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Effect of Aerobic Exercise on Uric Acid in Hyperuricemic Elderly

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Abstract: Background: It is generally believed that elevated serum uric acid is more common in elderly patients. There are many serious complications are associated with increased serum uric acid such as gout, metabolic syndrome, renal calculi and cardiovascular problems. **Purpose:** The aim of this study is to determine the effect of aerobic exercise on uric acid in hyperuricemicelderly. **Subjects and Methods:** thirty elderly patients, have elevated serum uric acid levels were selected randomly from Outpatient clinic of Department of physiotherapy and Rehabilitation in Al-Ahrar Teaching Hospital, Zagazig, their ages ranged from 65 to 75 years old and their body mass index (BMI) didn't exceed 30kg/m^2. The participants were assigned into two groups of equal number. **Group (A)** (15 males patients) and **group (B)** (15 females patients) treated by aerobic exercise 3 sessions per week for 8 weeks. All subjects in both groups were assessed through serum uric acid level test, visual analogue scale (VAS) to measure pain intensity and rated perceived exertion (RPE) before and after treatment. **Results:** It was revealed intensily that there was a statistically significant reducing serum uric acid level, pain level and increasing inrated perceived exertion in both group (A) and group (B) post treatment. **Conclusion:** The effect of aerobic exercise was effective in reducing serum uric acid level and pain intensity and increasing level of rate of perceived exertion in hyperuricemicelderly.

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1. Introduction

The world population is ageing rapidly. Since 1980, the number of people aged 60 years and over has doubled to approximately 810 million. The elderly population will continue to grow to approximately 2 billion in 2050. It has been predicted that 22% of the total population will be older than 60 years and around 5% will be older than 80 years in 2050. **(Louie GH and Ward M et al., 2010)**

Most studies among elderly people thus far have classified elderly adults into one group. Although there are different ways to classify this population, some studies have classified elderly adults between the ages of 65 and 74 years as youngest-old, those between ages 75 and 84 years as middle-old, and those aged over 85 years as oldest-old. **(Alterovitz and Mendelsohn GA et. al 2013)**

With age, the correlation between dual energy X-ray absorptiometry measures of muscle mass and strength weakens, and considerable decline in strength may occur in the absence of any detectable decline in mass although correlations may remain more stable if MRI-derived muscle mass is used. Aging is also associated with progressive reduction of biomechanical muscle quality, which is usually operationalized as the ratio between strength and mass. Low muscle strength (but less consistently low muscle mass), as well as excessive and long-term adiposity, are risk factors for age-related mobility loss. **(Moore AZ, Caturegli G, Metter EJ, et al.,2014).**

Hyperuricemia is an abnormally high level of uric acid in the blood. In the pH conditions of body fluid, uric acid exists largely as urate, the ion form. The amount of urate in the body depends on the balance between the amount of purines eaten in food, the amount of urate synthesized within the body (e.g., through cell turnover), and the amount of urate that is excreted in urine or through the gastrointestinal tract **(Al-Ashkar and Feyrouz, 2014).**

High plasma uric acid (UA) is a prerequisite for gout and is also associated with the metabolic syndrome and risk factors for cardiovascular diseases **(Kim et al., 2009).**

Population studies have reported the incidence of hyperuricemia in much of the developed world may be as high as 15-20% **(Mikuls et al., 2005).** And prevalence increases with age, in both sexes **(Doherty, 2009).**

Some studies have examined selected reproductive factors and its influence on gout prevalence. old age was shown to be a risk factor for gout **(Singh et al., 2011).**

Many factors contribute to hyperuricemia, including genetics, insulin resistance, iron overload, hypertension, hypothyroidism, hyperthyroidism, renal insufficiency, obesity, diet, use of diuretics (e.g. thiazides, loop diuretics), and consumption of excess alcoholic beverages. Of these, alcohol consumption is the most important **(Sam et al., 2010).**

Reproductive events which occur over the life-span of women are expected to influence hormonal levels, especially estrogen levels. Estrogens have an impact on the renal tubular handling of uric acid and therefore are possibly explaining the underlying relation between some reproductive parameters and uric acid levels, suggesting that premenopausal levels of estrogen in women cause a greater renal clearance of uric acid **(Sumino et al., 2012).**

