

A Study of the Effect of Angiotensin Converting Enzyme Inhibitors and Thiazides on Bone Mineral Density in Hypertensive Elderly

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Abstract

Background: Hypertension and osteoporosis are two major age-related disorders. Several studies have shown greater Bone Mineral Density (BMD) in people receiving thiazides diuretics compared with controls. The benefit of Angiotensin Converting Enzyme Inhibitors (ACEIs) to improve bone metabolism has been supported by some clinical studies. Therefore, these drugs might be a part of the therapeutic regime for osteoporotic hypertensive elderly.
Objective: to compare between the effect of ACEIs and thiazides on BMD when used separated or combined in hypertensive elderly.

Patients&method: A retrospective comparative study recruiting 171 participants who were aged 60 years and above from the outpatient clinics of Ain shams University Hospitals. The participants were divided into three groups: Group I: 57 participants receiving thiazides, Group II: 57 participants receiving combined ACEIs and thiazides, Group III: 57 participants receiving ACEIs. Each group was subdivided into two subgroups; older and younger than the median age (65years) of participants. Patients with systemic diseases or on drugs that affect BMD were excluded from the study. All participants were subjected to: BMD measurement at lumbar spine (L2-L4) and left femur neck using Dual-energy x-ray absorptiometry (DEXA) [lunar DPX DEXA system].

Results: As regard lumbar (L2-L4) BMD T-score ,there was no significant difference found between the groups as a whole sample (P-value 0.383), nor the age subgroups ,when subdivided into two subgroups older than the median age (65 years old)(P-value 0.832) and from 65 years old and younger (P- value0.259) (the same was found as regard z-score). As regard BMD of the Left Femur Neck T-score there was no significant difference found neither between the groups as a whole sample (P-value 0.921), nor among the age subgroups when subdivided into two subgroups older and younger (p-value 0.889), (the same was found as regard z-score). **conclusion:** the current study found no evidence that there is a difference between thiazides therapy and ACEIs therapy as regard their effect on BMD in elderly hypertensive patients when used separated or combined.

KEYWORDS: ACEIs, Thiazides, BMD.

Introduction

Osteoporosis and hypertension represent a problem that increases with age. (1) Aging is often associated with reductions in Bone Mineral Density (BMD) and consequently, with higher risk for falls and bone fractures. (2) Moreover, increasing age is associated with changes in the structure of walls of the blood vessels. These changes produce loss of vascular compliance and ultimately result in hypertension. (1)

Several studies have demonstrated abnormalities in calcium metabolism at the systemic level in hypertension (1). Olmos *et al*, suggested that thiazides are beneficial to prevent bone loss. (4), as they modify calcium metabolism and bone

mass(5). Moreover , Angiotensin II has been postulated to be able to act upon the cells involved in bone metabolism (1). Therefore, ACEIs may have possible benefits in treating not only hypertension but also osteoporosis (6) .Therefore, these drugs might be a part of the therapeutic regime of osteoporotic hypertensive elderly (5).

Patients and methods:

Design: retrospective comparative study.

Sample size:

171participants were aged 60 years and above were recruited from the outpatient clinics of Ain shams University Hospitals.

The participants were divided into three groups, group I:57 participants were receiving thiazides, group II:57 participants were receiving combined ACEI and thiazides and Group III: 57 participants were receiving ACEI. The drugs were received for at least 1 year. The 3 groups were matched for age, gender, Body Mass Index (BMI), nutrition screening, calcium supplement use, cigarette smoking, alcohol intake, physical activity level, family history of osteoporosis and history of fragility fractures.

Each group was subdivided; according to the median age of participants (65years) into two subgroups older and younger than the median age.

Patients with systemic diseases or on drugs that affect BMD were excluded from the study.

All participants were subjected to:

- 1-Oral Informed consent for acceptance of participation in the study.
- 2- Demographic, medical, nutritional and lifestyle information was obtained from face to face interviews using a questionnaire, and complete physical examination included anthropometry and brachial systolic blood pressures.
- 3- BMD measurement , of all participants, at lumbar spine (L2-L4) and left femur neck was assessed by Dual-energy x-ray absorptiometry (DEXA) using lunar DPX DEXA system

Data Management and Statistical Analysis

Qualitative data presented in the form of frequency tables. Quantitative data presented in the form of mean +/- SD. P value was set at 0.05 and all data manipulation and analysis were performed using the 17th version of SPSS.

Normality distribution of the variables was tested using one sample Kolmogorov Smirnov test. Two-sided t-test and ANOVA test was used to compare between 2 and 2 and several quantitative parametric data respectively. Mann-Whitney and Kruskal-Wallis tests were

used to compare between 2 and several quantitative non-parametric data respectively.

Results

24 patients were males and 147 patients were females.

Each group has 57 participants and was then subdivided into two subgroups older and younger than the median age (65 years old) (table 1).

Regarding lumbar (L2-L4) BMD T-score; there was no significant difference found between the 3 groups ($P= 0.383$). With subdivision of each group into younger and older than 65 years old; there was no significant difference between younger and elderly in each of the 3 groups ($P=0.73$, 0.728 and 0.121 consecutively) ; and there was no significant difference between the 3 groups of younger elderly ($P= 0.259$) or the 3 groups of older elderly ($P= 0.832$)(the same was found as regard z-score) (table 2).

