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Assessment of Simvastatin Effect and Compare It's with Combination of Calcium plus Vitamin D3 in Postmenopausal Women with Osteoporosis

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ABSTRACT

In osteoporosis, bone strength declines, which increases the chance of bone loss, making it a silent disease. In the elderly, it is the leading cause of bone loss. Forearms, hips, and backbones are among the bones most prone to breaking. There are no symptoms until the bones are destroyed. Bones eventually degenerate to the point that a fracture can occur spontaneously or as a result of simple force. Even after the bone has been destroyed, patients may still experience chronic discomfort and diminished mobility. The goal of this study was to examine the effectiveness of simvastatin with calcium and vitamin D3 in treating osteoporosis in postmenopausal women. Postmenopausal women suffering from bone loss were separated into two groups of twelve women each, with a total of twenty four participants. Twelve postmenopausal women who did not have osteoporosis were included as a control group. Six months of treatment were required. One group took 20mg of simvastatin twice a day, whereas the other took calcium and vitamin D3 (D3 500 I.U. plus 600mg of calcium) twice a day. T-scores, BMD, triglycerides, and total cholesterol were measured in both groups before and after treatment. Patients on simvastatin had significantly higher T-scores than those in the control and calcium + vitamin D3 treatment groups after six months of treatment. After six months of treatment, The simvastatin and calcium + vitamin D3 groups had significantly lower mean serum triglyceride and total cholesterol levels than the control group.

Keywords: **Bone Mineral Density, Osteoporosis, Triglyceride Vitamin D3+ Calcium , Simvastatin ,Osteoporosis .**

INTRODUCTION

As the condition progresses, the bones weaken, become brittle, thin, and more vulnerable to fracture. Osteoporosis is a term that refers to "porous bone." Depletion of bone mineral

density causes bone to thin (P. Lips and N. M. van Schoor 2005). Calcium and other minerals are needed for bone density, which aids in bone strength and bone protection. This is based on the findings of Johnell et al. (2004). After menopause, estrogen deficiency in women is related with accelerated bone resorption and loss of mineral density. Osteoporosis and fractures are more likely to occur in postmenopausal women because of this. (S. Y. Kim, S. Schneeweiss, J. Liu et al.2010) list the following risk factors for osteoporosis: decreased vitamin D3 levels; low body weight; cigarette and heavy alcohol usage; age 65 or older; female gender; family history of osteoporotic fractures; and menopause. Dietary modifications are a part of the treatment plan. Both preventing and increasing bone loss in women and men can be prevented and increased by a healthy diet. The risk of developing osteoporosis increases if your body does not get enough calcium and vitamin D. Calcium and vitamin D taken combined have been shown to lessen the risk of osteoporosis. Vitamin D and calcium are necessary for strong bones (Brian K Alldredge; Koda-Kimble, Mary Anne; et al.2009, Prince RL, Devine A, Dhaliwal SS et al. 2006). Exercising is crucial for those with osteoporosis because it slows the degenerative process of the illness. However, moderate exercise (for more than 90 minutes per week, on more than three days per week) lowers the risk of osteoporosis and fractures in older men and women, despite the fact that little exercise does not maintain the bones. Regular physical activity is essential. Decrease alcohol intake. Brittle bones are linked to heavy drinking. Caffeine has been linked to a decrease in the ability of the body to absorb calcium. Stop smoking because it is associated with developing osteoporosis as a result of cigarette smoking appears to diminish following cessation. Drugs that inhibit bone resorption, such as bisphosphonates, are used to treat and prevent osteoporosis after menopause (National Osteoporosis Foundation2008). Drugs used to prevent resorption include SERMs, bisphosphonates, and calcitonin, among othersBisphosphonates are the therapy of choice for osteoporosis, according to the National Institutes of Health's Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. According to Lau EM (2001) and Woo J (1998). Denosumab is among a number of newer antiresorptives (Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al. 2007). Resorption is inhibited, which slows down bone remodeling, but resorption isn't rebuilt by these medications (which prevent bone breakdown) (Daniel TB1996). Because resorption and reformation are both normal processes, limiting resorption could eventually lead to a reduction in bone growth. Anabolic (Bone building) medicines are those that aid in the growth and repair of bone (Reid IR, Bolland MJ, Grey A.2008). A low-dose parathyroid hormone injection is the principal anabolic drug. Broken bones can be prevented and restored with the use of this drug. As a novel medicine, the long-term effects of PTH are unknown. Fluoride is

