

## Does Administration of Vitamin C Improves Osteoporosis in Post-Menopausal Women? A Single Center Randomized Case Control Study

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### ABSTRACT

Osteoporosis in elderly is a worldwide problem with high cost on health care systems. Prevention of osteoporosis and its associated fractures, improves quality of life, and reduces the financial burden of treatment costs. Standard treatment regimen includes bisphosphonate, calcium, and Vitamin D3. In this paper we have studied the effect of daily administration Vitamin C on osteoporosis improvement. We studied 66 osteopenic to osteoporotic (T score <-1) patients referred to IMAM REZA hospital during 2012-2014 years. Cases were randomized in two groups of 33 patients. Both control and trial group were treated for osteoporosis with a regimen composed of alendronate 70mg weekly, 3 calcium carbonate (500mg) tablets per day and parenteral Vitamin D3 injection once a month. The trial group also received one Vitamin C tablet (250 mg) per day. Patient were followed for at least 12 month. After one year of treatment bone marrow density (BMD) was evaluated again. There was no statistically significant difference between controls and the trial group at the beginning of the study regarding demographic (age, weight, and height) and BMD. After one year of treatment the trial group, showed significantly better BMD than the control group (p<0.05). Addition of Vitamin C improves the outcome of osteoporosis. This is as safe and a low cost addition to standard treatment.

**Key words:** Osteoporosis, Osteopenia, Vitamin C, Ascorbic acid, Bone mineral densitometry.

### INTRODUCTION

Osteoporosis is a common problem in the elderly especially in postmenopausal women and a significant burden on health care systems. With increase in elderly population in societies around the world, prevention and treatment of osteoporosis treatment is becoming overwhelmingly important. Since osteoporosis increases the chance of fractures in any bone specially hips and spine, it has significant impact on quality of life in elderly population.

Diagnosis of osteoporosis according to world health organization (WHO) criteria is based

on measuring of bone density in hips and lumbar region by Dual-energy X-ray absorptiometry (DEXA) method. Dual-energy X-ray absorptiometry is the most widely used and most thoroughly studied bone density measurement technology. Two X-ray beams with different energy levels are aimed at the patient's bones. The BMD is determined from the absorption of each beam by bone after soft tissue absorption is subtracted out.<sup>1</sup>

Osteopenia is defined as bone loss more than one standard deviation from young adults means bone density (T score <-1) and decreased more than 2.5 standard deviation is indicative of osteoporosis (T score <-2.5).<sup>2</sup>

Several factors are responsible in development of osteoporosis. Decrease of estrogen in postmenopausal period is the leading cause in women. Alcohol abuse, low level activity, cigarette smoking, low body mass index (BMI), and age are among the other causative factors in both gender.<sup>3,4</sup> Rheumatoid arthritis, corticosteroid drugs<sup>5</sup>, and low dietary intake of Vitamins A, C, D, E that affect collagen metabolism can also cause osteoporosis.<sup>6,7</sup> Some reports also indicate excessive coffee consumption may worsen osteoporosis in postmenopausal women.<sup>8</sup>

Standard treatment of osteoporosis is triple therapy including calcium, bisphosphonate and Vitamin D3.<sup>9</sup> Hormone therapy such as parathyroid hormone (PTH) and calcitonin may be added to this treatment regimen.<sup>10</sup> Estrogen replacement therapy is also indicated in postmenopausal women who can't take bisphosphonate.<sup>10,11</sup> Addition of fluoride and strontium is a common practice in European countries but not in North America.<sup>13,14</sup>

Bone is a hybrid tissue of hydroxyapatite crystals embedded in a meshwork of collagen. In osteoporosis both of these elements are lost.<sup>3,6</sup> Treatment by factors which help collagen synthesis may have a positive effect on osteoporosis treatment.<sup>7</sup> Ascorbic acid or Vitamin C has an important role in collagen synthesis.<sup>15</sup> Several studies point to the positive role of Vitamin C in osteoporosis treatment. We performed current study to see if there is change in BMD measurement by

DEXA method, when Vitamin C is added to standard treatment in postmenopausal women.

## METHODS

In this study we investigated 73 women with osteopenia and osteoporosis, who were referred to orthopedic clinic of Imam Reza hospital (Tehran, Iran).

Inclusion criteria were: 1- Osteopenia or osteoporosis according to WHO criteria. 2- Normal level of calcium, phosphorus, and alkaline phosphatase. 3- At least 2 years post-menopausal. Exclusion criteria were: 1- Any prior treatment for osteoporosis before referral to our clinic. 2- Use of any kind of hormonal drug. 3- Menopause due to ovariectomy. 4- Cancer. 5- Diabetes mellitus. 6- Cigarette smoking. 7- Alcohol consumption. 8- use of corticosteroid drugs.

Subjects were divided in 2 groups, a control group (37 subjects) and a test group (36 subjects). Four patients in control group and 3 patients in test group were lost during study. Therefore results of 33 patients for each group were evaluated at the end of follow up period (Table).

