Impact of Mild versus Moderate Intensity Aerobic Walking Exercise Training on Markers of Bone Metabolism and Hand Grip Strength in Moderate Hemophilic A Patients.

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Abstract

Background: Patients with hemophilia A have low bone density than healthy controls. It is now widely recognized that physical activity and sports are beneficial for patients with hemophilia.

Objective: To compare the effects of mild and moderate intensity treadmill walking exercises on markers of bone metabolism and hand grip strength in male patients with moderate hemophilia A.

Material and Methods: Fifty male patients with moderate hemophilia, and age range from 25 to 45 years. The subjects were randomly assigned into 2 equal groups; the first group (A) received moderate intensity aerobic exercise training. The second group (B) received mild intensity aerobic exercise training.

Results: There was a 32.1% and 24.8% increase in mean values of serum calcium and hand grip strength respectively and 22.7 % reduction in mean values of parathyroid hormone in moderate exercise training group (A). While there was a 15.1 % and 15 % increase in mean values of Serum Calcium and Hand grip strength respectively and 10.3 % reduction in mean values of parathyroid hormone in mild exercise training group(B). The mean values of serum calcium and hand grip strength were significantly increased, while the mean values of parathyroid hormone were significantly decreased in both groups . There were significant differences between mean levels of the investigated parameters in group (A) and group (B) after treatment.

Conclusion: Moderate intensity aerobic exercise training on treadmill is appropriate to improve markers of bone metabolism and hand grip strength in male patients with hemophilia A.

Key Words: Aerobic exercise, bone metabolism, hand grip strength, hemophilia.

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Introduction

Haemophilia A is a hereditary X-chromosomal recessive disorder with an incidence of approximately 1:10,000 people caused by deficiency or absence of coagulation factors VIII (FVIII) in the blood. Depending on the concentration of FVIII or FIX coagulant activity in blood, the disorders may be classified as severe (<1% of normal activity), moderate (1–4%) or mild (5–25%) [1]. Patients with hemophilia often used to have a sedentary lifestyle, because of haemarthroses and subsequent synovitis and arthropathy [2].In haemophiliacs, the physical condition, muscular strength, aerobic resistance, anaerobic resistance and proprioception have all diminished. Muscle atrophy and instability, being more vulnerable to stressful motor demands, increase the risk of lesion and establish a vicious circle that is hard to break: pain, immobility, atrophy, articular instability and repeated bleeding episodes. In haemophilia, physical and/or sporting activities were not recommended until the seventies. Nowadays, the overall policy is to recommend certain physical activities to improve the patient's quality of life [3].

Patients with hemophilia are characterized by lower muscle strength and anaerobic power compared with age-matched controls. This may be related to their lower leisure-time activity. Low-physical activity is a risk factor for reduced bone mineral density in the haemophilics. This factor must be monitored to avoid a significant reduction in BMD that might contribute to further skeletal fragility and osteoporosis in later life [4-5].

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Adults with haemophilia have several predisposing factors for developing decreased bone mineral density (BMD) including prolonged periods of immobility, reduced weight bearing and co-morbidities associated with bone loss [6-7].

Fifty consecutive severe hemophilia patients aged between 20 and 50 years were evaluated for osteoporosis .Bone mass density values of lumbar spine and left hip of the patients were significantly lower than that of controls. The incidence of osteoporosis was significantly higher in hemophiliacs. Incidence of fractures in adult life was also significantly higher in hemophiliacs compared to controls [8].

Severe haemophilia and reduced bone density can negatively influence perception of patient's health-related quality of life (HRQoL), especially considering future aspects, which underscores the importance of early onset of adequate prophylactic treatment [9]. Physical activity has been considered as an important factor for bone density and as a factor facilitating prevention of osteoporosis [10].

As vigorous exercise have adverse effects, where both mild and moderate exercises were proved to have beneficial outcomes for hemophilic subjects, but the missed data in the body of knowledge and could considered a gap is to find an answer for the question: which is more better to apply moderate or mild exercises for hemophilic patients?. So the aim of this study was to compare the effects of mild and moderate intensity treadmill walking exercises on markers of bone metabolism and hand grip strength in patients with moderate hemophilia A.

Materials and Methods

Subjects

Fifty male patients with moderate hemophilia A (1%-5% of clotting factor activity) were selected from the Hematology Department at King Abdulaziz University Hospital and other Hospitals at Jeddah area. Inclusion criteria were age ranged from 25 to 45 years, the body mass index (BMI) ranged from 21 to 25 Kg/m^2 and participants received on-demand treatment. Participants who sustained a joint bleed in either the ankles or knees 2 weeks before testing were excluded. The subjects were included into 2 equal groups; the first group (A) received moderate intensity aerobic exercise training. The second group (B) received mild intensity aerobic exercise training. Informed consent was obtained from all participants.

