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A PROSPECTIVE INTERVENTIONAL STUDY ON COMBINATION OF CALCIUM CARBONATE AND VITAMIN D3 IN OSTEOPOROSIS PATIENT – AN OPEN LABELLED TRIAL

| Vijayakumar S ¹ , Parimalakrishnan S ² , Vijayakumar AR ³ , |
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| Yeshwanthkumar B ⁴ |

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Abstract

Background: Globally, Calcium and vitamin D 3 are widely used therapies for osteoporosis patients. However, addition of supplements to improve strengthens their bones, and reduced bone-related deficiencies such as osteopenia and osteoporosis. Though the effectiveness of these supplements may prove evidences of strengthen to the existing therapies.

Objective: This study aimed to assess before and after intake of calcium carbonate and vitamin D3 combination drugs among osteoporosis patients.

Methodology: The study group consist of 137 subjects from district headquarters hospital of Krishnagiri, Tamil Nadu. From these, 80 subjects with low level of 'T' score value (< -1.0 SD) were enrolled in the study population and they were administered with calcium (500mg) and Vit D3 (250I/U) day⁻¹ for the period of 18 weeks. At the end of the treatment 'T' scores were recorded in all patients, before and after study period. In addition to that patient's relevant data were collected through personal interview method.

Results: Before intervention prevalence of osteopenia and osteoporosis were found to be 33.7 % and 66.3 % respectively. Among study subjects 60 completed 18 week period of drug treatment, reported improvement of bone mineral density significantly ('p' <0.0001). In study group 60% subject fully recovered from osteoporotic to osteopenic condition. The data reports base line characteristics revealed that high risk features of osteoporosis was observed in both groups of smokers and alcohol consumption study subjects were found to be 11.6 % and 60 % respectively.

Conclusion: The present study highlighted that intake of calcium supplements increase bone mineral density and however, decreases in risk of osteoporosis condition targeting these groups.

Keywords: Calcium; Vitamin D3; Bone Mineral Density (BMD); Osteoporosis; 'T' Score.

¹Research Scholar, Annamalai University, Chidambaram, Tamilnadu, India,

²Associate Professor, Annamalai University, Chidambaram, Tamilnadu, India,

³Department of Pharmacology, Sree Balaji Medical College and Hospital,

BIHER, Chromepet, Chennai-600044. Tamil Nadu, India.

⁴Department of Pharmacy Practice, Padmavathi College of Pharmacy and Research Institute, Dharmapuri, Tamil Nadu, India.

Correspondence : S. Vijayakumar, M. Pharm., Research Scholar, Annamalai University, Annamalai Nagar, Chidambaram. Tamilnadu. Email. vijaykumarsasikala@gmail.com

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1. INTRODUCTION

Osteoporosis, is a major public health concerned worldwide today. It is a condition of compromised bone strength as a predisposing factor for increased risk of fracture. [1,2] Osteoporosis is a multifactorial disease involving multiple risk factors few are not modifiable factors such as gender, advancing age, hereditary and race while others are considered as modifiable factors such as knowledge, health belief, offer an opportunity to delay the onset or progression of osteoporosis[3,4]. However, people may not know that they have osteoporosis until a sudden fall or strain [5,6]. The financial burden of treating fractures is enormous, and the consequences of this fracture can be serious and even fatal[7-9]. The most common fractures related to osteoporosis are hip, wrist and spine. Among them vertebral fracture can cause back pain, decreased pulmonary functions, loss of height, deformities and immobility [10-14] with result antiimpact on patient's health related quality of life [15]. Reduced consumption of essential elements like calcium and vitamin D supplement in day to day life might be the reason for progressive bone loss in osteoporosis. Several studies demonstrated the external supplement of calcium and vitamin D improves the bone strength [16,17]. This study aimed to assess before and after intake of calcium carbonate and vitamin D3 combination drugs among osteoporosis patients

2. MATERIAL & METHODS

2.1.Study design and population

Present open label prospective intervention study was undertaken at a DEFF=Design effect for cluster design, tertiary care district headquarters hospital of Krishnagiri district of Tamil Nadu, India during June 2019 to April 2020. A total of 137 osteoporosis patients' with given consent of age group of 20 to 85 years were screened for the study. All subjects underwent physical examination and routine bone mineral density was investigated. The subjects with a history of chronic glucocorticoid excess due to over consumption or secondary to Cushing syndrome, malignant tumour, Rheumatoid arthritis, Inflammatory Bowel Disease (IBD), Parathyroidism, Cystic fibrosis and Chronic liver disease whose clinical data were incomplete were excluded from the study. Among all reviewed patients n=80 were recruited in intervention group and finally the n=60were carried out the studied (Figure Institutional ethics committee 1). reviewed approved the protocol.

