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Effect of Alendronate on Bone Mineral Density in Puerto Rican Males with Osteoporosis

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Osteoporosis in men was not recognized as a major health problem until recently, and increased research in this area resulted in the approval of alendronate for the treatment of osteoporosis in men at the beginning of this decade. Low bone mineral density (BMD) has been demonstrated to be a strong predictor of fracture in men as it is in women. The causes of osteoporosis in men are variable and can be classified as primary or secondary. The aim of these report is to present the response of BMD in 10 Puerto Rican men with secondary causes of osteoporosis treated with alendronate. A significant increase of BMD in spine, total hip, trochanter and intertrochanteric regions were noted. A non-significant increase in femoral neck was observed.

Key words: Osteoporosis, Men, Alendronate, Bone mineral density

The burden of osteoporosis in men was not realized until recently and previously it was thought that osteoporosis was a post-menopausal women's health problem. It has been estimated that the lifetime risk for a clinical osteoporotic fracture in men is approximately 13 % (1). About 20 % of symptomatic vertebral fractures and 30 % of hip fractures occur in men, leading to considerable morbidity, excessive mortality and increased use of health and social services (2). This recognition of the importance of osteoporosis as a public health concern in men had led to increased in research in this area, resulting in the approval of alendronate (Fosamax ® Merck, Co.) for the treatment of osteoporosis in men at the beginning of this decade.

The International Society for Clinical Densitometry has recommended that osteoporosis be defined for males as a bone mineral density (BMD) T-score of -2.5 or below the young normal mean for men (3). Low BMD has been demonstrated to be a strong predictor of fracture in men as it is in women (4).

The causes of osteoporosis in men are variable and can be classified as primary or secondary. Primary causes include age-related osteoporosis, which tends to occur in men older than 70 years and is speculated to result from a combination of a decreased absorption of calcium, reduced activation of vitamin D, a decline in the lifespan and function of osteoblast, and decreased concentrations of sex hormones; and idiopathic (1). Secondary causes, which occur in one-half to two-thirds of men with osteoporosis, include hypogonadism, glucocorticoid excess, alcoholism, tobacco abuse, use of anticonvulsants and a variety of other systemic conditions (5).

The aim of this report is to present the results of the change in BMD in ten Puerto Rican men treated for osteoporosis with oral alendronate at the Endocrinology and Metabolism Clinics of the University District Hospital in the Puerto Rico Medical Center.

Methods

The study group comprised adult male patients with osteoporosis evaluated and followed at the Endocrinology and Metabolism Clinics of the University Hospital at the Medical Sciences Campus. Osteoporosis was defined, on the basis of the recommendation of the International Society for Clinical Densitometry, as a lumbar spine or hip BMD T-score of -2.5 or below the mean BMD of a reference data of young male controls provided by the densitometer manufacturer. The medical records of the identified male patients with osteoporosis were reviewed and the patient's information was included for analysis if the following criteria were met: a) a baseline BMD measurement by dual energy x-ray absorptiometry (DEXA) of spine and hip with osteoporosis, b) was started on oral alendronate 10 mg every day after the baseline DEXAC, c) had a DEXA done at least one year after starting treatment with alendronate and d) did not discontinue treatment with alendronate before DEXA follow up. A total of 10 patients satisfying

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above criteria were identified and constitute the study subjects. The BMD measurements by DEXA of the lumbar spine, total hip, trochanter, intertrochanter and femoral neck were performed at the Endocrinology and Metabolism Section on a Hologic QDR 1000 bone densitometer, with a defined least significant change for lumbar spine, femoral neck, total hip, trochanter and intertrochanteric of 0.035 g/cm², 0.053 g/cm², 0.024 g/cm², 0.033 g/cm² and 0.039 g/cm², respectively. The BMD measurements of trochanter, intertrochanter and femoral neck were not available for three patients, so for these measurements, the data of the other seven patients were used for analysis.