Standard drugs used for osteoporosis were given to both groups; calcium carbonate tablets (500 mg) 3 times daily, alendronate tablet (70 mg) weekly, and Vitamin D3 injection (600,000 IU) monthly. In test group daily 250 mg Vitamin C tablet was added. Before starting the treatment BMD in

**Table. 1: Vital measurements & BMD (mg/cm<sup>2</sup>) of subjects in control and test groups Before & after treatment**

			Test (n=33)	Control (n=33)	p
Vital measurements	Height (cm)	Mean± Standard deviation Range	156.42±6.48 145-170	158.21±7.16 144-178	N.S
	Weight (kg)	Mean± Standard deviation Range	66.97±12.63 47-115	67.12±13.12 40-94	N.S
	Age (yr)	Mean± Standard deviation Range	63.52±10.87 40-84	62.58±12.63 40-89	N.S
BMD (mg/cm <sup>2</sup> )	Before therapy	Mean± Standard error	696.27±20.53	713.51±17.68	N.S
	After therapy	Mean± Standard error BMD Increase	720.57±117.25 24.3±5.33	731.45±102.20 17.94±4.15	N.S <0.05

hip region were studied was measure by DEXXA method using Hologic instrument (Bedford, MA). After one year of follow up another BMD was performed by the same instrument. Numerical results were evaluated using two tailed Student t-test for using IBM SPSS software v.18 (Armonk, NY).

## RESULTS

In this study control group with mean age of 62.58 years and mean BMD of 713.51 mg / cm<sup>2</sup>(hip region) and test group with mean age of 63.52 mean BMD 696.29 mg/cm<sup>2</sup>were investigated for effect of Vitamin C on bone density (table).

After one year of treatment BMD was measured in both groups. Mean BMD in control group was 731.25 and in test group was 720.57 mg/cm<sup>2</sup>. Mean increment of BMD was 17.9 mg / cm<sup>2</sup> in control group and 24.3 mg/ cm<sup>2</sup> in test group, which corresponds to 2.52% and 3.60 % increase in BMD respectively.

There was a statistically significant increase in BMD of both groups after receiving treatment for one year compared to initial BMD ( $p < 0.05$ ). Furthermore, BMD increase in test group was significantly more than the controls group.

According to significance level in BMD1 and BMD2 variables and percentage of this variable with respect to absolute value of the calculated ts with 64 degrees of freedom is more than means the t of the table (1.96) so we can conclude by 95% confidence that means of the variables are different in 2 groups and increment of bone density in test group was more than control group which indicates positive effect of vit C on bone density .

## DISCUSSION

Osteoporosis is a major health issue in postmenopausal women. Chronic pain due to micro fractures or overt fractures especially in lower extremities and spine results in disability. Considering the heavy financial burden on health system, findings an effective and economic way to prevent and treatment of osteoporosis is worthwhile.

Several lines of evidence point to vitamin C role in bone metabolism. In animal models of osteoporosis Vitamin C is shown to have protective effect. Arsalan *et al* showed adding Vitamin C to ovariectomized rats diet results in amelioration of osteoporosis .<sup>16</sup>Park *et al* showed that addition of Vitamin C to Vitamin C deprived mice improved osteoporosis .<sup>17</sup>Similarly, Turan and coworker reported that in heparin-induced osteoporotic rabbits, addition of Vitamins C,E and selenium added to diet, is curative .<sup>18</sup> Most interestingly, Mohan *et al* shows increased rate of fracture in mice with a gene mutation causing Vitamin C deficiency .<sup>19</sup>These and many other studies using animal models, prove the positive effect of Vitamin C on bone health.

In clinical studies, a number of articles report positive role of Vitamin C on outcome of osteoporosis. <sup>20,21,22,23,24</sup> The reduction rate of fractures may indicate indirectly to increased bone density but this item was not measured by DEXA method except in two study in elderly men.<sup>15,21</sup> Therefore, our study is one of few well controlled studies that show positive effect of vitamin C in osteoporosis treatment by increasing BMD.

Ramirez *et al* have shown that low level of Vitamin C is associated with osteoporotic hip fracture .<sup>20</sup> However, the net effect of Vitamin C was unknown, because of confound role of vitamin B12 and folate.

Ramos *et al* report that high dose of Vitamin C (1000mg/day)in conjunction with vitamin E(400IU/day) in elderly men prevents bone loss and this effect was attributed to their anti-oxidant action.<sup>21</sup> Like the previous study Vitamin C was not studied alone and its contribution could not be ascertained.

Sahni and coworkers have reported that low plasma level of Vitamin C increases the rate of hip fracture .<sup>22</sup> In their study 952 cases were followed up for hip fracture occurrence up to 17 years. They did not study BMD or the effect of Vitamin C prescription.

Zang *et al*, studied effect of high dose Vitamin C on BMD in 344 men and 540 women .<sup>23</sup>

After four years follow up, daily high dose of Vitamin C, has increased bone density in nonsmoker men. Their study has compared the effect of high dose Vitamin C consumption on elderly men and women but we have studied its effect on postmenopausal women in conjunction with standard treatment for osteoporosis.

Like any other drugs Vitamin C is not without adverse effect. High dose Vitamin C consumption is a known risk factor for renal stone formation.<sup>26</sup> Daily recommended dose of Vitamin C is 200mg.<sup>25</sup> We prescribed a 250mg of Vitamin C tablet daily which is similar to daily recommended dose, and is much lower than 1000mg prescription in other studies.

Among limitation of our study is low number of cases in and lack of Vitamin C blood level measurement. One can argue for cost benefit ratio of added expense of vitamin C measurement in treatment of osteoporosis.

### CONCLUSION

In this study we have shown that Vitamin C, an affordable drug, in combination with standard therapy of osteoporosis; calcium carbonate tablets (500 mg) 3 times daily, alendronate tablet (70 mg) weekly, and Vitamin D3 injection(600 000IU )monthly, has positive effect on increase of BMD in osteoporosis

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