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Effect of Weight Bearing Exercises on Osteoporosis in Prostate Cancer Patients Undergoing Androgen Deprivation Therapy

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ABSTRACT

Background: Most men diagnosed with prostate cancer (PCa) are aged 50 years old or more treated by androgen deprivation therapy (ADT) treatment has been associated with interconnected adverse effects as decreased bone mineral density (BMD) and a loss in the structure and strength of bone leading to osteoporosis. Exercise has been proposed as a treatment to mitigate side effects of ADT.

Objective: This study was conducted to evaluate the effect of weight bearing exercises on osteoporosis in prostate cancer patients undergoing androgen deprivation therapy.

Patients and methods: The current study was conducted during a period of 3 months starting from 1st October 2019 till 31st December 2019.Thirty PCa patients who had osteoporosis induced by ADT were participated in this study, their ages were over 50 years old. They were selected from the Oncology Hospital Menoufia University and randomly distributed into two equal groups, group A: included 15 patients who received 30 minutes of weight bearing exercises through walking on treadmill, in addition to conventional medical care 3 days /week and group B: included 15 patients who on their conventional medical care.

Results: Our study showed that there was a statistically significant improvement in BMD and T-score mean of spine, femoral neck and total femur post treatment compared to that pre-treatment in the group A and B.

Conclusion: It can be concluded that weight bearing exercises had fruitful effects in cases of osteoporosis in prostate cancer patients undergoing androgen deprivation therapy as evidenced by the significant increase in BMD and T-score mean.

Keywords: Prostate Cancer, Osteoporosis, Androgen Deprivation Therapy, Weight Bearing Exercises, Bone Mineral Density.

INTRODUCTION

Prostate cancer (PCa) is the most commonly diagnosed male cancer. Treatment for PCa includes surgery, radiotherapy, androgen deprivation therapy (ADT) and chemotherapy, which is influenced by the stage and aggressiveness of the cancer **(1).** The vast majority men diagnosed for PCa were 50 years old or more seasoned. And, as men get older, their risk for osteoporosis likewise increases **(2)**. Those pervasiveness for osteoporosis over men with PCa on ADT may be great documented, with dependent upon 53 % influenced by this bone condition **(3).**

In spite of the fact that ADT has been shown to improve survival outcomes, treatment-induced hypogonadism with multiple interconnected side effects such as reduction in bone mineral density (BMD) and a loss in the structure and strength of bone. What's more an expanded hazard about falls and What's more resulting fractures in this clinical population group **(4)**.

Weight bearing exercise is more adapted to improve bone mass over whatever viable physical activity, they assume a double part over stressing the bones as they set both gravitational and muscular stress on bones **(5)**. One of the most well-known types of weight bearing exercise is walking, an exercise delicately very well and accepted by the older, as it is harmless, self-managed and effortlessly practicable. The impacts of walking on BMD have been widely considered **(6)**.

Treadmill exercise fortifies bone formation what's more suppresses bone resorption, increase serum 1,25-dihydroxyvitamin D3 level, what's more declines the serum parathyroid hormone level, leading to an increase in bone mass with incitement for longitudinal bone growth, particularly during weight-bearing sites **(7).**

AIM OF THE STUDY

The aim of this work was to evaluate the effect of weight bearing exercises on osteoporosis in prostate cancer patients undergoing androgen deprivation therapy.

PATIENTS AND METHODS

The current study was a prospective case-control study which was conducted during a period of 3 months, starting from Oct 1st, 2019 till Dec 31st, 2019. Thirty PCa who had osteoporosis induced by ADT participated in this study, their ages were over 50 years old. They were selected from the Oncology Hospital

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Menoufia University and randomly distributed into two equal groups:

Group A (Study group): included 15 patients who received 30 minutes of weight bearing exercises through walking on treadmill, in addition to drug therapy (vitamin D supplements and calcium) 3 days /week. **Group B (Control group):** included 15 patients who received only drug therapy (vitamin D supplements and calcium).