The statistical analysis was done using STATA version 8.2. The BMD data for each skeletal region was subjected to a Shapiro-Wilk W test of normality and if the data passed the test, defined as obtaining a p value < 0.05, then the differences in BMD before and after treatment with alendronate was compared by using the Wilcoxon signed-rank test. If the data did not pass the Shapiro-Wilk W test, defined as obtaining a p value ≥ 0.05, then the differences in BMD before and after treatment with alendronate were compared using paired t-test. Differences were considered as statistically significant if p < 0.05. Since each of the patients had the post-alendronate treatment BMD measurement at different time intervals, data was analyzed as obtained from the medical record and then averaged for reporting as annualized. Results are reported as means ± standard deviation. This current retrospective study was approved by the internal review board of the Medical Sciences Campus of the University of Puerto Rico.

Results

Ten patients with osteoporosis were identified and used in the current report. Age ranged from 26 to 78 years old with a mean of 45.1 ± 17.7 years old. Among the causes of osteoporosis identified, in 5 patients it was attributed to hypogonadism secondary to pituitary insufficiency due to hypothalamic-pituitary tumors such as craniopharyngioma (3 patients), ependymoma in 1 patient, and growth hormone- producing tumor also in 1 patient. In 2 patients it was due to the use of corticosteroids, in two other patients it was secondary to hyperparathyroidism; and in 1 patient the cause of osteoporosis was ascribed to the long-term use of anti-epileptic drugs. The length of treatment with alendronate for analysis ranged from 1 year to 2.75 years, with a mean of 1.6 ± 0.6 years. All patients were on calcium supplementation.

At the lumbar spine, the mean pre-treatment BMD was 0.711 ± 0.113 g/cm², and the annualized mean percentage change in BMD with alendronate was + 6.82 ± 6.53 % (p = 0.0038) (See Table 1). All patients had gain of BMD at the lumbar spine during treatment. Increases in BMD ranged from 0.401%/year to 22.381%/year. Figure 1 shows relationship between lumbar spine BMD before and after alendronate treatment in each patient.

For the total hip, the mean pre-treatment BMD was 0.771 ± 0.144 g/cm² and the annualized mean percentage change in BMD with alendronate was + 2.67 ± 4.53 % (p = 0.0469) (See Table 1). Two patients had decreased BMD of the total hip; one patient had a total percentage decrease of 5.75 % in 2.75 years of treatment. He had a diagnosis of hypogonadism due to pituitary insufficiency. During treatment with alendronate he was also using phenytoin (Dilantin®; Pfizer US Pharmaceutical). The other patient had a total percentage decrease of 0.35 % in 1 year of treatment and had a history of hyperparathyroidism corrected with parathyroidectomy concurrently with the starting of alendronate. Of the patients with increases in total hip BMD, the range was from 0.41 %/year to 15.49 %/year. Figure 2 shows the relationship between total hip BMD before and after treatment with alendronate for each patient.

At the trochanter region, the pre-treatment BMD was 0.552 ± 0.133 g/cm², and the annualized percentage change in BMD was 2.94 ± 3.45 % (p = 0.0144) (Table 1). Two

Table 1. Changes in Bone Mineral Density after Alendronate Treatment

Site	No. of subject	Mean duration of Tx	Mean baseline BMD	Mean after Tx BMD	Mean % change in BMD	Mean annualized % change BMD	P Value
Spine	10	1.6 ± 0.7	0.711 ± 0.113	0.785 ± 0.124	+10.96 ± 11.04	+6.82 ± 6.53	0.0038
Total hip	10	1.6 ± 0.7	0.771 ± 0.114	0.805 ± 0.163	+4.29 ± 7.71	+2.67 ± 4.53	0.0469
Trochanter	7	1.5 ± 0.6	0.552 ± 0.132	0.576 ± 0.133	+4.55 ± 4.99	+2.94 ± 3.45	0.0144
Intertrochanter	7	1.5 ± 0.6	0.852 ± 0.174	0.888 ± 0.178	+4.27 ± 4.25	+2.76 ± 2.84	0.0229
Femoral neck	7	1.5 ± 0.6	0.696 ± 0.176	0.705 ± 0.175	+1.44 ± 3.28	+0.93 ± 1.62	0.1550

