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Research Article

A STUDY OF THE CONSEQUENCE OF THIAZIDES AND ANGIOTENSIN CONVERTING ENZYME INHIBITORS ON BONE MINERAL DENSITY IN ELDERLY HYPERTENSIVE PATIENTS

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Abstract:

Background: Hypertension and osteoporosis are the two major age-related conditions. Several studies have shown higher bone mineral density (BMD) in people receiving thiazide diuretics compared with controls. The benefits of angiotensin converting enzyme (ACEI) inhibitors in improving bone metabolism have been confirmed in some clinical trials. Therefore, these medications may be part of a therapeutic regimen for the elderly with hypertension and osteoporosis.

Objective: To compare the effects of ACEI and thiazides on BMD when used alone or in combination in elderly hypertensive patients.

Place and Duration: In the Medicine Unit-II of Bahawal Victoria Hospital, Bahawalpur for one-year duration from October 2019 to October 2020.

Patients and Method: A retrospective comparative study recruiting 171 participants aged 60 years and older. The participants were divided into three groups: Group I: 57 participants receiving thiazides, Group II: 57 participants receiving combined ACEI and thiazides, Group III: 57 participants receiving ACEI. Each group was divided into two subgroups; older and younger than the average age (65) of participants. Patients with systemic diseases or taking medications affecting BMD were excluded from the study. All participants underwent: lumbar spine BMD (L2-L4) and left femoral neck BMD measurements using dual energy X-ray absorptiometry (DEXA) [Lunar DPX DEXA system].

Results: For the BMD T-score in the lumbar region (L2-L4), there was no significant difference between the groups as the whole sample (p-value 0.383), nor between the age subgroups after the division into two subgroups older than the median age. (P-value of 65) (p-value 0.832) and those aged 65 and younger (p-value of 0.259) (the same was found for the z index). Regarding the left femoral BMD T-score, there was no significant difference either between the groups as a whole sample (p-value 0.921) or between the age subgroups divided into two older and younger subgroups (p-value 0.889) (the same was found for the result from).

Conclusion: In the present study, no evidence was found that there is a difference between thiazide therapy and ACEI therapy with respect to their effect on BMD in elderly hypertensive patients when used alone or in combination.

Keywords: ACEI, Thiazides, BMD.

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INTRODUCTION:

Osteoporosis and high blood pressure is a problem that increases with age. Aging is often associated with a decrease in bone mineral density (BMD) and therefore a greater risk of falls and bone fractures. In addition, the structure of blood vessel walls changes with age. These changes cause a loss of vascular compliance and ultimately lead to hypertension. Several studies have shown abnormalities in calcium metabolism at the systemic level in hypertension. Olmos et al. Suggested that thiazides are beneficial in preventing bone loss because they modify calcium metabolism and bone mass. Moreover, it has been postulated that angiotensin II may act on cells involved in bone metabolism. Therefore, ACEIs may be of benefit not only in the treatment of hypertension but also in the treatment of osteoporosis, and therefore these drugs may be part of the therapeutic regimen of elderly people with osteoporotic hypertension.

PATIENTS AND METHODS:

A retrospective comparative study was held in the Medicine Unit-II of Bahawal Victoria Hospital, Bahawalpur for one-year duration from October 2019 to October 2020. 171 participants aged 60 years and older were recruited. The participants were divided into three groups, group I: 57 people received thiazides, group II: 57 participants received a combination ACEI and thiazides, and group III: 57 people received ACEI. Drugs have been taken for at least 1 year. These 3 groups were matched for age, sex, body mass index (BMI), nutritional screening, calcium supplement use, smoking, alcohol consumption, physical activity level, family history of osteoporosis, and brittleness history. Each group was divided; according to the median age of

participants (65 years) into two subgroups older and younger than the median age. Patients with systemic diseases or taking medications affecting BMD were excluded from the study.

All participants were subjected to:

1. Oral Informed consent to participate in the study.
2. Demographic, medical, nutritional and lifestyle information was obtained from personal interviews using a questionnaire, and the complete physical examination included anthropometry and systolic blood pressure in the arm.
3. Measurement of BMD of all participants in the lumbar spine (L2L4) and left femoral neck was assessed by Dual Energy X-ray Absorptiometry (DEXA) using the Moon's DPX DEXA System

Data Management and Statistical Analysis:

Qualitative data presented in the form of frequency tables. Quantitative data presented as means +/- SD. The P value was set at 0.05 and all manipulations and data analysis were performed using the 17th version of SPSS. The normality distribution of variables was tested with the Kolmogorov Smirnov test on one sample. Two-tailed t-test and ANOVA were used to compare between 2 and 2, respectively, and several quantitative parametric data. The Mann Whitney and Kruskal-Wallis tests were used to compare from 2 to several quantitative nonparametric data, respectively.

RESULTS:

24 patients are men and 147 patients are women. Each group has 57 participants and was then divided into two subgroups older and younger than the median age (65 years) (Table 1).

Table 1: Age distribution among groups

Age group		Groups			
		Group I	Group II	Group III	Total
≤ 65	N	25	27	24	76
	%	43.86	47.37	42.11	44.44
>65	N	32	30	33	95
	%	56.14	52.63	57.89	55.56
Total	N	57	57	57	171
	%	100.00	100.00	100.00	100.00
Chi-Square	X ²	0.331			
	P-value	0.847			

Regarding the T-index of BMD in the lumbar region (L2-L4); no significant difference was found between the 3 groups ($P = 0.383$). Each group is divided into younger and older than 65 years; there was no significant difference between younger and older

people in each of the 3 groups ($P = 0.73, 0.728, \text{ and } 0.121$, respectively); and there was no significant difference between the 3 groups of younger elderly ($P = 0.259$) or the 3 groups of older elderly ($P = 0.832$) (same was found for the z score) (Table 2).

