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Role Of Alendronate and Parathyroid Hormone in Postmenopausal Osteoporosis: A Randomized Clinical Trial

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Abstract

Aim: To compare the role of Alendronate and Parathyroid Hormone in Postmenopausal Osteoporosis

Study Design: Randomized Clinical Trial

Place and duration: This study was conducted in Peoples University of Medical & Health Sciences Nawabshah, Pakistan from Jan 2019 to Jan 220

Methodology: Total 238 women with deficient bone mineral density in the hip or spine were examined by dual-energy X-ray absorption spectroscopy **(**DxA) and Quantitative **CT** (QCT) over the course of a year for bone mineral density. They were randomly allocated to alendronate, parathyroid hormone and both alendronate and parathyroid hormone (Combination therapy) groups. Individuals who were fasting were subjected to a blood test to search for indicators of bone turnover.

Result: There was no statistically important alteration in the improvement of spinal bone mineral density between the parathyroid hormone and combination-therapy groups. There was an improve in trabecular bone volumetric density at the spine in all three groups, although it was approximately twice as great in the parathyroid hormone group. Only in the group taking parathyroid hormone did bone development rise significantly. Both the combined therapy and alendronate groups had a reduction in bone resorption.

Conclusion:

There was no sign that parathyroid hormone and alendronate functioned together in a synergistic manner. When alendronate is used with parathyroid hormone, it's likely that changes in volumetric bone density, hip cortical volume, and indicators of bone turnover will occur, counteracting the parathyroid hormone's anabolic benefits. An extensive amount of fracture research must be conducted over an extensive period of

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time in order to discover any anti-resorptive medications may be utilized in combination with parathyroid hormone treatment.

Keywords: osteoporosis, parathyroid hormone, alendronate, postmenopausal

Introduction

The use of antiresorptive medicines to prevent osteoporotic fractures is a firm treatment technique for individuals with osteoporosis. (1, 2) Bisphosphonates containing nitrogen, including such alendronate and risedronate, have been demonstrated in several randomized, double-blind studies to lower fracture risk while simultaneously enhancing bone mineral density by reducing bone resorption. (3-6)

When provided occasionally for osteoporosis, parathyroid hormone, unlike bisphosphonates, is anabolic. Both parathyroid hormones (1–84) stimulate bone formation rather than inhibiting bone resorption to improve bone density. (7, 8) For the treatment of osteoporosis and fracture risk, parathyroid hormone, a 34-amino acid fragment, has recently been shown to lessen the risk of fracture. It is unclear if combining a bisphosphonate with parathyroid hormone for fracture prevention would give a therapeutic benefit by combining various processes. Thyroid hormone (1–34) has been explored as a supplement to continuing estrogen (an antiresorptive agent), (9, 10) but no equivalent studies with bisphosphonates have been done. No antiresorbtive medicine (such as estrogen or a bisphosphonate) has been tested in previously untreated persons with Parathyroid hormone from the beginning of treatment. Our study compared the effects of parathyroid hormone (1–84) or alendronate monotherapy with those of alendronate and parathyroid hormone combination treatment in postmenopausal women with osteoporosis. We provide here the outcomes after a period of one year.

Methodology:

Females who had gone through menopause and were between the ages of 55 and 85 were selected. Women who were 55 years or older, had a past history of postmenopausal fractures, or had a family history of hip fracture were eligible to participate in the study. A woman was eligible to participate if her bone mineral density at the femoral neck, hip, or spine had a T score of less than –2.5. It was decided to exclude females with conditions or medicines recognized to effect bone metabolism, as well as those using bisphosphonates for more than four weeks in the preceding year. Before participating in the trial, all women were required to submit written informed permission, which was authorized by the official assessment panels at each of the take part clinics. Permission was also taken from the ethical review committee of the institute.

Alendronate (10mg/daily), calcium carbonate (50mg) parathyroid hormone (1-84) 100 µg daily, and multivitamin including 400 IU of vitamin D was given to women. Using a pen with a cartridge filled, the ladies were injected parathyroid hormone (1–84) or a matched placebo in the morning. Every two weeks, the cartridges were replaced. After an overnight fast, participants took either Alendronate or a matched placebo in the morning.