Informed consent was obtained from all participants. This study was approved by the Scientific Research Ethical Committee, Faculty of Applied Medical Sciences at King Abdulaziz University. All participants were free to withdraw from the study at any time. If any adverse effects had occurred, the experiment will be terminated and the Human Subjects Review Board will be informed. However, no adverse effects occurred, and so the data of all the participants were available for analysis.

Methods

Equipment

1) Electronic treadmill (Zan 800; made in Germany) was used for application of the aerobic exercise training. The speed and the inclination of treadmill were controlled by pre-selected soft ware (Bruce standard protocol) and it also provided with control panel to display the exercise parameters.
2) Jamar hand dynamometer (Sammons Preston Rolyan, Cedarburg, WI, USA) was used for hand grip strength measurements which is an index for general fitness.

1. Evaluated parameters

A. Chemical analysis:

- Markers of bone metabolism: samples of venous blood were taken from fasted patients between 8-10 hours to be analyzed for markers of bone metabolism included serum calcium and parathyroid hormone

B. Hand Grip Strength:

Grip strength of the dominant hand was measured using three successive repetitions with a Jamar hand dynamometer (Sammons Preston Rolyan, Cedarburg, WI, USA). The elbow was flexed at a 90° angle and not allowed to contact any body part. Resting time between subsequent measurements was 30 s. The mean value of the two best performances was used in the analyses. The intraclass correlation coefficient (ICC) of the grip strength measurements has been shown to be 0.87 for absolute grip strength values.

All measurements were taken before the starting of the study (pre-test) and after three months at the end of the study (post-test).

2. The aerobic exercise training program

The aerobic treadmill-based training program (Track master 400E, gas fitness system, England) was at 65 %

to 75 % of the maximum heart rate (HRmax) achieved in a reference ST performed according to a modified Bruce protocol for group (A) who received moderate intensity aerobic exercise training, where group (B) received mild intensity aerobic exercise training at 50 % to 60 % of the maximum heart rate (HRmax). This rate was defined as the training heart rate (THR).After an initial, 5-minute warm-up phase performed on the treadmill at a low load, each endurance training session lasted 30 minutes and ended with 5-minute recovery and relaxation phase. All patients performed three sessions / week (i.e. a total of 36 sessions per patient over a 3-month period).

Statistical analysis

The mean values of the investigated parameters obtained before and after training program in both groups were compared using paired "t" test. Independent "t" test was used for comparison between the two groups ($P<0.05$). Pearson's product moment correlation coefficients (r) were applied to examine the degree of correlation between changes in hand grip strength, parathyroid hormone and calcium.

Results

The two groups were considered homogeneous regarding the baseline descriptive characteristics (Table 1).

Table (1). Comparison of baseline characteristics between patients on mild and moderate exercise.

Variable	Mean ± SD		p value
	Moderate exercise Group (A)	Mild Exercise Group (B)	
Age (year)	38.14± 8.32	37.97± 9.15	P>0.05
Weight (Kg)	67.46 ± 8.51	69.16± 7.83	P>0.05
Height (cm)	167.83± 7.11	169.15 ± 6.52	P>0.05
RBC (million/uL)	4.23 ± 1.61	4.18 ± 1.86	P>0.05
WBCs(thousands/m3)	13.76 ± 2.94	13.83 ± 3.15	P>0.05
Plt counts109/L	386.7 ± 5.25	395.4 ± 5.67	P>0.05
Bleeding time(min)	8.41 ± 1.6	8.62 ± 1.8	P>0.05
Serum Calcium (ng/dl)	8.26 ±1.47	8.14 ±1.52	P>0.05
Parathyroid Hormone (ng/dl)	14.91 ± 2.85	14.63 ± 2.97	P>0.05
Hand grip strength (mmHg)	138.45 + 8.61	134.98 + 7.96	P>0.05

RBC = Red blood cells WBCs = White blood cells Plt = Platelets

There was a 32.1% and 24.8% increase in mean values of Serum Calcium and Hand grip strengthrespectively and 22.7 % reduction in mean values of parathyroid hormone in moderate exercise training group (A). While, There was a 15.1 % and 15 % increase in mean values of Serum Calcium and Hand grip strength respectively and 10.3 % reduction in mean values of parathyroid hormone in mild exercise training group(B). The mean values of Serum Calcium and Hand grip strength were significantly increased, while the mean values of parathyroid hormone were significantly decreased in both groups (Table 2 &3).

Table (2): comparison of changes in markers of bone metabolism in patients on moderate exercise before and after training.