Regarding BMD of the Left Femur Neck T-score; there was no significant difference found neither between the groups, nor among the age subgroups when subdivided into two subgroups older and younger than the median age (65 years old) (the same was found as regard z-score). While there was a significant difference found among the age subgroups of group II and group III, the younger subgroup of each, had a higher T-score than the older subgroup($P= 0.047$ and 0.027 consecutively) (table3).

The results showed that there was no significant difference in the distribution of subjects as normal, osteopenic or osteoporotic between the 3 groups regarding lumbar BMD (L2-L4) or left femur neck BMD T-score according to the WHO definition ($P= 0.597$ and 0.304 consecutively)(data were not presented).

Discussion

The current study was designed to compare between ACEIs and thiazides effects upon BMD when used combined or separated in hypertensive elderly people. Untreated control group of hypertensive patients was not included due to ethical reasons.

In the current study, no significant difference was found between the effect of ACEIs and thiazides on BMD among the

elderly participants of the three groups. Moreover, when the groups were subdivided into subgroups above and below the median age, no significant difference was found in BMD at the lumbar spine and femur neck T-score, Z-score or gm/cm².

These results concur with the results of a study by Jose' *et al.* (6) who clarifies the therapeutic effect of three treatments on bone remodeling markers and BMD in hypertensive patients. This study included 134 patients (82 women and 52 men), aged between 36 and 76. Seventy four women were postmenopausal (90%). Patients were randomly allocated to one of the three treatments: quinapril, quinapril plus hydrochlorothiazide, and enalapril. Densitometric studies on lumbar spine were performed. No baseline differences were observed in patients other than their genotype. Patients were monitored for 1 year and they were seen every 3 months. During the follow-up period of 1 year, BMD remained unchanged and there was no physiologic loss, which is common in this age group. No differences were found among the three groups at the beginning and the end of the treatment.

This study(6) demonstrated a relationship between ACE polymorphism and BMD response and ACEIs treatment. It was found that women with the ACE II_ID polymorphism had a poor BMD response to ACEIs. Therefore, it was proved that BMD of women with the ACE DD polymorphism was better than BMD of women with the II_ID polymorphism.

Jose' *et al.* (6) had provided one explanation for the absence of change in BMD with ACEIs. The authors of this study speculate that genetic factors in response to other antihypertensives may also play a role.

Lynn *et al.* (7) hypothesized that ACEIs and thiazides decrease the rates of bone loss in older people. A cross-sectional study of 3887 Chinese men (n = 1958) and women (n = 1929) was used to explore the association between ACEIs use and BMD.

The participants were aged 65 years and above and were divided into females and males of ACEI users and non users. In multiple regression analyses, after adjusting for age, weight, height, thiazide, beta-blocker, calcium channel blocker, statin, corticosteroid, and calcium supplement use, history of diabetes, heart disease, peripheral vascular disease, cigarette smoking, alcohol intake, and physical activity level; BMD measurements at femoral neck, total hip, and lumbar spine were done.

Lynne and his colleagues found that both ACEI and thiazide users had an increase in BMD in males and females. After adjusting for other antihypertensive medications and potential confounders, they found that thiazides users in both genders give an additional increase in BMD.

The limitation of this study and conflict with the results of the current study may be due to the fact that they didn't exclude diabetic or cardiac patients. As ACE inhibitors were usually prescribed for hypertension and cardiac failure, it was not surprising that ACE inhibitor users were heavier and more likely to be diabetic and users of related drugs such as statins and nitrates, these subjects were not excluded from the previous study. Diabetes and body weight were associated with higher BMD in lumbar spine and total hip in previous studies. (8)

To avoid such influence on the results cardiac and diabetic patients were excluded from the current study. Hence after excluding diabetics and cardiac patients in the current study no difference in BMD was found between thiazides and ACEIs users.

The results of current study do question the preventive or therapeutic role of thiazides and ACEI diuretics in osteoporotic hypertensive elderly.

In 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.

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	χ^2	0.331			
	P-value	0.847			

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 \pm SD	Mean \pm SD		Mean \pm SD	
Group I	-1.856 \pm 0.392	-1.991 \pm 0.552	0.340	0.735	-1.932 \pm 1.473
Group II	-1.681 \pm 0.271	-1.793 \pm 0.146	0.349	0.728	-1.740 \pm 1.197
Group III	-1.225 \pm 0.464	-1.827 \pm 0.398	1.574	0.121	-1.574 \pm 1.445
ANOVA	F	1.375	0.184		0.964
	P-value	0.259	0.832		0.383

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 \pm SD	Mean \pm SD		Mean \pm SD	
Group I	-1.080 \pm 0.135	-1.463 \pm 0.834	1.467	0.148	-1.295 \pm 0.987
Group II	1.135 \pm 0.084	-1.593 \pm 0.959	2.029	0.047	-1.333 \pm 1.048
Group III	-0.929 \pm 0.197	-1.709 \pm 0.332	2.276	0.027	-1.381 \pm 1.324
ANOVA	F	0.118	0.433		0.083
	P-value	0.889	0.650		0.921

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