In this randomized clinical trial total 238 females were allocated randomly to one of three treatment regimens after a two-week "run-in" period, and then observed for a year. All 119 women received alendronate, 59 women received parathyroid hormone and alendronate, and 60 women received an alendronate. All of the women took calcium and vitamin D daily. Women in the first category of parathyroid hormone were given alendronate or a placebo in the 2nd year of the study, that is still going on. During the second year of the experiment, it would be split into two groups. Because of this, the first parathyroid hormone group was two times larger than any of the other groups. The first year of the study is covered in this report, and parathyroid hormone was the sole experimental reagent employed. Participants, physicians, and researchers were all unaware of the treatment group tasks, with the exception of a single clinician at the organizing center who was in charge of reporting to the information & protection checking panel. Various pharmaceutical firms offered funding for medication products and quantitative computed tomography (CT), but they had no influence in the study's design or interpretation.

We made an effort to track down and conduct all study visits and procedures for all women who were arbitrarily allocated to a treatment regimen. The intention-to-treat concept was employed in all analyses unless otherwise noted. Variables measured by dual-energy-x-ray absorptiometry & quantifiable CT had their significance determined by their percent changes from baseline. T-tests & Wilcoxon tests were used to relate the mean percent change in the combination-therapy group to the other 2 groups, and the mean variation in markers of bone turnover was compared. There were no multi-comparison adjustments made. For continuous variables, one-way ANOVA was used to compare groups, while 2/3 chi-square testing for dichotomous variables was used to compare groups. We were able to discern a difference in bone mineral density of 2.2% in the hip and 2.8% in the spine with a power of 90%.

Results:

Table 1 outlines the women's baseline characteristics. The mean (SD) T score for the femoral neck bone mineral density was 2.20.7. After menopause, 112 women (47%) reported a fracture, increasing the total to 165 (69 percent). There were no statistically important variations in baseline values across treatment groups, except for spinal bone mineral density (which remained almost 6% more in the combination-therapy group than any other group; P=0.03 for the three-way comparison). The spine's volumetric density did not show a similar trend.

The alendronate and parathyroid hormone treatment groups both reported similar increases (6.3 percent), however the alendronate group observed a smaller increase (4.6 %; alteration among the combination-therapy & alendronate groups, 1.5 % points; 95 % confidence interval, 0.5 to 3.6). The BMD of the parathyroid hormone group stayed the same, whereas the BMD of the combined therapy and alendronate groups increased. The overall hip growth was substantially greater in the combination therapy group than in the parathyroid hormone group. Alendronate seemed to reduce bone mineral density loss in the distal radius in the combined therapy group. The alendronate group's decrease was comparable to the combination-therapy groups. (As shown in figure 1)

Quantitative CT was used to evaluate volumetric bone mineral density in trabecular bone. The spine's cortical & trabecular bone volumetric density increased. All groups' bone volumetric density increased. The combined treatment group grew almost twice as fast as this one (25.5 % vs. 12.9 %; alteration, 12.6 % points; 95 % confidence range, 2.8 to 22.4). Alendronate-treated groups improved 10.5%, as did those treated with both drugs. Trabecular bone volumetric density enhanced in all treatment groups. The variation in trabecular bone volumetric density at the spine was similar across groups, although not statistically. (As shown in figure 2)

Cortical-bone variables changed in a different way than trabecular bone variables (Fig. 3). The parathyroid hormone group had a substantial decline in volumetric density of cortical bone at the entire hip, whereas the combination treatment group did not, and the alendronate group had an increase. The cortical bone density of the femoral neck increased. The parathyroid hormone group had more cortical bone volume in the hip (3.5 percent) & femoral neck (3.4 percent) than the other groups. The parathyroid hormone and combination treatment groups had varied changes in cortical size at the femoral neck. (3) 3.1 % points difference; 95% confidence interval (0.8-7) No treatment enhanced cortical BMD (As shown in figure 3).

Over a 12-month period, the quantity of N-pro peptide of type I collagen in the parathyroid hormone individuals grew immediately & drastically (an increase of 150 percent), and this increase was sustained over the course of the study (As shown in Fig. 4).

Following parathyroid hormone treatment, a rise in serum C-terminal telopeptide of type I collagen, a marker of bone loss, was linked to bone resorption. However, this increase happened more slowly than the alteration in N-pro peptide absorption. The concentration of N-pro peptide in the combination-therapy group increased after one month, but by three months, it had decreased to a level that was only slightly lower than the baseline value. After one month, the C-terminal telopeptide concentration in the

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combination-therapy group had reduced by 50% and stayed at that level for another month. Within one month of starting the study, the C-terminal telopeptide level in the alendronate group had reduced by 58 percent, followed by a decline in the N-propeptide level that was almost identical (by 59 percent after three months).

Percentages and rates of adverse events associated with parathyroid hormone therapy did not vary complication related to injection site, nausea, fatigue, pain in limbs and head, fatigue.