	Mean ±SD		T-value	Significance
	Before	After		
Serum Calcium (ng/dl)	8.26 ±1.47	10.91 ± 1.36	6.52	P <0.001
Parathyroid Hormone (ng/dl)	14.91 ± 2.85	11.52 ± 2.61	6.61	P <0.001
Hand grip strength (mmHg)	138.45 + 8.61	172.74 + 7.78	8.93	P <0.001

Table (3): Comparison of changes in markers of bone metabolism in patients on mild exercise before and after training.

	Mean ±SD		T-value	Significance
	Before	After		
Serum Calcium (ng/dl)	8.14 ±1.52	9.37 ± 1.42	3.41	P <0.001
Parathyroid Hormone (ng/dl)	14.63 ± 2.97	13.12 ± 2.75	3.62	P <0.001
Hand grip strength (mmHg)	134.98 + 7.96	155.24 + 7.18	5.25	P <0.001

Also, there were significant differences between mean levels of the investigated parameters in group (A) and group (B) after treatment (Table 4).

Table (4): Comparison of changes in markers of bone metabolism in patients on moderate and mild exercise after training.

	Mean ±SD		T-value	Significance
	Moderate exercise Group (A)	Mild Exercise Group (B)		
Serum Calcium (ng/dl)	10.91 ± 1.36	9.37 ± 1.42	3.34	P <0.001
Parathyroid Hormone (ng/dl)	11.52 ± 2.61	13.12 ± 2.75	3.16	P <0.001
Hand grip strength (mmHg)	172.74 + 7.78	155.24 + 7.18	4.35	P <0.001

The Pearson's correlation coefficients test for the relationship between the hand grip strength and parathyroid hormone in both groups showed a strong direct relationship of 0.87 and 0.85.
There was an inverse direct relationship between the hand grip strength and serum calcium in both groups, that is 0.85 in group A and 0.83 in group B

Discussion

In recent decades, quality of life and life expectancy of individuals with haemophilia have been improved by better quality in treatment and more availability of blood coagulation products. Recently, new concerns have been directed to the reduced bone density (RBD). RBD in bleeding disorders is becoming an escalating burden worldwide due to an increased in life expectancy. Also, haemophilics have lower levels of fitness and strength than their healthy peers. The physical therapist, along with the haemophilia care team, can assist in preparing an individual to begin or progress to a physical activity program that enhances fitness level, body composition and overall well-being, so this study aimed to compare the effects of mild and moderate intensity treadmill walking exercises on markers of bone metabolism and hand grip strength in male patients with moderate hemophilia A.

Moreover results of the present study concerning the mean values of serum calcium were significantly increased, while the mean values of parathyroid hormone were significantly decreased in group (A) and group (B). Also, there were significant differences between mean levels of the investigated parameters in group (A) and group (B) after treatment. These results agreed with Bradney etal. and Welton etal. Who reported that weight-bearing exercise is critical to ensure adequate bone mass accrual in childhood and may be even more important than dietary calcium intake [11-12].

However, Lanyon etal., said that the exact mechanism by which weight loading increases bone mass is not known but is likely related to dynamic strains in bone tissue regulating bone formation and resorption.6 Unusually high strains and high strain rates are particularly osteogenic [13]. Also, Lester etal. , conducted a previous study to determine whether aerobic, resistance, or combined aerobic and resistance exercise programs conducted over eight weeks and compared to a control group could produce changes in biochemical markers of bone turnover indicative of bone formation. Biomarkers of bone formation were increased in the

resistance and combined groups, while biomarkers of bone resorption were decreased and increased, respectively, after training in all groups. Small changes in BMD were observed in the distal tibia in the Aerobic and Combined groups, respectively. The results of the present study demonstrate that participation in an eight week physical training program that incorporates a resistance component by previously inactive young women results in alterations in biomarkers of bone remodeling indicative of increased formation without substantial alterations in markers of resorption [14].

Finally results of the present study concerning the mean values of hand grip strength were significantly increased in group (A) and group (B). Also, there were significant differences between mean levels of the investigated parameters in group (A) and group (B) after treatment. These results approved by Hilberg et al. documented improvements in isometric leg strength and proprioception in adults with severe haemophilia following
a physical training program, but this study had small numbers and was not randomized and therefore give limited information about the effect of exercise on muscle performance [15]. Also, Marin etal., stated that Body weight was strongly and positively related to BMD in all sites, but the most important component of body composition was lean mass, also significantly related to all BMD sites, whereas fat mass
was weakly related to the femoral neck BMD. The handgrip strength was most importantly related to lumbar spine, femoral neck, and total body BMD [16]. A major limitation of this study is the lack of female patients who suffer from hemophilia that is why we involve only male patients. Finally, our sample size may have been too small to detect significant changes in all variables.

Conclusion

Moderate intensity aerobic exercise training on treadmill is appropriate to improve markers of bone metabolism and hand grip strength in male adult patients with hemophilia.

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