Results are presented as means ± SD
Tx = treatment with alendronate
BMD = bone mineral density
% = percent

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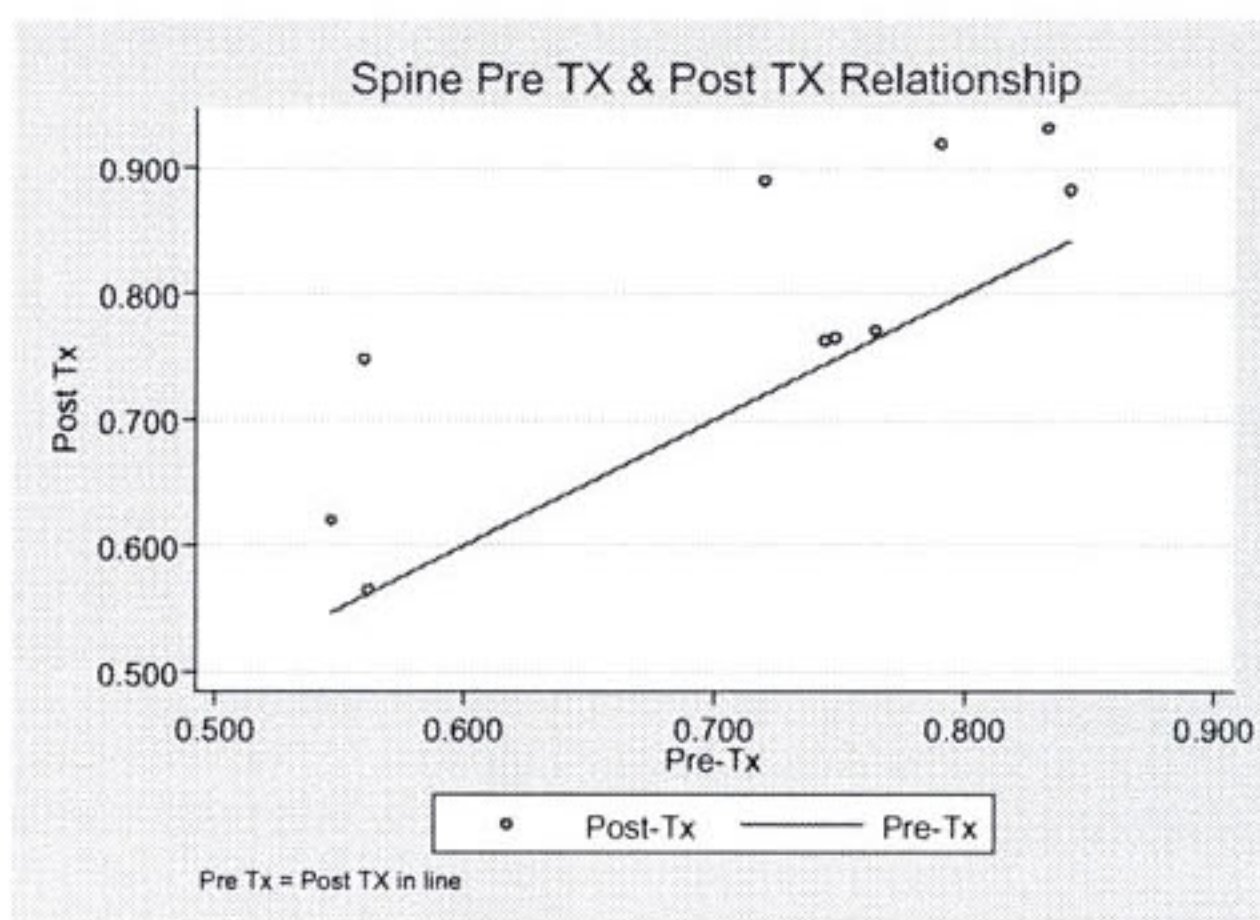Martinó A, et al.