During the experiment, two females in the Parathyroid hormone group died, both of whom had quickly developing dementia. One of the women had merely received one parathyroid hormone dosage. The two fatalities were determined to be unconnected to the study drug by the data & protection checking panel.

Both the parathyroid hormone (1.03 mg per deciliter [61 mol per liter]) and combination-therapy (0.85 mg per deciliter [51 mol per liter]; P0.001 for both increases) groups had substantial increases in mean serum uric acid concentrations, but the alendronate group did not. One person in the parathyroid hormone group & 2 people in the combined therapy group both developed gout as a result of their treatment

Table 1: Women's baseline characteristics and he mean (SD) T score for the femoral neck bone mineral density

Characteristics	**Parathyroid hormone group**	**Combination-therapy group**	**Alendronate group**	**P value**
Mean Age (Years)	69.4	70.2	70.6	0.47
Mean Age at menopause	46.6	47.3	48.2	0.27
Race			**0.50**	
White	111	57	58	
Others	8	2	2	
Height loss since 25 year of age	40.3	40.8	34.5	0.35
Body Mass Index	25.6	27.1	25.1	0.07
Clinical feature since 45 year of age	57	30	25	0.64
Previously use of alendronate	13	4	10	0.23
On dual energy x-ray bone mineral density				
Lumber spine	0.771	0.819	0.778	0.03
Total hip	0.710	0.738	0.712	0.13
Femoral neck	0.599	0.612	0.596	0.50
Distal one third of radius	0.556	0.566	0.551	0.49
Volumetric density on quantitative CT				
Integral spine	0.174	0.178	0.178	0.56
Trabecular spine	0.083	0.087	0.085	0.68
Integral total hip	0.211	0.220	0.217	0.14
Trabecular total hip	0.073	0.074	0.076	0.71

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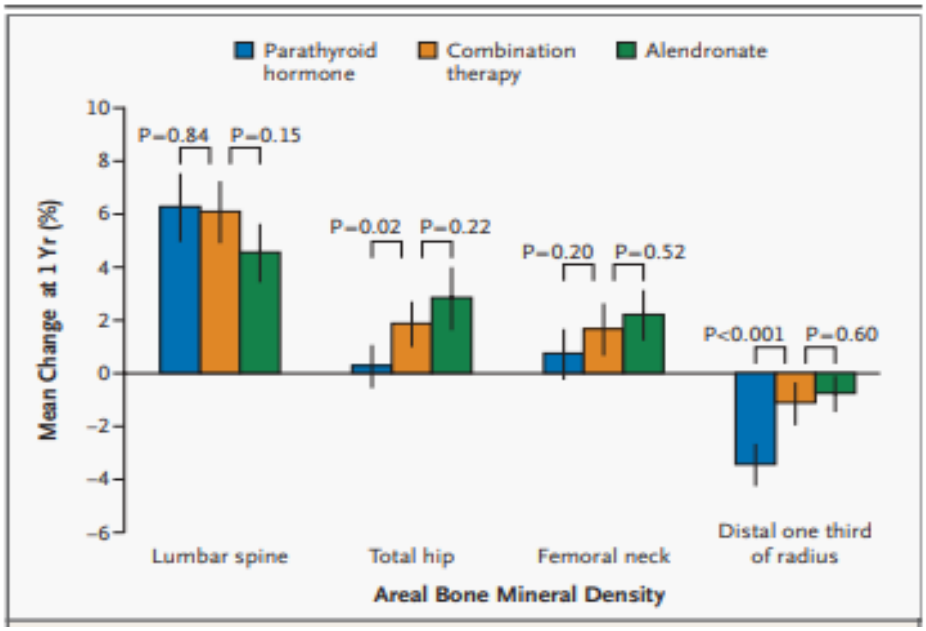

Figure 1: shows the mean percent changes in areal bone mineral density measured by dual-energy X-ray absorption spectroscopy.