Sample size calculation

Sample size calculation took into consideration the known prevalence of osteoporosis (50%), a 95% level of confidence (CI), an error rate of 5%, and a design effect equivalent to 2 for cluster design, the investigator calculated the sample size through Software Open Epi Version 2.3, using the following equation.

Sample size n= [DEFF*Np (1-p)/ $[d2/z21-\alpha(N-1) + P^*(1-p)]$

Where,

n=sample size,

N=Population size,

Z=Z statistic for a level of confidence 95%,

P=Expected proportion,

Sample size calculated was 137 eligible for study population [18].



Figure 1: Study Design

2.2. Data collection and Intervention procedure

After confirmation of preliminary council plan bv the research of Government headquarters district hospital, Krishnagiri, Tamil Nadu and recovering the ethical code from the Institutional ethical committee of the college, finally those subjects who provided consent letters for the participation of the study were recruited. the Objectives of study and its significance were explained clearly at the time of consent to the study subjects. Primary data was collected using a checklist containing questions about demographic information including age, gender, clinical examination and paraclinical information. All the subjects were underwent Bone Mineral Density (BMD) test was performed using ultra sound densitometer scan with encompasses grades as per WHO criteria **'**T' score greater than -2.5 were considered to have osteoporosis, individuals with 'T' score ranging from -1 to -2.5 were considered to have osteopenia and those with 'T' score greater than or equal to -1.0 were considered normal individual. There upon subjects with low bone mineral density were treated with combination drug Calcium (500 mg) and Vitamin D3 (250I/U) (LUPIN 500 mg; LUPIN LTD, 159 C.S.T road, Kalina, Santacruz (E) Mumbai-400098 India) twice daily for 18 weeks period. At the end of treatment period all subjects were evaluated for BMD and the results of the pre and post bone mineral density were evaluated by DXA scan. The treatment has been continued after completion of the study to the patients those who had deficient /insufficient calcium and vitamin D. Body mass index was calculated as weight in kg per height in square meter. Those with a BMI of 25.0 - 29.9kg/m were consider as very obese.

2.3. Ethical consideration

This study was approved by the committee ethical institutional of Padmavathi College of Pharmacy and Research Institute and Government headquarters hospital Krishnagiri. [EC/00108/2019]. The checklist was anonymous and included only raw data and statistics. Subjects were assured that their information would remain confidential and they are free to withdraw from the study at any stage of the research work.

2.4. Statistical method

Data was analysed using graph pad prism statistical software of version 8.0.2. The results were expressed in mean \pm SD to study difference in total score for different group of continuous variable. P value < 0.05 was considered to be statistical significance.

3. RESULTS

The total number of osteoporosis subjects were included during the study period based on inclusion/ exclusion criteria were found to be 137 subjects (Male n=49 and Female n=88)with a mean age of male and female was found to be 48.83 ± 14.73 and 50.45 ± 14.78 years respectively. The mean BMI of study population was found to be underweight male

 $23.37 \pm 4.61 \text{ kg/m}^2$ and female 23.85 ± 4.41 kg/m². Whereas mean BMI overweight male23.23±4.55 kg/m^2 and female 23.58 ± 4.64 kg/m². However, the results of smokers and non smokers, alcohol and non-alcohol consumption study subjects were found to be 16.7% and 83.3%, 20% and 80% respectively. A total of 58% of participants were found to have mixed diet habit. The majority of the enrolled patients were from rural area (77%) and the 51% were literate can able of read and write (Table 1 & 2)

| Variables | Male | Female | |
|--------------------------------------|-------------|-------------|--|
| Number of participants (n=137) | 49 | 88 | |
| Age in Years | 48.83±14.73 | 50.45±14.78 | |
| Body Mass Index (kg/m ²) | | | |
| ≤ 25 | 23.37±4.61 | 22.85±4.41 | |
| ≥ 25 | 23.23±4.55 | 23.58±4.64 | |
| Socio demogra | phic data | | |
| Smokers | | 16.7% | |
| Non-smokers | | 83.3% | |
| Alcohol consumption | | 20% | |
| Non-alcohol consumption | | 80% | |
| Mixed diet habit | 58% | | |
| Literate | | 51% | |
| Illiterate | | 49% | |
| Rural | | 77% | |
| Urban | | 23% | |