Figure 1. Relationship of lumbar spine BMD before and after alendronate treatment for each patient.

patients had loss of BMD at this region during treatment. One patient with the diagnosis of pituitary insufficiency due to growth hormone-producing tumor post adenoma resection had a total percentage decrease of 0.497 % in 2.5
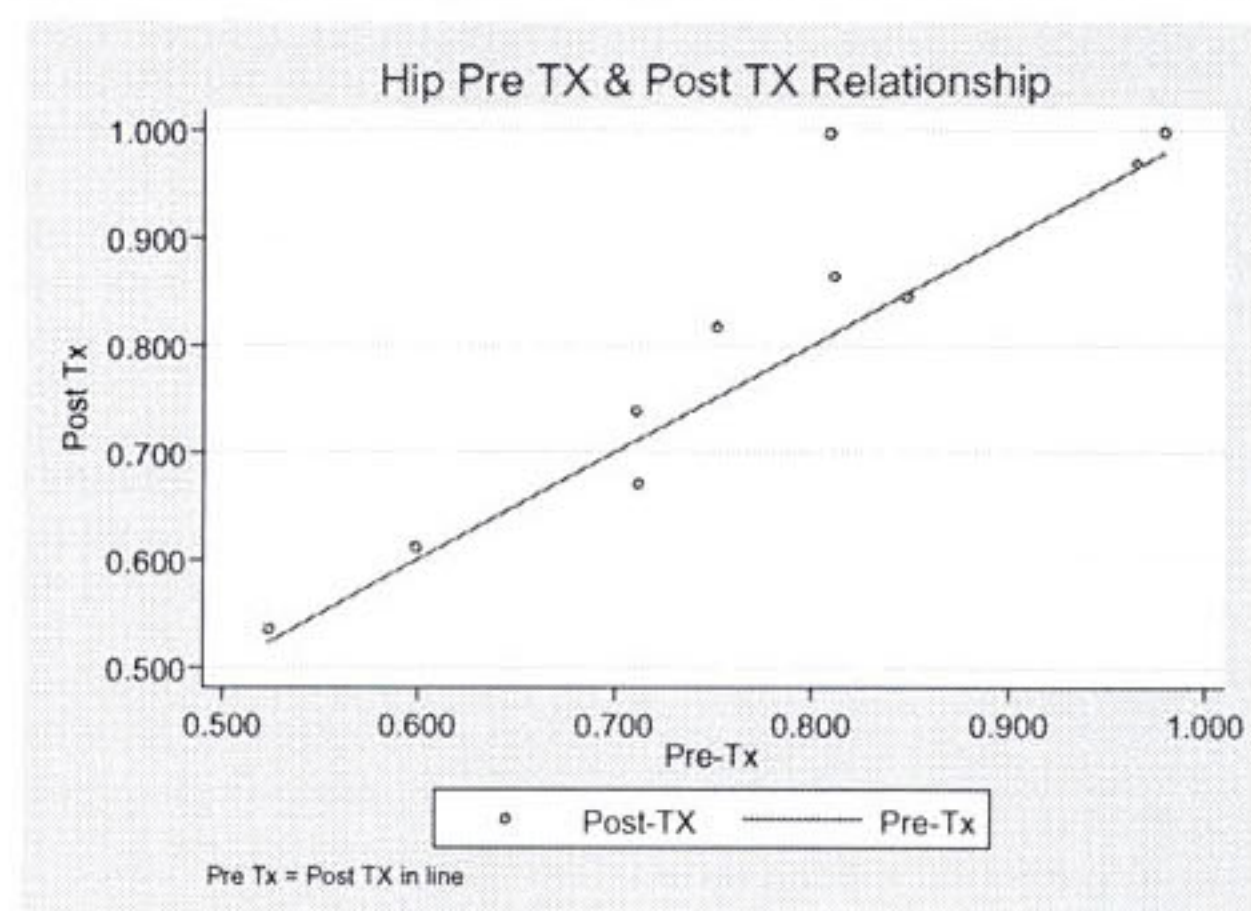

Figure 2. Relationship of total hip BMD before and after treatment with alendronate for each patient.

years of treatment, The other patient had a total percentage decrease of 1.309 % in 1.33 year of treatment, also had a diagnosis of pituitary insufficiency secondary to craniopharyngioma, was on testosterone replacement and used phenytoin for a seizure disorder. In the patients who had an increase in BMD the percentage change ranged from 3.00 %/year to 8.6 %/year. Figure 3 shows the relationship between trochanteric region BMD before and after treatment with alendronate in each patient.