Ethical approval:

Research Ethics Committee and quality control approvals were obtained. The study purpose and procedures were explained in details and in plain terms to each of the subjects before being asked to give an informed written consent to participate in the study. Quality control of screening, handling of data and verification of adherence to protocols were done on a regular basis by the trial coordinator.

Criteria for the patient selection:

a- Inclusion Criteria:

- Age over 50 years old.
- Prostate cancer patients with osteoporosis as a result from androgen deprivation therapy.
- All patients are clinically and medically stable.
- All patients enrolled to the study signed their informed consent.

b- Exclusion Criteria:

The study excluded Patients with any of the following:

- Cardiac diseases.
- Pulmonary diseases.
- Orchiectomy.
- Unstable head or neck damage.
- Dementia
- Physical/mental incapacity to perform study prerequisites.
- Chronic kidney disease.
- Hypothyroidism**.**

Procedures of the study:

The procedure of this study was divided into two main procedures

A) Measurement procedures:

Estimation of Bone mineral density by DEXA

DEXA is commonly made on the lower spine and hips**,** T-scores was calculated by taking the difference between patients measured BMD and the mean BMD in healthy young adults matched for gender and ethnic groups and expressing the difference relative to the young adult population standard deviation **[8].**

Measurements will be taken as following:

- Before starting any protocol (pretreatment).
- After three months (post-treatment).

B) Therapeutic procedures:

Electronic Treadmill (BIODEX 945-480; Made in U.S.A)

During the three months intervention period, full weight bearing program included 30 minutes walking session three times a week at intensity of 60-80% of target heart rate. The training program consisted of treadmill exercises of progressive increasing intensity and frequency. These exercises divided into 3 phases as follow:

Warm up phase: Simple stretching exercises for all muscle groups then walking for 5 minutes on the treadmill at lowest speed (5 kilometer/hour and at 2 degrees angle of inclination).

Active phase: Then gradually increased at 2 minute intervals until it reached the initial intensity of 50- 55% of the maximal heart rate (MHR) in the first 2 weeks, then increased gradually until reaching 55-60 % of MHR in the second 2 weeks, 60-65% in the third 2 weeks and 65-75% in the forth 2 weeks, then increase till reach 80% of MHR by the end of the last 2 weeks.

Cool down phase: by simple stretching exercises for all muscle groups then walking for 5 minutes on the treadmill at lowest speed (5 kilometer/hour and at 2 degrees angle of inclination) **[9].**

The patients were instructed to stop training if they felt any dizziness, headache, palpitations, nausea, anxiety, exhaustion or any other side effects. The patients' vital signs were examined at least once during the practice **[10].**

Statistical analysis

Descriptive statistics and unpaired t-test were conducted for comparison of age between both groups. Normal distribution of data was checked using the Shapiro-Wilk test for all variables. Levene's test for homogeneity of variances was conducted to test the homogeneity between groups. Unpaired t-test was conducted to compare the mean values of BMD of spine, femoral neck and total femur between groups A and B. Paired t-test was conducted for comparison between pre- and post-treatment in each group. The level of significance for all statistical tests was set at p equal or < 0.05. All statistical analysis was conducted through the statistical package for social studies (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA**)** **[11].**

RESULTS:

***- Subject characteristics*:**

Thirty patients with prostate cancer who had osteoporosis induced by androgen deprivation therapy participated in this study. The mean ± SD age of the group A was 55.26 ± 3.2 years old, with maximum

value of 60 years old and minimum value of 50 years old. The mean age of group B was 54.86 ± 3.68 years old, with maximum value of 60 years old and minimum value of 50 years old. There was no significance difference between both groups in the mean age values (p = 0.75).

Effect of treatment on Bone mineral Density (BMD):

- Within group comparison:

There was a statistically significant increase in BMD of spine, femoral neck and total femur post-treatment compared to that pretreatment in groups A and B (p < 0.001). The percent of increase in BMD of spine, femoral neck and total femur in group A were 38.94, 40.6 and 38.46% respectively, while that in group B were 14.63, 15.86 and 15.29% for BMD of spine, femoral neck and total femur respectively. (Table 1 and figure 1).