Table 1: Base line characteristics of study subjects.

| Ш | U | nderwe | eight | Normal | | Obese | | | Overweight | | | |
|-------------------------------|-----|---------------|--------------------|--------|--|-------|-----|--------------------|------------|---------|------------------|-------|
| BI | (< | :18.5 kg | g/m ²) | (18. | $(18.5-24.9 \text{ kg/m}^2) \qquad (25.0-29.9 \text{ kg/m}^2)$ | | | g/m ²) | (≥ | 30 kg/m | l ²) | |
| 'T' Score (SD) | >-1 | -1 to -2.5 | <-2.5 | >-1 | -1 to - 2.5 | <-2.5 | >-1 | -1 to - 2.5 | <-2.5 | >-1 | -1 to - 2.5 | <-2.5 |
| Before treatment (n=80) | 0 | 02 | 13 | 0 | 15 | 19 | 0 | 07 | 13 | 0 | 03 | 08 |
| After treatment (n=60) | 01 | 07 | 02 | 05 | 15 | 05 | 05 | 10 | 04 | 0 | 04 | 02 |

Table 2: Age-Gender wise distribution of study population.

(BMI-Body Mass Index; n-Number of Subjects; SD- Standard Deviation)

3.1. Prevalence of osteopenia and osteoporosis

Age and gender distribution of the intervention study subjects for 18 weeks were summarized in Table 3. The prevalence of osteoporosis in study participants were 66.3%, among them 16.25% were male and 50% female.

| Age group (in Years) | Male (n=25) | Female (n=55) | Total n (%) | Mean ± SD |
|----------------------------|----------------|------------------|-------------|-----------|
| 25-30 | 01 | 2 | 03 (3.75) | 58±20.1 |
| 30-40 | 02 | 7 | 09 (6.5) | 56.2±13.4 |
| 40-50 | 06 | 11 | 17 (21.2) | 54.8±13.1 |
| 50-60 | 08 | 10 | 18 (22.5) | 55.5±13.2 |
| 60-70 | 08 | 18 | 26 (18.9) | 56.8±13.2 |
| 70-80 | 0 | 6 | 06 (4.3) | 57.0±14.5 |
| 80-90 | 0 | 1 | 01 (0.7) | 85±0 |

Table 3: Treatment characteristics of study subjects

(n- Number of Subjects; %- Percentage)

Baseline Characteristic of 80 subjects enrolled in our study depicted in Table 4. Before intervention, prevalence of osteopenia and osteoporosis was found to be 33.7% and 66.3 %.In our study data high risk of smoking and alcoholic subjects was found with 11.6 % and 60% respectively. A significant (p < 0.0001) improvement of BMD in n=60 was observed in subjects completed 18 weeks of treatment with Calcium and Vitamin D3. This study observed that prevalence of osteopenia was found to be 33.7% among them 15% were male and 18.7% female. In addition to that the data reports

that high risk feature of osteoporosis in both smokers and alcohol consuming subjects were found to be 11.6% and 60% respectively.

| Variables I | | moking subj (n=12) (%) ollow up n= | ects) 9/3 | Alcoholic subjects (n=10) (%) Follow up n= 7/3 | | | Bone mineral density (g/cm ³) | | | 'P' value |
|---------------------------------|--------------|--|------------------|--|--------------|--------------|--|--------------|--------------|--------------|
| T' Score (SD) | >-1 | -1 to -2.5 | <-2.5 | >-1 | -1 to -2.5 | <-2.5 | >-1 | -1 to -2.5 | <-2.5 | |
| Before treatment n=80 (%) | 0 | 05 (8.3) | 07 (11.6) | 0 | 04 (40) | 06 (60) | 0 | 27 (33.7) | 53 (66.3) | < 0.0001 |
| After treatment n=60 (%) | 03 (33.3) | 05 (55.5) | 01 (11.1) | 01 (14.2) | 05 (71.4) | 01 (14.2) | 11 (18.3) | 36 (60) | 13 (21.6) | |

Table 4: Duration of Calcium with Vitamin D3 therapy of subjects.