a bone-building medication, however it is not widely used and has several drawbacks. Bone and fracture loss can be prevented with both types of drugs, although severe side effects can occur (Ganong WF.1995). Patients who have been diagnosed with osteoporosis by the US Preventive Services Task Force (USPSTF) should only be given these drugs (Bischoff-Ferrari HA, Kiel DP, Dawson-Hughes B, et al.2009). Evidence from an animal study published in 1999 by Mundy et al. suggests that statins may have a bone-rebuilding effect. BMP-2 (bone morphogenic protein-2) is required for osteoblast cell development, and statins control its production. Statins may have more bone-forming effects if they increase BMP-2 expression. In addition to inhibiting protein synthesis, statins reduce the osteoclast enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. Edwards CJ, Russell RG, and Spector TD.2001.

METHODS

Patients

Clinical trials are being conducted in a randomized fashion in this investigation. The research was conducted in Iraq at Merjan Teaching Hospital at the Rheumatology Department's dual-energy x-ray absorptiometry facility. The study was conducted from August 2015 to January 2016. Gold-standard equipment for measuring bone mineral density is DXA (dual-energy x-ray absorption) (Schousboe JT, Shepherd JA, Bilezikian JP, et al. 2013, Gosfield E 3rd, Bonner FJ Jr. 2000). Patients with a very low fracture risk may benefit greatly from peripheral DXA, which measures bone mineral density at the wrist. Using DXA, we can determine patient's T-score, which represent the difference between their bone mineral density and that of the control group's peak bone mineral density. (Kanis J.A., McCloskey E.V, Johansson H. et al.2008, S.L. Silverman 2007. Czerwinski E., J.E. Badurski et al. 2007. In a healthy young adult, a normal T-score value is defined by WHO guidelines as being within one standard deviation (SD) of the mean BMD value. Those values that deviate more from the mean are described as follows(Czerwinski, Badurski, Marcinowska-Suchowierska, et al.2007): -

- A T-score between 1 and 2.5 SD indicates osteopenia.
- A T-score of less than –2.5 standard deviations is used to diagnose osteoporosis.
- Fragility fractures and a bone density of less than –2.5 standard deviations are both signs of advanced osteoporosis.

- More than 150mg/dl is considered normal triglyceride.

- A total cholesterol level of less than 200 milligrams per deciliter is considered normal.

The sample size

A total of 24 osteoporotic postmenopausal women made up the study's sample. There are two groups of 12 patients each, and each group is split evenly. Treatment lasts for six months.

The Group Study

Group I:- vitamin D3 and calcium hydrogen phosphate (600 mg) daily.

Group I I:- Taking 20 mg of simvastatin every day.

All groups had their BMD, T-score, total cholesterol, and triglyceride levels checked at the start and six months into the treatment.

The collecting of data:-

Patients are interviewed in a dedicated room attached to the DXA unit to gather information about their medical history. The data was gathered using a questionnaire that had been prepared and a structured interview technique that was employed with patients. Data were gathered in a systematic and individual fashion. A 30-minute interview with the patient was allotted because data collection was only done on Mondays and Wednesdays, from Monday through Wednesday, beginning at 8 am and lasting until 2 pm.