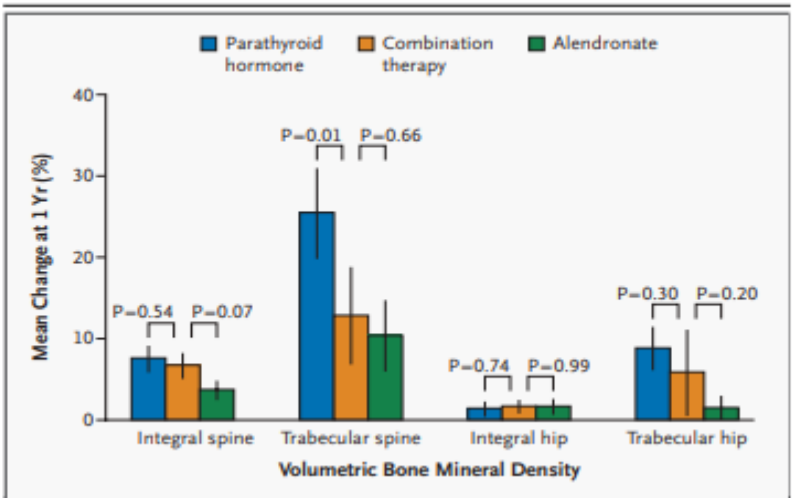

Figure 2: Using Quantitative CT, the mean percentage change in volumetric bone mineral density for both Integral and Trabecular Bone

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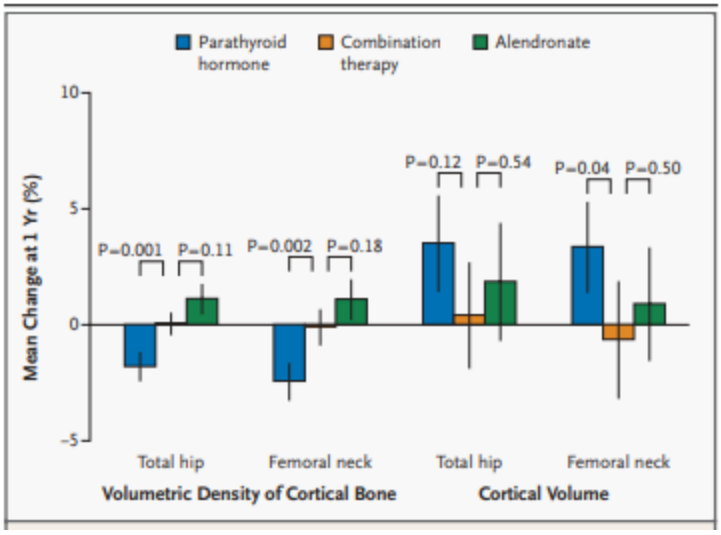

Figure 3: Mean % Changes in Cortical Bone Volumetric Density and Cortical Volume on Quantitative CT at the Hip

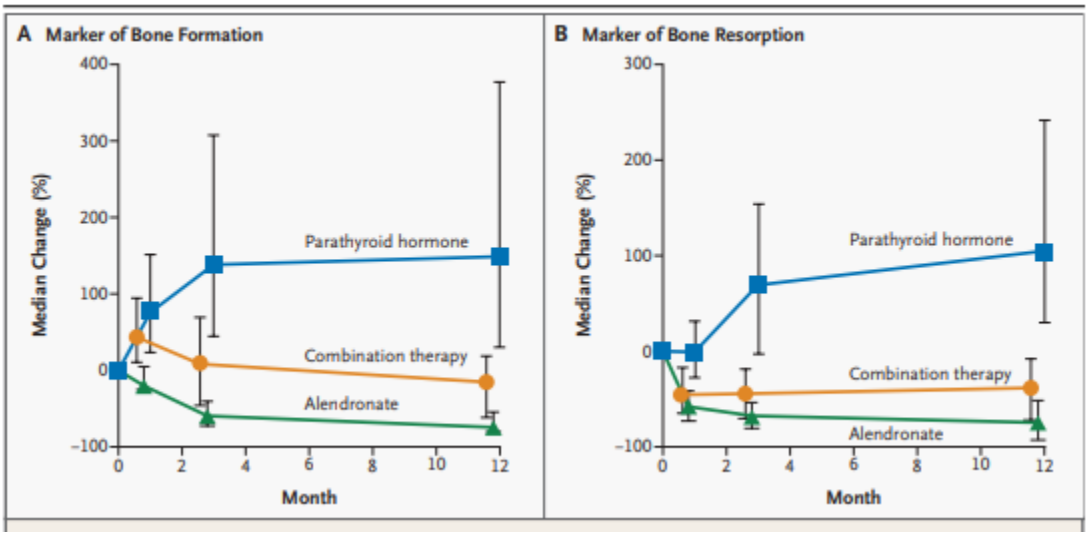

Figure 4: Median percentage change in blood concentrations of biochemical indicators of bone production and resorption.

