1	0.52 ± 0.3
Fe Potassium percentage	10.3 ± 2.3	11.2 ± 2.1	11.5 ± 1.2	12.1 ± 2.1	11.4 ± 3.2	10.9 ± 2.3
Group-2						
Plasma renin activity	1.32 ± 1.3**	1.42 ± 0.31**	1.22 ± 0.31	1.41 ± 0.4	1.31 ± 1.2	0.32 ± 3.2
Plasma renin concentration	3.46 ± 0.34	2.31 ± 0.31	2.20 ± 0.21	3.21 ± 2.1	2.04 ± 0.32	2.01 ± 0.41
Aldosterone	15 ± 2.2	14 ± 2.4*	14 ± 1.4	15 ± 2.2	15 ± 1.5	14 ± 5.1
Fe Sodium %	0.68 ± 1.2	0.78 ± 3.2**	0.61 ± 1.3	0.5 ± 31	0.39 ± 2.1	0.37 ±2.3
Fe Potassium %	13.2 ± 3.1	12.1 ± 2.1**	12.4 ± 1.3	14.5 ± 3.1	12.3 ± 2.1*	12.2 ± 1.2

Plasma renin activity PRA (ng/ml/h), Plasma renin concentration PRC (ng/ml/h), Aldosterone (ng/l) P-value <0.05 =*, P-value<0.01= **

DISCUSSION

A small study of 40 participants for 7 days study trial of normotensive subjects on low salt intake showed a non-substantial difference in systolic and diastolic blood pressure between the two groups one was treated with naproxen 500 mg and 2nd was treated with 2 doses of celecoxib 200 mg. Both groups showed a reduction in sodium, water, and potassium excretion.[13] In the same way, one more study about the non-specific NSAIDs indomethacin 50 mg and COX-2 inhibitor rofecoxib 50mg used in 14 day trial of normotensive older adults concluded that an increase in diastolic blood pressure in each group. With indomethacin increase in 2.6 mm Hg, rofecoxib 1.7 mm Hg, and 1.5 mm Hg in the placebo group but statistically all the results were non-significant.[14] Another attempt demonstrated that the elderly group of participants received celecoxib 200 mg 2 times/day thereby decrease in systemic prostaglandin synthesis.[15]

In the present study, the blood pressure profile and renin-angiotensin-aldosterone among both groups did not show any difference under the influence of specific COX-2 inhibition by celecoxib. Similarly no significant difference in COX-2 inhibition by diclofenac. Although slight elevation of mean arterial pressure was measured in group 2. These findings showed the similarity between the two trials of celecoxib and rofecoxib.[16-17] Although in the current study the suppression of renin release was not significant by celecoxib treatment as compared to diclofenac treatment. Plasma renin activity was used to determine the state of renin-angiotensin-aldosterone.[18]

CONCLUSION

We concluded that the overall mean arterial blood of group 2 was slightly higher than group one of young members. The 14 days dose of celecoxib and diclofenac had non-significant alternation in blood pressure and renal function in both groups.

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