Statistical data analysis:-

SPSS 16.0 for Windows. lnc was used for the statistical analysis. The testing was aided by a statistician who was brought in especially for the job. Numbers were expressed as means and standard errors of means. A student's t-test was utilized to compare treatment durations within the same group. Multiple groups' data were compared using analysis of variance and post hoc LSD tests (ANOVA). An event was considered statistically significant if its P-value was lower than 0.05.

RESULTS AND DISCUSSION

Anthropometry

In this investigation, no significant difference was seen in anthropometric measurements between the two groups (1)

Table 1. study's patients' anthropometric measurements

Anthropometric data	Mean ±SEM	Anthropometric data
59.9±1.86	56.15±1.84	Age
82.95±4.06	81.2±2.54	Weight
154.6±1.52	152.4±1.22	Height

The demographics of osteoporosis patients and those who are in good health

Table 2. Age, weight, and height mean standard error of the mean (SEM) in healthy individuals and those with osteoporosis.

P-value	**Patients with osteoporosis**	**Healthy**	**P-value**
N.S.	58.13±1.42	60.25±1.62	Age(years)
N.S.	78.18±3.14	79.12±2.16	Weight(Kg)
N.S.	156.16±1.16	158.18±1.28	Height(cm)

T-score, total cholesterol, and triglyceride concentrations were all affected by the two therapy regimens.

T-score and bone mineral density (BMD) increased significantly (P0.05) at 6 months compared to baseline, as illustrated in figure(1,2) and figure(1,3), respectively (3,4). Serum total cholesterol and triglycerides were considerably lower in the group treated with simvastatin for six months (P0.05) than in the control group (5,6). There was also a considerable rise in BMD and the mean T score relative to the baseline, as seen in figure (7,8). As demonstrated in the table, calcium and vitamin D3 were found to be more beneficial than simvastatin in treating postmenopausal osteoporosis (3)

Table 3. Many patients with osteoporosis continue to have symptoms and show signs of improved bone health (osteopenia) following their therapy

Group	**Osteopenia (No. %)**	**Osteoporosis (No. %)**
Calcium + vitamin D3	(6 ,50%)	(6 ,50%)
Simvastatin	(5,41.7%)	(7,58.3%)

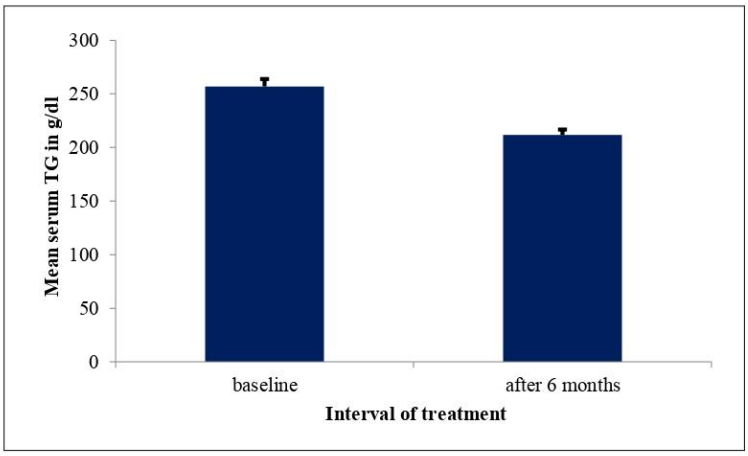

Figure 1. Calcium plus vitamin D3 effects on mean blood triglycerides at various time points.