At the intertrochanteric region, the pre-treatment BMD was 0.882 ± 0.174 g/cm^2, and the annualized percentage change in BMD was $+ 2.76 \pm 2.84$ % (p = 0.0229)(Table 1). Two patients had decreased in BMD at this region. One patient had a total percentage decrease of 0.563 % in 1.25

year of treatment, had a diagnosis of *pemphigus vulgaris* in remission and at the moment of treatment with alendronate was using low-dose corticosteroids. The other patient had a total percentage decrease of 0.939 % after 1
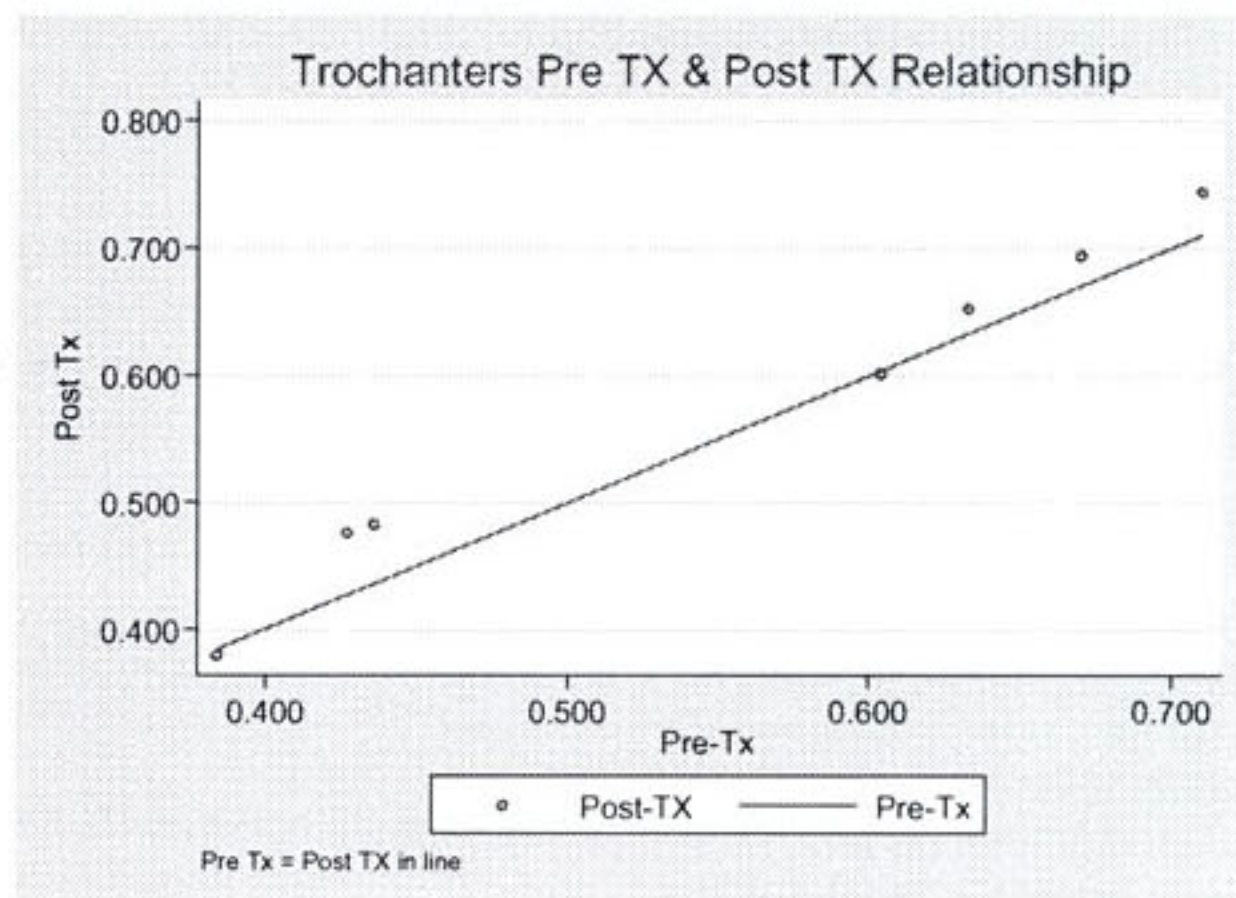