- Between groups comparison:

There was no statistically significant difference in BMD of spine, femoral neck and total femur between both groups pre-treatment (p > 0.05). Comparison between both groups post treatment revealed a statistically significant increase in BMD of spine, femoral neck and total femur of group A compared to that of group B (p < 0.001). (Table 1 and figure 1).

Table (1): Mean BMD of spine, femoral neck and total femur pre and post treatment of the group A and B

BMD (g/cm²)	Group A $\bar{x}$ ± SD	Group B $\bar{x}$ ± SD	MD	t-value	p value
Spine					
Pre treatment	-3.57 ± 0.42	-3.35 ± 0.43	-0.22	-1.39	0.17
Post treatment	-2.18 ± 0.26	-2.86 ± 0.32	0.68	6.21	0.001*
MD	-1.39	-0.49			
% of change	38.94%	14.63%			
t- value	-18.84	-6.19			
	p = 0.001*	***p = 0.001****			
Femoral neck					
Pre treatment	-2.98 ± 0.42	-2.9 ± 0.27	-0.08	-0.61	0.54
Post treatment	-1.77 ± 0.34	-2.44 ± 0.39	0.67	4.96	0.001*
MD	-1.21	-0.46			
% of change	40.6%	15.86%			
t- value	-13.91	-9.43			
	p = 0.001*	***p = 0.001****			
Total femur					
Pre treatment	-3.38 ± 0.5	-3.4 ± 0.34	0.02	0.12	0.9
Post treatment	-2.08 ± 0.28	-2.88 ± 0.33	0.8	7.06	0.001*
MD	-1.3	-0.52			
% of change	38.46%	15.29%			
t- value	-13.78	-7.16			
	p = 0.001*	***p = 0.001****			

$\bar{x}$, mean; SD, standard deviation; MD, mean difference; p-value, probability value; *, significant

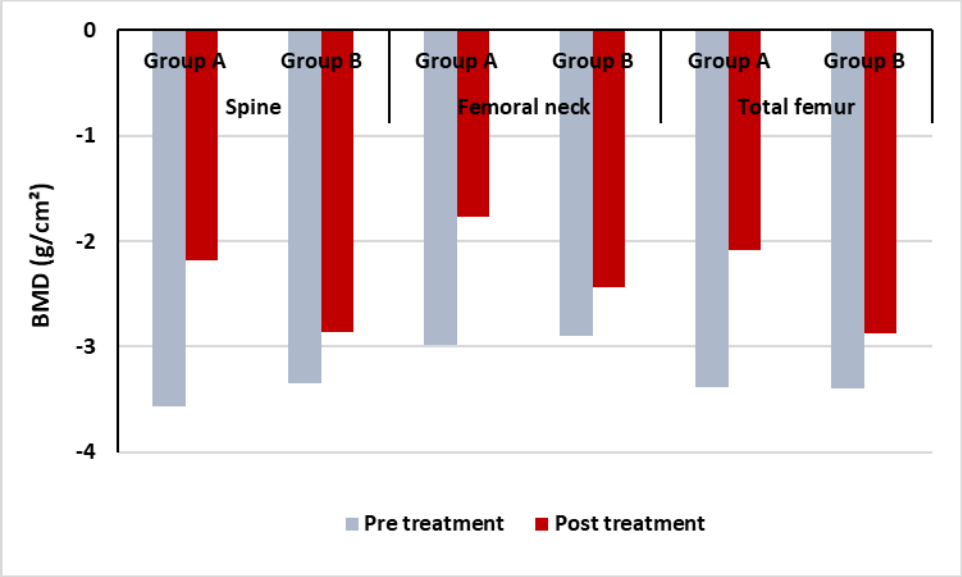

Figure (1): Mean BMD of spine, femoral neck and total femur pre and post treatment of the groups A and B

DISCUSSION

In the present study, effect of weight bearing exercises on osteoporosis in prostate cancer patients undergoing androgen deprivation therapy was investigated. Thirty PCa patients who had osteoporosis induced by ADT participated in this study, their ages were over 50 years old. They were selected from the Oncology Hospital Menoufia University and randomly distributed into two equal groups:

Group A (Study group): included 15 patients who received 30 minutes of weight bearing exercises through walking on treadmill, in addition to drug therapy (vitamin D supplements and calcium) 3 times / week for 3 months.