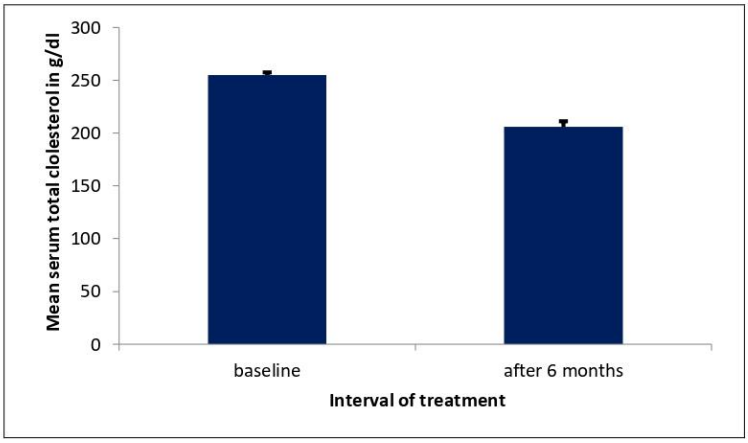

Figure 2. Different time intervals of calcium and vitamin D3's influence on the mean blood total cholesterol.

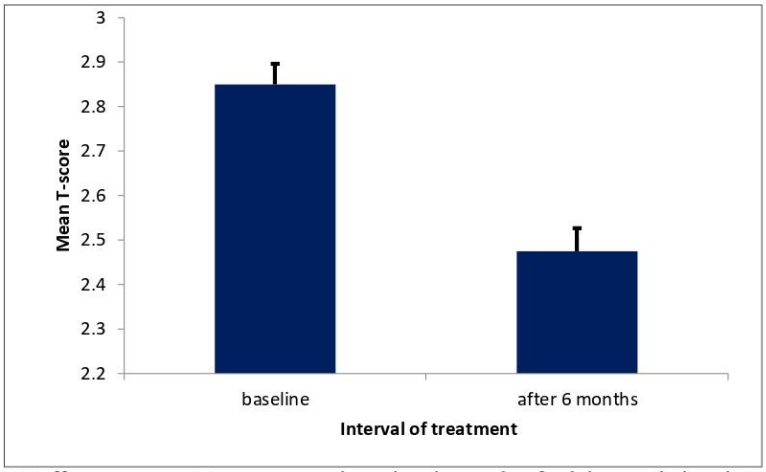

Figure 3. Effects on mean T-scores at various time intervals of calcium and vitamin D3 comparison.

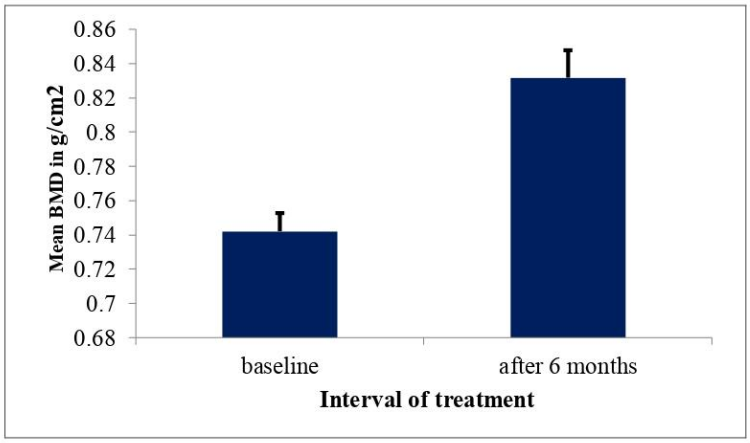

Figure 4. At various time points, a comparison of the effects of calcium plus vitamin D3 on mean bone mineral density

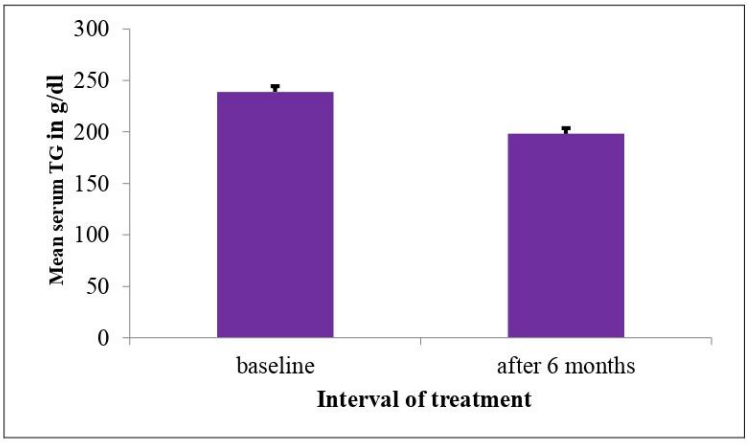

Figure 5. Analyzing how simvastatin affects triglyceride levels over time.