Figure 3. Relationship of trochanter BMD before and after treatment with alendronate in each patient.

year of treatment and was the same patient with hyperparathyroidism that had loss of total hip BMD described previously. In the patients with gain in BMD at this region, the range of percentage increase was from 1.59 % to 4.32 %. Figure 4 shows the relationship between intertrochanteric region BMD before and after treatment with alendronate for each patient.

At the femoral neck, the pre-treatment BMD was 0.696 ± 0.175 g/cm^2 and the annualized percentage change in BMD was $+ 0.93 \pm 1.62$ % (p = 0.1550)(Table 1). One patient did not change BMD in this region after 1.33 years of treatment with alendronate and two other patients have a loss of BMD at this same region. One of the patients with loss of BMD had a total percentage decrease of 1.40 % in 1.25
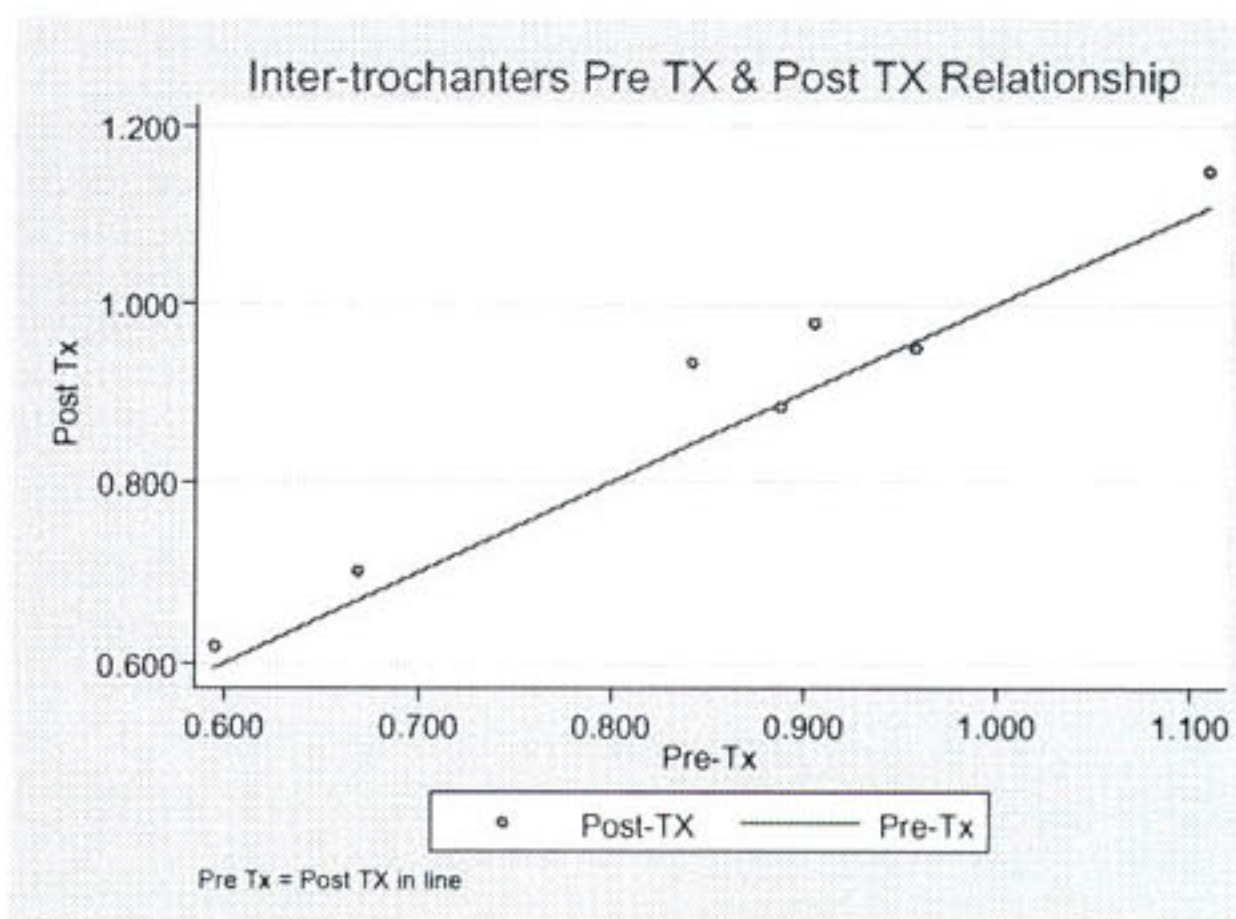