.Discussion

Utilizing a randomized clinical trial design, we sought to determine whether using both parathyroid hormone as well as a bisphosphonate was superior than using either one of the two. Bone mineral density may be improved & the threat of fractures, such as vertebral & non-vertebral, can be decrease by everyday inoculations of parathyroid hormones (1–34) or parathyroid hormones (1–84). (7) When it comes to bone health, therapy with parathyroid hormones improves equally bone development & resorption, although during the first few months, the former takes primacy. However, alendronate, a bisphosphonate, has been reported to increase bone mineral density & decrease the danger of fracture, but it acts differently than parathyroid hormone, which prevents bone resorption rather than bone development.

Combination treatment, which stimulates bone formation while reducing bone resorption at the equal period, may be more successful than parathyroid hormone or alendronate therapy alone. Combination

therapy with parathyroid hormone and alendronate was predicted to improve bone mineral density, maintain bones formation, as well as minimize osteoporosis when compared to parathyroid hormone treatment alone. We found no convincing evidence that this combination is preferable to either therapy alone when it came to alterations in areal & volumetric bone mineral density, cortical volume, as well as stages of biochemical indicators of bone turnover.

We were able to analyses trabecular bone independently from cortical bone using quantitative CT. While alendronate and combination treatment did enhance spinal trabecular bone volumetric density, the effects of parathyroid hormone were more dramatic. Researchers observed that the cortical volume at the hip enhanced, but the volumetric density reduced & the bone mineral content stayed constant when contrasting the parathyroid hormone as well as placebo groups. These findings are consistent with previous studies. (11, 12) and the Parathyroid hormone has been shown to have previously shown activities, like the introduction of new bone that is not completely mineralized and the increase in cortical porosity (13, 14) These alterations were not linked to decreased bone strength in nonhuman primates in investigations. However, it is unknown if the alterations in cortical bone found with parathyroid hormone treatment devise a favorable, -ve or unbiased impact on bone power & fracture danger in individuals. General, the alterations in cortical and trabecular bone caused by parathyroid hormone treatment were not perceived with combination therapy or alendronate monotherapy, indicating that combination therapy affects the particular impacts of parathyroid hormone on bone.

Ending with the conclusion that further research is required to establish the impact of parathyroid hormone–based combination treatment on fracture danger. The levels of the bone formation marker rose clearly and fast in the parathyroid hormone group, while the levels of the bone resorption marker enhanced slowly but considerably. These findings are consistent with previous study findings. (8) Although the data were inconclusive, they did not support the idea that combination therapy would keep the enhanced bone formation understood with parathyroid hormone only though simultaneously decreasing resorption. The projected considerable and persistent improvements in bone formation were found to be non-existent a month after the commencement of the combined treatment regimen was initiated. The fact that improvements in bone formation are suggestive of parathyroid hormone's effects on bone suggests that combined therapy may not fully realize the anabolic advantages of parathyroid hormone.

We only looked at the effects of antiresorptive treatment & parathyroid hormone therapy in female who weren't previously on osteoporosis medication, so we can't answer issues about whether antiresorptive therapy should be started before or after parathyroid hormone therapy. The utility of parathyroid hormone treatment following antiresorptive medication is poorly understood. The addition of parathyroid hormone to continuing estrogen treatment, on the other hand, did not seem to decrease parathyroid hormone's potential to accelerate bone turnover. (10) The impacts of combining estrogen & parathyroid hormone therapy on bone mineral density were equivalent to those of parathyroid hormone alone. After 6 months of alendronate monotherapy, a recent research in males indicated that 24 months of combination alendronate and parathyroid hormone (1–34) (40 g) treatment resulted in lower gains in bone mineral density than 24 months of parathyroid hormone monotherapy. (15) Nevertheless, no trials of parathyroid hormone monotherapy have been conducted after any sort of antiresorptive medication has been discontinued. Our study was unable to determine if antiresorptive medication given following a course of parathyroid hormone therapy is clinically beneficial. Though 1 minor, nonrandomized research found an extra increase in bone mineral density following parathyroid hormone treatment (1–84), whether antiresorptive medicines must be given following parathyroid hormone treatment is a question that needs to be responded.

Conclusion

There was no sign that parathyroid hormone and alendronate functioned together in a synergistic manner. According to changes in trabecular bone volumetric density, cortical volume at the hip, & stages of bone turnover indicators, the anabolic benefits of parathyroid hormone might be decreased if alendronate is

administered at the same time. Longer-term fracture studies are required to investigate whether & how antiresorptive medicines may be used with parathyroid hormone treatment to get the best results.

Permission:

It was taken from the ethical review committee of the institute

Conflict of interest:

None

Funding Source:

None

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