Table 2: Comparison of BMD at the lumbar (L2-L4) BMD T -score

L2-L4 T-score		Age group		T-Test		All subjects
		≤ 65	>65	T	P-value	
		Mean ± SD	Mean ± SD			Mean ± SD
Group I		-1.856±0.392	-1.991±0.552	0.340	0.735	-1.932±1.473
Group II		-1.681±0.271	-1.793±0.146	0.349	0.728	-1.740±1.197
Group III		-1.225±0.464	-1.827±0.398	1.574	0.121	-1.574±1.445
ANOVA	F	1.375	0.184			0.964
	P-value	0.259	0.832			0.383

Regarding the BMD T-score of the left femur; there was no significant difference either between groups or between age subgroups when they were divided into two subgroups older and younger than the median age (65 years) (the same was found for z-score). Although there was a significant difference between the age subgroups of groups II and III, the younger subgroup had a higher T-score than the older subgroup ($p = 0.047$ and 0.027 respectively) (Table 3).

Table 3: Comparison of the BMD at the Left Femur Neck (Lt F.N) T-score

Lt F.N T score		Age group		T-Test		All subjects
		≤ 65	>65	T	P-value	
		Mean ± SD	Mean ± SD			Mean ± SD
Group I		-1.080± 0.135	-1.463± 0. 834	1.467	0.148	-1.295±0.987
Group II		1.135± 0.084	-1.593± 0 .959	2.029	0.047	-1.333±1.048
Group III		-0.929± 0.19 7	-1.709± 0.332	2.276	0.027	-1.381±1.324
ANOVA	F	0.118	0.433			0.083
	P-value	0.889	0.650			0.921

The results showed that there was no significant difference in the distribution of healthy people with osteopenia or osteoporosis between the 3 groups in terms of lumbar BMD (L2-L4) or left femoral BMD T-score as defined by WHO ($P = 0.597$ 0.304 consecutively) (data were not presented).

DISCUSSION:

The current study was designed to compare the effects of ACEI and thiazides on BMD when used together or separately in elderly hypertensive patients. An untreated control group of patients with arterial hypertension was not included for ethical reasons. In the present study, no significant difference was found between the effects of ACEI

and thiazides on BMD among the older participants in the three groups. Moreover, when the groups were divided into subgroups above and below the median age, there was no significant difference in BMD in the lumbar spine and femoral neck T-scores, Zscore or gm / cm². These results are in line with the results of a study by Jose et al. which explains the therapeutic effect of the three treatments on markers of bone remodeling and BMD in patients with hypertension. 134 patients (82 women and 52 men) aged 36 to 76 participated in this study. Seventy-four women were postmenopausal (90%). Patients were randomized to one of three therapies: quinapril, quinapril with hydrochlorothiazide, and enalapril. Densitometric examinations of the lumbar spine were performed. No baseline differences were observed in patients other than their genotype. Patients were monitored for 1 year and were followed up every 3 months. During the follow-up period of 1 year, BMD did not change and there was no physiological loss that is common in this age group. There were no differences between the three groups at the beginning and end of treatment. This study showed an association between ACE polymorphism and BMD response and ACEI treatment. Women with ACE II_ID polymorphism were found to have a poor BMD response to ACEI. Therefore, it was proved that the BMD of women with ACE DD polymorphism was better than that of women with II_ID polymorphism. Jose et al. provided one explanation for the lack of change in BMD with ACEI. The authors of this study speculate that genetic factors may also play a role in response to other antihypertensive drugs. Lynn et al. It has been hypothesized that ACEI and thiazides reduce the rate of bone loss in the elderly. A cross-sectional study of 3,887 Chinese men (n = 1,958) and women (n = 1,929) was used to investigate the relationship between ACEI use and BMD. Participants were 65 and older and were divided into male and female ACEI users and non-ACEI users. In multiple regression analyzes for age, weight, height, thiazides, beta blockers, calcium channel blockers, statins, corticosteroids, and calcium supplements, diabetes history, heart disease, peripheral vascular disease, smoking, alcohol consumption, and activity level physical; BMD measurements of the femoral neck, the entire hip and the lumbar spine were performed. Lynne and his colleagues found that both ACEI and thiazide users had increases in BMD in both men and women. After adjusting to other antihypertensive medications and potential confounders, researchers found that people using thiazides in both genders resulted in an additional increase in BMD. The limitation of this study and inconsistency with the results of the current study may be due to the fact that patients with diabetes or

cardiology were not excluded. Since ACE inhibitors were usually prescribed for hypertension and heart failure, it was not surprising that people using ACE inhibitors were more severe and more likely to have diabetes, and those taking related medications such as statins and nitrates were not excluded from the previous study. In previous studies, diabetes and body weight were associated with higher BMD in the lumbar spine and the entire hip. To avoid this impact on the results, heart and diabetes patients were excluded from the current study. Therefore, after excluding diabetic and heart patients, the present study found no differences in BMD between thiazide and ACEI users. The results of current studies question the prophylactic or therapeutic role of thiazides and ACEI diuretics in elderly people with osteoporotic hypertension.

CONCLUSION:

The current study found no evidence for a difference between thiazides therapy and ACEIs therapy as regard their effect upon BMD in elderly hypertensive patients when used separated or combined

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