Group B (Control group): included 15 patients who only on drug therapy (vitamin D supplements and calcium).

Measurements were conducted before starting the treatment as a first record and at the third month of the treatment as final record.

ADT is a basic treatment for PCa patients which can prolong survival rate and reduce disease-related morbidity [(12)]. But, treatment-induced hypogonadism with multiple interconnected side effects such as reduction in bone mineral density (BMD) and a loss in the structure and strength of bone what's more an expanded hazard about falls what's more resulting fractures in this clinical population group [(4)]. Poor physical function (such as impairment in rising, walking, and balance tasks) is reliably connected with low BMD, bone loss and hip fractures. Men with PCa receiving ADT ought to subsequently a chance to be determinedly urged to maintain bone health, muscle strength and physical function through an active lifestyle [(13)]. Exercise has been proposed as a treatment to relieve adverse effects of ADT [(14)]. Weight bearing exercise is more adapted to improve bone mass than any other physical activity. They play a dual role in stressing the bones as they put both gravitational and muscular stress on bones [(5)].

The results of the present study showed that there was a significant increase in BMD of spine, femoral neck and total femur post treatment compared to that of pretreatment in groups A and B ($p < 0.001$). The percent of increase in BMD of spine, femoral neck and total femur in group A were 38.94, 40.6 and 38.46% respectively, while that in group B were 14.63, 15.86 and 15.29% for BMD of spine, femoral neck and total femur respectively. The finding of our study are supported by the finding of a study in Turkey, which used regular walks on a treadmill three times a week for three months at an intensity of 55-75% of maximal heart rate. Bone turnover rate was determined by measurements taken before the experiment, at one week, and again after the three-month program. The measurements determined levels of crosslinked C-terminal telopeptides of type 1 collagen and N-terminal pro-peptides of type 1 procollagen, both of which are biomarkers of bone formation [(15)].

The results of the present study agree with **Mauney *et al.*** [(16)] who stated that walking is weight bearing activity that has its impact on bone and bone marrow. Also, **Dimo *et al.*** [(5)] and **Iwamoto *et al.*** [(7)] found that weight bearing exercises in form of walking on treadmill at intensity of 80% of maximal heart rate was more adapted to improve bone mass than any other physical activity as it fortifies bone formation, what's more suppresses bone resorption, increase serum 1,25-dihydroxyvitamin D3 level and what's more declines the serum parathyroid hormone level leading to an increase in bone mass with incitement for longitudinal bone growth, particularly during weight-bearing sites.

Moreover, the results of the present study are consistent with works reported by **Douchi *et al.*** [17] and **Hind *et al.*** [18] that regular weight-bearing exercise sessions, two to three times weekly, over a period of at least 6 months recognized as a major and effective prophylaxis against osteoporosis. Firstly stimulate bone accretion during growth, secondly to stimulate bone accretion once bone loss has occurred and thirdly to prevent bone loss.

The study was limited to physical and psychological conditions of the patients that might affect the evaluation and treatment.

CONCLUSION

Within the limitations of this study, the following conclusion is warranted:

It can be concluded that weight bearing exercises had fruitful effects in cases of osteoporosis in prostate cancer patients undergoing androgen deprivation therapy as evidenced by the significant increase in BMD and T-score mean, so decrease risk of fractures and enhance physical performance.

Future studies and recommendations:

The results of this study indicated a need to consider the following recommendations:

Further researches are needed to study efficacy of weight bearing exercises on osteoporosis in prostate cancer patients undergoing androgen deprivation therapy.

Further researches should be conducted to determine the potential adverse effects of weight bearing exercises. Further researches are needed to study other physical therapy modalities and another osteoporosis type.

Greater sample number could be used to assure the results and for a longer period than 3 months

Further survey studies are needed to determine the prevalence of prostate cancer in Egypt and to detect its causes.

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