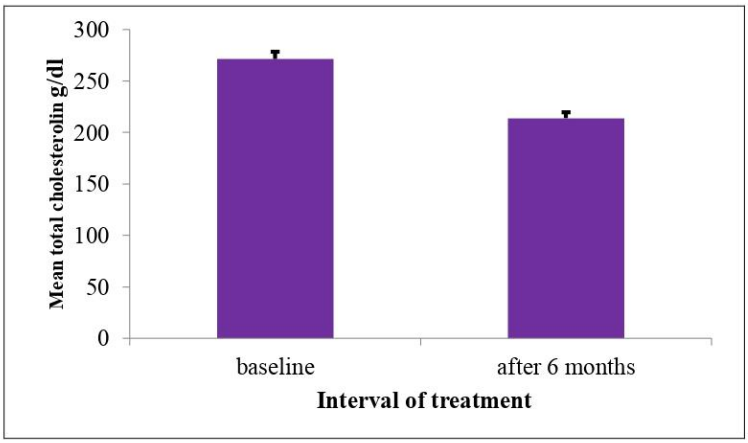

Figure 6. Comparison of simvastatin's effect on the mean serum total cholesterol at various time intervals.

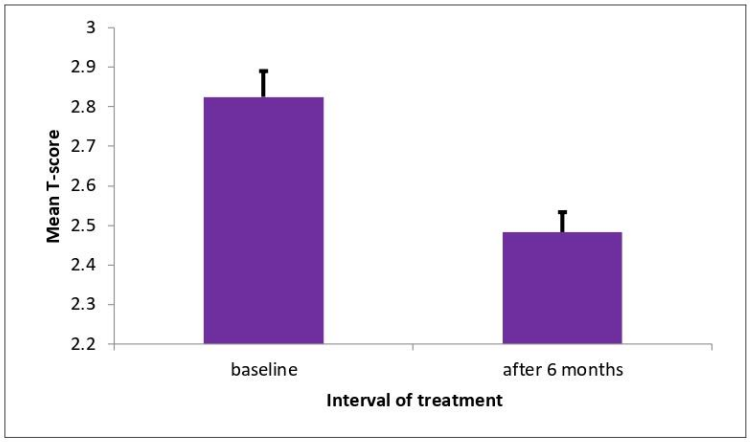

Figure 7. A comparison of the effects of simvastatin on the mean T-score at various intervals.

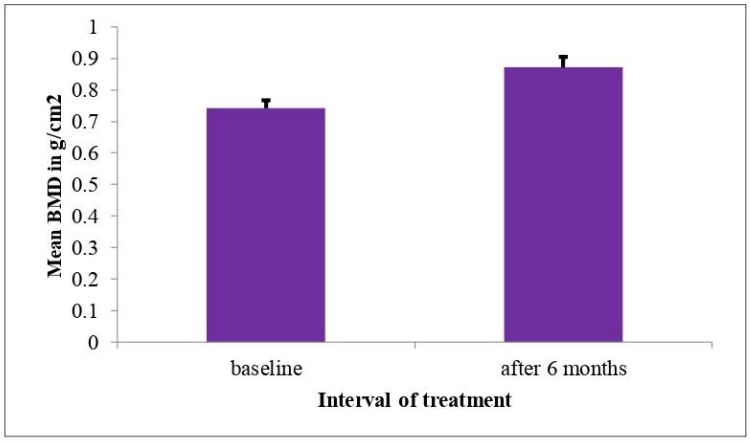

Figure 8. Different time points were used to compare the effects of simvastatin on the mean bone mineral density.