Figure 4. Relationship of intertrochanteric area BMD before and after treatment with alendronate for each patient.

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years of treatment with alendronate and was the same patient who had a loss of BMD at the intertrochanteric region and had a diagnosis of *pemphigus vulgaris*. The other patient had a total percentage loss of BMD of 1.31 % in 1 year of treatment with alendronate, had a history of hyperparathyroidism, and as the other patient with hyperparathyroidism, this patient started alendronate treatment concurrently with parathyroidectomy. In the patients with increases in BMD at this region the range of annualized percent change was from 0.25 %/year to 3.07 %/year. Figure 5 shows the relationship between femoral neck BMD before and after treatment with alendronate.
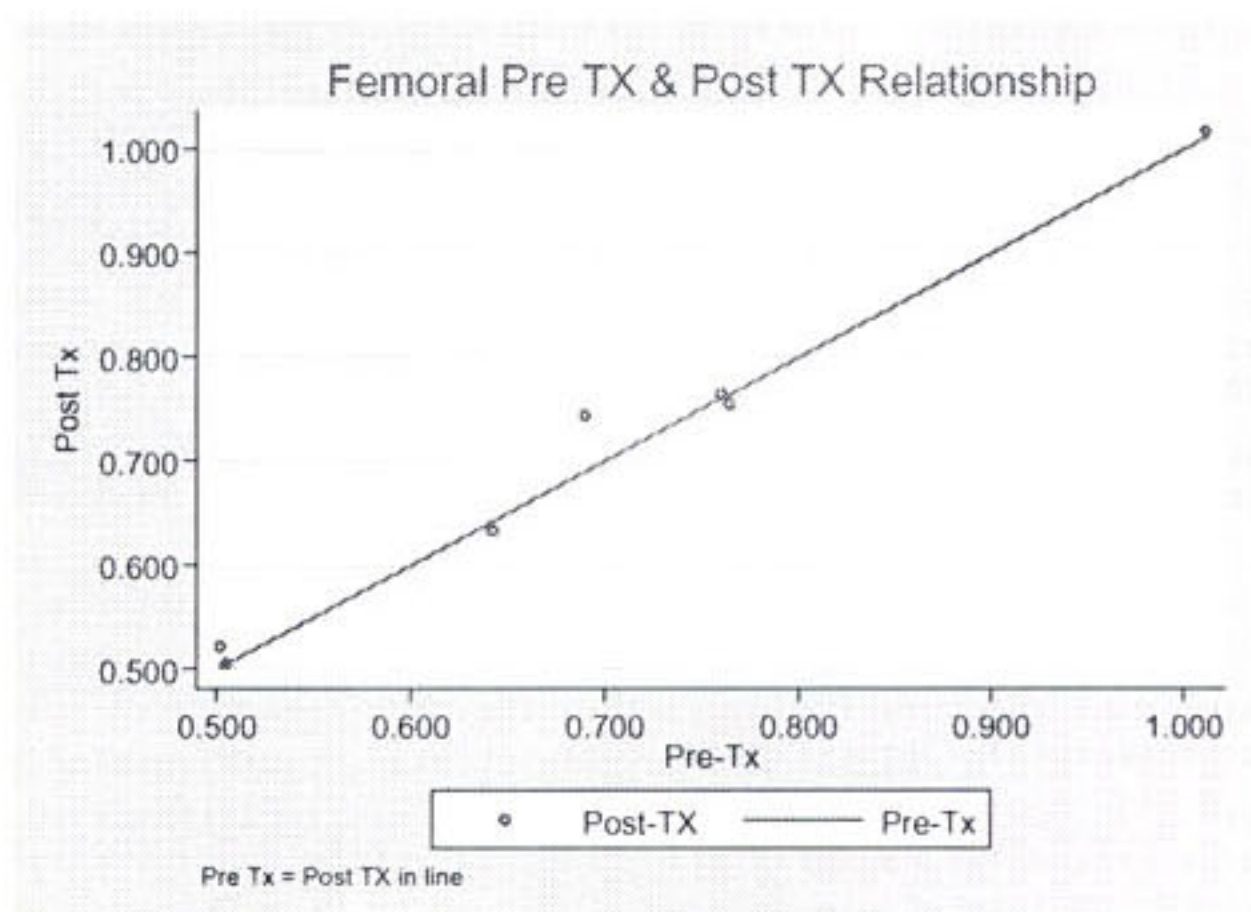