*n- Number of Subjects; %- Percentage; SD- Standard Deviation

However subjects who did not achieve the outcome of treatment because of irregular followup, renal complications and died due to Covid-19 infection (Table 5).

(n-Number of Subjects; % - Percentage)

| | Follow up | | | Follow up | | | |
|------------------------------|-----------|-----------------|---------------------|-----------|---------|------------|--|
| Duration of treatment | Continued | (n=60) | Discontinued (n=20) | | | | |
| (in weeks) | Male | Female | Total | Male | Female | Total | |
| | (%) | (%) | (n) | (%) | (%) | (n) | |
| 1-3 weeks | 07 (11.6) | 13 (21.6) | 60 | 02 (10) | 03 (15) | 05 | |
| 4-12 weeks | 07 (11.6) | 13 (21.6) | 60 | 03 (15) | 05 (28) | 08 | |
| < 16 weeks | 07 (11.6) | 13 (21.6) | 60 | 02 (10) | 05 (25) | 07 | |

4. DISCUSSION

The goals of present study were to assess the efficacy of combination calcium (500mg) and vitamin D3 (250I/U) day⁻¹in osteoporosis subjects. The result shows strong and positive correlation between 'T' Score measured by ultrasound densitometer. Osteoporosis is a common medical problem with over 50 million fractures occurring annually in India. [2]

Although the majority of gender population shows women were more susceptible (68.75%)

than men. Present study results correlates fragility hip fractures are more common in women

compared to men. Vitamin D deficiency is a very common phenomenon all over the world. It is found to be more commonly in elderly home bound adults and is one of important the risk factor for an osteoporotic fracture. So whether an association exist between the incidence of such fractures and the deficiency of been vitamin D has a matter of exploration. The cause for such high prevalence of vitamin D deficiency in the present study might be a multifactorial. Inadequate dietary calcium and vitamin D intake, lack of food fortification with vitamin D, pigmented skin, environmental pollution and traditional dress code causing less exposure to sunlight in most Indian.[19]With the findings of our study, these multifactor are again evident as risk for osteoporosis.

In a hospital based study among 158 women age greater than 25 years utilising calcaneal qualitative ultrasound 20.2% and 36.8% were suffering from osteoporosis and osteopenia respectively. Another retrospective study of 40-60 years old Indian women documented 18.4% osteoporotic and 47% osteopenics. A study in 158 female (mean age 42.5 years) reported osteoporosis and osteopenia rates as 13.3% and 48.1% respectively. Increasing age of women, higher gravidia status and postmenopausal status, low body weight and lesser physically active status were identified as risk factor. Our results correlate with above finding [20]. In current study, osteoporosis positively correlated with lower educational level were more likely to have osteoporosis than individual with higher educational level the finding agree with the previous literature [21] that demonstrated the association between educational level and risk of osteoporosis.

This study also demonstrated a positive correlation between BMI and BMD. High BMI is associated with high bone density while low BMI is linked with low bone density. Since BMI and fat mass are closely related, it can be deduced that fat mass is also positively correlated to BMD in both males and females. The positive correlation between high BMI and BMD indicates that the accumulation of fat results in an increase in bone density. Alternatively, poor nutritional state may causes a decrease in bone mineral density, which in turn increases the risk of osteoporosis. The associations between fat and bone density described above may explain why BMD increased in proportion to increased BMI [22].

5. LIMITATIONS OF THE STUDY

This study has few limitations. Though the effectiveness of these supplements is proven, add on evidences strengthen the existing therapies and while the current study attempted to establish an evidence base, it might have been more effective if it had been done in larger groups. Study subjects are taken the medication and adherence was monitored but the patients were not given with any food regulations to be followed. A dietary supplement rich in calcium and Vit D3 may confer the better outcomes of the subjects.

6. CONCLUSION

A clear improvement of bone mineral density with combination drug of calcium (500mg) and vitamin D3 (250I/U) day ⁻¹ as play an important role current treatment guidelines in of osteoporosis. However subjects with established osteoporosis reported that smokers and alcoholic are the most prevalent risk factors for osteoporosis. Intervention to raise the calcium level in bone mass achieved through proper medication (21.6%) was observed. Our study suggests that regular intake of Calcium and Vitamin D increase bone mineral density and reduces the risk of osteoporosis.

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