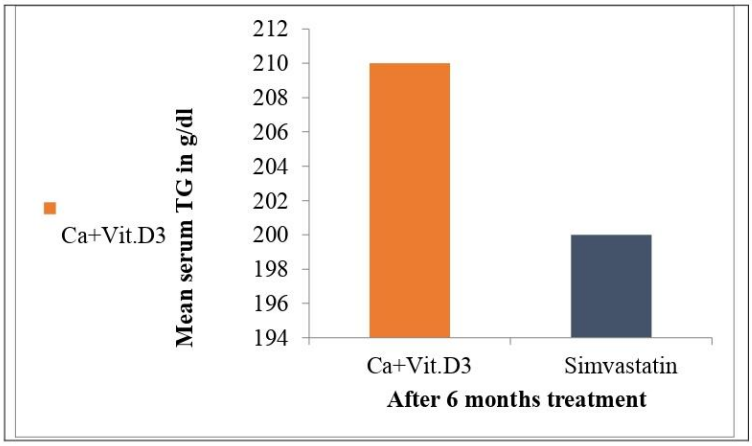

Figure 9. After six months of treatment, researchers compared the effects of calcium with vitamin D3 and simvastatin on mean serum triglycerides.

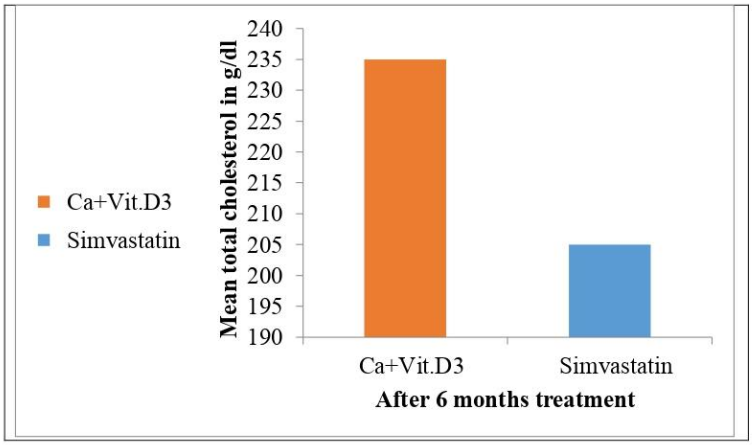

Figure 10. After six months of treatment, a comparison of the effects of calcium and vitamin D3 and simvastatin on the mean total cholesterol.

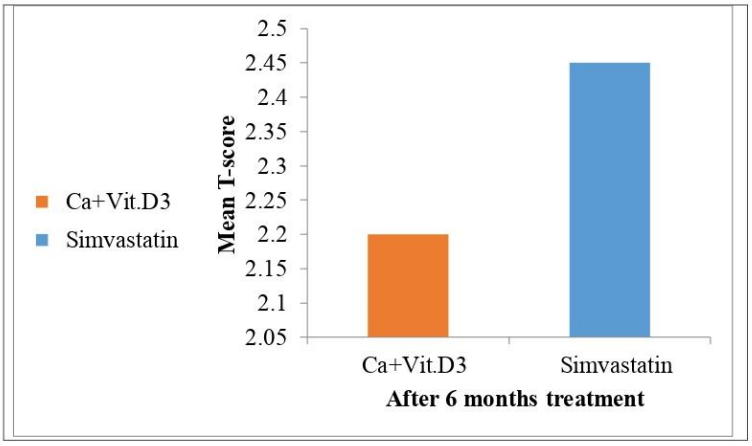

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Figure 11. A six-month study comparing the effects of calcium with vitamin D3 and simvastatin on the mean t-score.