About 20-25% of asymptomatic patients with raised serum uric acid exhibit monosodium urate crystal deposits in their joints – especially the knees and the first MTP joint) and yet do not suffer from attacks of gout – suggesting that other factors must be at play **(Pineda et al., 2011).**

It was demonstrated that, about 81% of the patients with hyperuricemia presented with pain in the knee and metatarsophalangeal joints **(Neugebauer et al., 2009).**

As a marker of atherosclerotic diseases, it has been demonstrated that the serum uric acid level is associated with cardiovascular risk factors and subclinical atherosclerosis, such as hypertension, metabolic syndrome, kidney disease, coronary artery calcification and carotid atherosclerosis **(Coutinho et al., 2013).**

There were significant benefits of the exercise regimen such as improved exercise tolerance as judged by falling rated perceived exertion (RPE) scores for the same achieved exercise and broad improvements in the quality of life and health. The quality of life improvements is of interest in view of evidence that the psychological benefits of exercise may be an important contributor to the accompanying physical improvements in health **(Kosmadakis et al., 2011).**

Moreover, aerobic exercise improved arterial stiffness, an effect that had reversed by 1 month after training had ceased. This reduced arterial stiffness may also explain the improved glomerular filtration rate after aerobic exercise in our patients **(Mustata et al., 2010).**

Long-term aerobic exercise has been associated with better arterial compliance, and antidiabetic and anti-inflammatory benefits. It was hypothesized that in patients with diabetes and chronic kidney disease, better aerobic capacity is associated with less inflammatory state and arterial stiffness **(Lesniewski et al., 2011).**

2. Subjects

This study was carried out on thirty elderly patients, have elevated serum uric acid levels were selected randomly from Outpatient clinic of Department of physiotherapy and Rehabilitation in Al-Ahrar teaching Hospital. This study was conducted from August 2019to December 2019.

Inclusion criteria:

1- Elderly patients had elevated uric acid levels.
The female uric acid levels ≥6.0 mg/dL.
The male uric acid levels ≥7.0 mg/dL.
2- Their age ranged from 65-75 years old.
3- All patients suffered from musculoskeletal pain only without swelling or redness especially in small joints.
4- BMI was less than 30 kg/m2.

Exclusion criteria:

1- All patients suffered from unstable medical conditions as uncontrolled diabetes mellitus and malignant hypertension.
2- Patients on specific hormonal medications.
3- Patients who had history of kidney disease such as chronic kidney disease or microalbuminuria.
4- All the patient with unstable cardiac and chest diseases.
5- Uncooperative patients or patients unable to perform exercise regularly.

Design of the study:

1- Group A: (males group)

This group consisted of fifteen male patients with hyperuricemia. They received aerobic exercise in the form of walking on a treadmill 3times/week and each session lasted for 45 minutes for 8 weeks.

2- Group B: (females group)

This group consisted of fifteen female patients with hyperuricemia. They received aerobic exercise in the form of walking on a treadmill 3times/week and each session lasted for 45 minutes with for 8 weeks.

Methods

A) Evaluation methods:

1. Serum uric acid level: a sample of blood was used to assess the level of uric acid in the blood for both groups A & B before and after treatment.

2. Weight and height scale: a universal height and weight scale will be used to determine the subjects' height and weight to calculate the body mass index for all participants before the study for the two groups.

3. Visual analogue scale: will be used to measure the level of pain for both groups A & B before and after treatment.

4. Rated Perceived Exertion (RPE): will be used to measure the level of exertional effort for both groups A & B before and after treatment.

B) Treatment methods:

1-Aerobic exercise:

Moderate aerobic exercise was applied once daily three times / week for 45 minutes for all patients participated in both groups (A and B) in the form of walking on a treadmill. Before starting aerobic exercise, every patient was instructed briefly and clearly about the nature of exercise and its effect in order to gain their confidence and cooperation of all through the period of this study (8 weeks).

Exercise session for the study group consisted of:

Warm-up phase:

The patient started the exercise session with warm-up exercise at a speed of 1 km/h for 5min to allow for conditioning of the body for the exercise.

Training phase:

The patient walked at the level of speed obtained at warm-up phase and, after that the speed was increased in increments of 1.0 km/h every 2min until the participant reached level 75% of max heart rate for 30–35min.