Figure 5. Relationship of femoral neck BMD before and after treatment with alendronate in each patient.

Discussion

As in other studies, alendronate 10 milligrams daily increased significantly lumbar spine BMD in our patients almost to the same extent as those studies, in spite of our study group been composed of male with secondary causes of osteoporosis, in contrast to the majority of reported studies (6,8,9,10) where patients with secondary causes of osteoporosis were excluded. This result suggest alendronate is effective in increasing lumbar spine BMD without regard of the cause of osteoporosis.

At the total hip, trochanteric and intertrochanteric areas, alendronate also demonstrated significant increases in BMD at these sites, although to a lesser extent than at the lumbar spine, a tendency seen also on studies of men and women with osteoporosis treated with alendronate (6,11). The lessesr increase in BMD at these skeletal areas as compared to the lumbar spine can be explained by the fact that the lumbar spine has greater amount of trabecular bone, and hence greater remodeling, and the increase in BMD in response to alendronate is believable to be due to the filling of the greater remodeling space in the trabecular

bones (7). Therefore, skeletal areas abundant in trabecular bone will respond greater to antiresorptive treatment than areas with less presence of trabecular bone.

At the femoral neck, our study group had a nonsignificant increase in BMD, a similar finding reported in another study (7) that included men with primary and secondary osteoporosis treated with alendronate, and in studies that used etidronate (10,13). In two other studies that included only males with primary osteoporosis (6,9),the increase in femoral neck BMD was significant. No plausible explanation can be given for this difference in response to alendronate at the femoral neck.

Conclusion

This study demonstrates that oral alendronate is effective in significantly increasing BMD at the lumbar spine, total hip, trochanter and intertrochanteric areas in Puerto Rican males with secondary causes of ostoporosis. A nonsignificant increase was observed at the femoral neck. The clinical significance of these findings in terms of reduction of fracture incidence in our patient population needs to be determined with larger, prospective studies.

Resumen

La osteoporosis en hombres no ha sido reconocida como un problema mayor de salud hasta muy poco tiempo atrás, y el aumento en la investigación en esta área resultó en la aprobación de alendronate para el tratamiento de osteoporosis en el hombre al principio de esta década. La densidad mineral ósea baja ha demonstrato ser un predictor contundente de riesgo de fracturas tanto en la mujer como en el hombre. Las causas de osteoporosis en hombres son varias y pueden clasificarse en primarias y secundarias. El propósito de este artículo es presentar la respuesta de densidad mineral ósea en 10 hombres puertorriqueños con causas secundarias de osteoporosis tratados con alendronate. Se notó un aumento significativo de densidad mineral ósea en espina lumbar, cadera total, área trocantérica y en área intertrocantérica. En cuello femoral, el aumento de densidad mineral ósea no fue significativo.

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