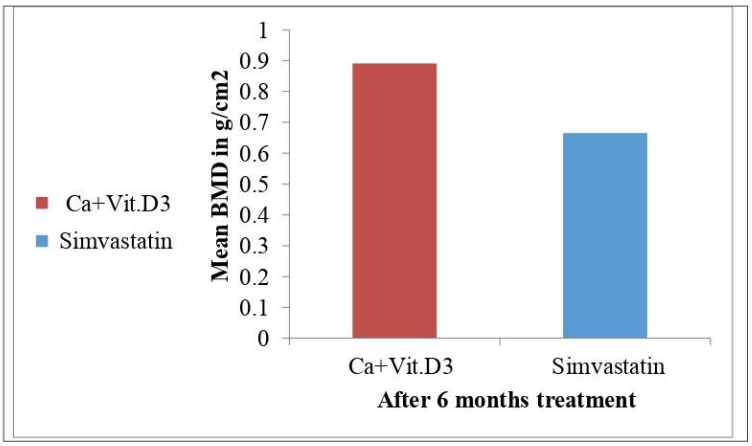

Figure 12. After six months of treatment, researchers compared the effects of calcium with vitamin D3 and simvastatin on mean bone mineral density.

Osteoporosis increases the risk of fracture because it causes both a loss of bone mass and a modification of the bone's microarchitecture. Main and secondary osteoporosis have long been recognized as distinct entities. Primary osteoporosis is associated with aging and diminished gonadal function, such as decreased estrogen levels, whereas secondary osteoporosis is the outcome of a variety of health conditions. Inactivity is a major contributor to bone loss, which can lead to osteoporosis (A.Howard,2011).

Effects of simvastatin on several study parameters

After six months of treatment with simvastatin, total cholesterol and mean serum triglyceride levels reduced significantly compared to baseline (Figure 5,6). Researchers found that patients with hyperlipidemia who took a single daily dose of 20mg simvastatin tablet at night, as reported by Nissen SE, et al. (2004), experienced significant reductions in their serum lipid profiles, including triglycerides and total cholesterol (Nissen SE, et al.2004). After six months of simvastatin treatment, the mean T-score and BMD significantly increased in comparison to the baseline figure(7,8), according to the findings of the current study. The results of this study were comparable to those of Skoglund et al. Statins have been shown to enhance bone growth in mice and aid the healing of fractures (Skoglund et al.2008). Staining of osteoblastic cell lines from mice, humans, and murine embryonic stem cells has been found to improve bone density by raising the rate of BMP-2 production and encouraging osteoblastic development. (Sugiyama M, Kodama T, Konishi K, et al. 2000). (.Philips BW, Belmonte N, Vernochet C, et al.2001). Statins have been demonstrated to induce osteogenesis in MC3T3-E1 cells (a clonal pre-osteoblastic cell line derived from the mouse calvaria) and murine embryonic stem cells (Friedenstein AJ, Chailakhyan RK, Gerasimov UV. 1987). (Erben R.G., A.M.Scutt, D.Miao, and et al. Statin therapy upregulated osteocalcin mRNA expression in human femur bone fragment-derived osteoblast cells in primary culture (Ohnaka et al., 2001). A statin-induced differentiation of osteoblasts is supported by all of these data and discoveries. Simvastatin's favorable effect on bone metabolism allows statins to become an