Cooling down phase:

Afterward, the speed was decreased to 1 km/h and the session was terminated with cooling down for 5min as warming up.

Statistical analysis

Descriptive statistics and unpaired t-test were conducted for comparison of subject characteristics between both groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levene's test for homogeneity of variances was conducted to ensure the homogeneity between groups. Paired t test was conducted for comparison between pre and post treatment mean serum uric acid, VAS and RPE in each group. Unpaired t test was conducted for comparison of percent of improvement of serum uric acid, VAS and RPE between males and females. The level of significance for all statistical tests was set at $p < 0.05$. All statistical analysis was conducted through the statistical package for social studies (SPSS) version 22 for windows (IBM SPSS, Chicago, IL, USA).

3. Results

- Subject characteristics:

Table (1) showed the subjects' characteristics of males and females. There was no significant difference between both groups in age, weight, height and BMI ($p > 0.05$).

Table (1). Comparison of subject characteristics between group A and B.

	Males Mean ± SD	Females Mean ± SD	t-value	p-value
Age (years)	66.6 ± 2.8	65.53 ± 3.62	0.9	0.37
Weight (kg)	75.33 ± 7.23	74.46 ± 5.56	0.36	0.71
Height (cm)	167.73 ± 6.01	166.26 ± 5.61	0.69	0.49
BMI (kg/m²)	26.8 ± 2.5	27.04 ± 3	-0.25	0.8

SD, Standard deviation; p value, Probability value

Effect of treatment on serum uric acid, VAS and RPE:

- Within group comparison:

There was a significant decrease in serum uric acid and VAS post treatment in males and females compared with that pretreatment ($p > 0.001$). Also, there was a significant increase in RPE post treatment in males and females compared with that pretreatment ($p > 0.001$). (Table 2).

- Between groups comparison in percent of improvement:

There was a significant increase in the percent of improvement of serum uric acid and VAS of males compared with that of females ($p > 0.001$). There was no significant difference in the percent of improvement of RPE between males and females ($p = 0.21$). (Table 3, figure 1).

Table (2). Mean serum uric acid, VAS and RPE pre and post treatment in males and females:

	Pre	Post			
	Mean ± SD	**Mean ± SD**	**MD**	**t- value**	**p value**
Serum uric acid (mg/dl)					
Males	7.5 ± 0.3	5.36 ± 0.42	2.14	19.05	0.001
Females	6.5 ± 0.21	5.12 ± 0.28	1.38	21.85	0.001
VAS					
Males	8.06 ± 0.7	3.86 ± 0.63	4.2	29.01	0.001
Females	8.13 ± 0.64	4.66 ± 0.61	3.47	16.1	0.001
RPE					
Males	11 ± 1.46	16.4 ± 1.18	-5.4	-19.81	0.001
Females	9.66 ± 1.3	13.93 ± 1.43	-4.27	-23.48	0.001

SD, Standard deviation; MD, Mean difference; p value, Probability value

Table (3). Comparison of the percent of improvement of serum uric acid, VAS and RPE between males and females.

% of improvement	**Males**	**Females**	**MD**	**t- value**	**p value**
	Mean ± SD	**Mean ± SD**			
Serum uric acid	28.43 ± 5.35	21.12 ± 3.61	7.31	4.38	0.001
VAS	52.16 ± 6.08	42.32 ± 8.58	9.84	3.62	0.001
RPE	50.6 ± 14.31	44.93 ± 9.64	5.67	1.27	0.21

SD, Standard deviation; MD, Mean difference; p value, Probability value

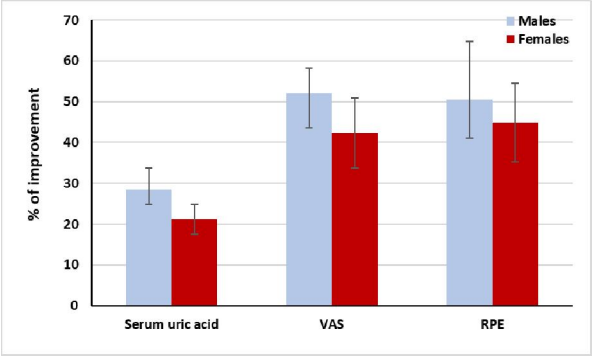

Figure (1): Mean serum uric acid, VAS and RPE pre and post treatment of the group A and B:

4. Discussion

The aim of this study was to evaluate the effect of aerobic exercise on uric acid inhyperuricemic elderly. Thirty elderly patients, have elevated serum uric acid levels were selected randomly from Outpatient clinic of Department of physiotherapy and Rehabilitation in Al-Ahrar Teaching Hospital, Zagazig, their ages ranged from 65 to 75 years old and their body mass index (BMI) didn't exceed 30kg/m2. The participants were assigned into two groups of equal number. **Group (A)** (15 males patients) and **group (B)** (15 females patients) treated by aerobic exercise 3 sessions per week for 8 weeks. All subjects in both groups were assessed through serum uric acid level test**,** visual analogue scale (VAS) to measure pain intensity treatment and rated perceived exertion (RPE) to measure the level of exertional effort before and after. Serum uric acid level through a sample of blood was used to assess the level of uric acid in the blood and visual analogue scale was used to measure the level of pain for both groups A & B before and after treatment.

The result of the present study revealed that there was a significant improvement in serum uric acid, visual analogue scale and rated perceived exertionin post treatment in compare with pretreatment in both groups (A and B). and there was a significant improvement at percent of improvement at serum uric acid and visual analogue scale in group A in compared with improvement of group B, these results were approved by **Casas et al., 2014** through study conducted to test blood purines which stated that when doing physical exercises (especially the long term aerobic physical training), ATP turnover is accelerated which thereby reduces uric acid production ideally.

Our results are supported by **Banfi et al., 2012** who found that physical exercise is known to induce metabolic changes intensifying catabolic processes. Thus, the uric acid concentration is one of the most important biochemical parameters indicating changes in purine nucleotides distribution.

Our results are in agreement with **Meyer and Meister, 2011**who stated that aerobic exercise affected the UA plasma concentration in female football players. It decreased significantly after the exercise post-exercise as well as during recovery in comparison to the measurements pre exercise in this studied group. A significant decrease in the uric acid level in female football players during the entire training season was also found by Meyer and Meister.

Data in this report of **Hedrington and Davis, 2015**also suggested that exercise may help controlling uric acid and serum lipids and alleviating gastroesophageal reflux. A large number of reports also confirm that exercise may help to control hypoglycemia and hyperlipidemia.

The results also in agreement with **Aucella et al., 2015** who stated that exercise is beneficial in ameliorating cardiovascular risk factors such as hypertension, dyslipidemia, hyperglycemia, hyperuricemia, obesity, inflammation, and oxidative stress. Moreover, it has been reported that inactivity is associated with the development of major chronic kidney disease precursors, including albuminuria, reduced glomerular filtration rate, and initiates diabetes.

Jackson AS and Sttanfforth PR et al., 2002 reported that for the same body mass index (BMI), women typically present with ~10% higher body fat compared to men. Aging increases adiposity in both sexes, but again, women are characterized by higher percent body fat throughout the entire life span.

At 2010 Dillon EL reported that for men, decreasing levels of testosterone over time can lead to a decrease in lean muscle mass and muscle strength, which may have roles in decreased physical activity, higher fall risk, depression, and other medical problems such as obesity and its role in the development of type II diabetes. With testosterone supplementation, however, it is possible to slow or even reverse this trend. Similarly, in women, lower levels of estrogen lead to decreased muscle mass and increasingly fragile bones, which can contribute to decreased activity levels and can be reversed with hormone replacement therapy.

Also Giannoulis MG, Martin FC et al.,2012 confirmed that estrogen may play a significant role in stimulating muscle repair and regenerative processes, including the activation and proliferation of satellite cells. The pathways by which hormones regulate muscle protein metabolism are complex and multifactorial.

Lovejoy JC, Champagn et al.,2008 reported that menopause is followed by redistribution of adipose tissue towards a more central/android phenotype. Importantly, it is visceral adiposity that rises in women during the peri-menopausal transition, presumably due to the fall in estrogen levels. As testosterone declines with age, visceral adiposity also increases in men.

Conclusion

Aerobic exercise was effective in reducing serum uric acid level pain intensity and increasing rated perceived exertion in hyperuricemicelderly so it is recommended to use aerobic exercise at treatment of hyperuricemic elderly.

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