effective osteoporosis treatment medication. As far as the authors are aware, there has never been any research on the impact of statins on cellular development and proliferation. Defects in bone formation may be caused by a variety of causes, including a lack of bone marrow stromal cells, a decrease in osteoblastic growth and/or function, and a drop in the rate of osteoblast precursor proliferation (Hock JM, Onyia J, Bidwell J.1995). Proliferation and differentiation are both critical in the production of new bone, but it is difficult to determine the entire impact of both. Statins have considerable effects on differentiation, however the net effects would be reduced if cell growth and proliferation were taken into account. In order to settle these arguments, additional randomized, prospective studies with the use of the appropriate statins, dosages, and methods would be beneficial. Simvastatin, an HMG-CoA reductase inhibitor, was found to increase alkaline phosphatase activity, mineral deposition in human BMSCs, and osteocalcin expression, according to this study. According to these results, simvastatin appears to have anabolic effects on bone, presumably through promoting osteoblastic differentiation. Despite this, simvastatin's capacity to decrease bone cell proliferation has been proven to have an effect on bone synthesis. If statins reduce proliferation or promote differentiation in the vivo process of osteogenesis, this topic must be addressed in the near future.

Effects of calcium and vitamin D3 on several measured variables were analyzed. After Graph demonstrating the considerable reduction in mean blood triglyceride and total cholesterol after six months of treatment with calcium and vitamin D3 (1,2) In postmenopausal women, decreased bone mineral density has been linked to high levels of LDL cholesterol and low levels of good cholesterol (HDL) (BMD). As reported by (Yamaguchi T, Sugimoto T, Yano S.2002). Aggregation of LDL-cholesterol in the subendothelial space of vertebral arteries reduces bone synthesis in the subendothelium, leading to enhanced arterial mineralization (Anagnostis P, Karagiannis A, Kakafika AI, et al.2009). When the oxidized low density lipoprotein fraction of cholesterol is overproduced,

it stimulates an excess of osteoblast cells in the arterial pool, leading to atherogenesis and plaque calcification. High levels of low-density lipoprotein (LDL) cholesterol were associated with an increased risk of vertebral fractures in postmenopausal women with low levels of triglyceride (TG) (Yamaguchi T, Sugimoto T, Yano S.2002). There were no connections detected in certain research between serum lipid levels and bone marrow The mineral density (Solomon DH, Avorn J, Canning CF, et al.2005), bone density (Parhami F, Garfinkel A, Demer LL. 2000, Orozco P. 2004, Sivas F, Alemdarog lu E, Elverici E) and other studies have even found a positive correlation between them. (Sivas F, Alemdarog lu E, Elverici E, et al.2009, Solomon DH, Avorn J, Canning CF, et al.2005, Adami S, Braga V, Zambolini M.2004,. Brownbill RA, Ilich JZ. 2006). The study of Sivas et al. 2009 found that blood lipids, rather than bone mineral density variations, have an impact on vertebral fracture occurrence. Postmenopausal women with only one vertebral fracture had lower levels of total cholesterol, triglycerides, and LDL-C. The presence of vertebral fractures was strongly linked to a person's total cholesterol level. Vertebral fracture risk was lowered by 2.2% when total cholesterol was raised by 1 milligram/deciliter. For postmenopausal women exclusively, the authors of a 2010 study by Jeong et al. adjusted for laboratory and clinical variables and discovered a weakly positive correlation between HDL-cholesterol and lumbar spine bone mineral density In line with Yamaguchi et alfindings . 's from 2002, which found that lower HDL-cholesterol and greater LDL-cholesterol were associated with bigger bone mass, but no explanation could be provided. We conclude that lipid profile and skeletal mineral density are not consistently linked, neither within nor between studies (Jeong IK; Cho Sw; Kim SW; 2010). Further clinical investigations are needed to further understand the association between calcium and vitamin D3 supplementation and the reduction of total cholesterol and triglyceride and the improvement of bone mineral density and T-score in postmenopausal women with osteoporosis. The Vonhurst2010 research shows that one's diet can alter bone mineral density, and the L'Abbe et al. (2004) study demonstrated that calcium and vitamin D intake are

particularly important for reaching one's maximal bone mineral density (Lochmuller EM, Muller R, Kuhn V,2003).

Conclusion

Osteoporosis treatment with simvastatin results in increased bone mineral density and decreased T-score for those with osteoporosis, although it is less effective than calcium and vitamin D3 supplementation.

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