

Response of testosterone and semen parameters to a 14-week aerobic training in sedentary obese men with hyperglycaemia

DOI: <https://doi.org/10.5114/pq.2023.123525>

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Abstract

Introduction. Obesity, sedentarism, and insulin resistance are strongly associated with increased deoxyribonucleic acid fragmentation index (DFI) of sperms, reduced total testosterone (TT), and low semen quality, which can be prevented by lifestyle modification. This study aimed to investigate the effect of 14-week moderate-intensity aerobic exercise on serum TT, semen parameters, and DFI in centrally obese men with hyperglycaemia.

Methods. Overall, 40 men aged 26–39 years with waist circumference (WC) > 102 cm, body mass index (BMI) limited from 30 to 34.9 kg/m², and fasting blood glucose (FBG) levels of 100–125 mg/dl were assigned to the study and control groups. The study group ($n = 20$) received supervised 14-week moderate-intensity aerobic exercise on a treadmill for 40 minutes, 3 times weekly, in addition to 1-hour home walking (on the alternative days of aerobic exercise), while the control group ($n = 20$) received general advice on increasing physical activity.

Results. In the study group, exercise significantly improved BMI, WC, FBG, serum TT, sperm DFI, and semen parameters, including motility (progressive and static) and morphology ($p < 0.05$), while the volume and count of semen showed no significant difference. The control group presented no significant changes.

Conclusions. The deteriorating effect of central adiposity, hyperglycaemia, and sedentarism on semen quality and nuclear damage of sperms (assessed by DFI) is prevented or counteracted by increased exercise-induced TT production, resulting from decreased BMI, FBG, and WC.

Key words: aerobic exercise, testosterone, semen quality, DNA fragmentation index, hyperglycaemia, central obesity

Introduction

Obesity is a chronic epidemic disease associated with abnormal excessive fatty accumulation that produces many negative health consequences [1]. Insulin resistance (IR), diabetes mellitus (DM), and metabolic syndrome (MetS) may be developed from obesity, low physical activity, and the elevated rate of visceral fat accumulation that increases free fatty acids (FFA) release into the portal circulation [2].

In addition to the estimated 60–70% of overweight and/or obese population aged 15–60 years in the 2015 Egyptian health survey, the anticipated number of Egyptian patients with DM will be 16.7 million by the year of 2045 [3].

Men's reproductive health is negatively affected by a body mass index (BMI) over 30 kg/m² [4], the elevated production of oestrogen instead of total testosterone (TT), increased temperature of scrotum, damaged chromatin integrity of sperms, and impaired semen parameters (volume, count, morphology, and motility) [5, 6].

The decline of the molecular composition of semen with raised BMI may be explained by the increased deoxyribonucleic acid (DNA) fragmentation of sperms since MetS deteriorates the mitochondrial function, plasma membrane, and DNA of spermatozoa through the MetS-induced elevated production of systemic inflammatory cytokines, reactive oxygen species, and oxidative stress in addition to the decreased synthesis of seminal antioxidative enzymes [7].

DNA fragmentation index (DFI) is the percentage of sperm with nuclear DNA double or single strand breaks. A DFI value

of $\geq 30\%$ is considered not suitable for fertility in men [6]. Hyperglycaemia induces high DFI values, perhaps owing to the extensive production of spermatozoa with severe structural deformations [8].

Normal TT levels are strongly associated with increased insulin sensitivity, low IR, and maintained normal blood glucose levels. Hence, a low TT level is the main risk factor for DM development. Besides hyperglycaemia, low TT declines spermatogenesis and/or semen quality in sedentary men (TT is involved in the synthesis of sperms from the testicular cells) [9].

Even in men with normozoospermia (semen with normal parameters), future attention must be directed toward weight control measures – especially in those with abdominal obesity [10]. Preventive glycaemic control measures must be considered in patients with hyperglycaemia to decrease the risk of poor semen quality [8]. To enhance the sperm function and quality in obese men, exercise and/or diet are the most available therapeutic interventions with low costs [11].

Physically active men with decreased television-watching exposure time revealed higher spermatozoa parameters (motility and morphology) than sedentary ones [12]. As a result of the low attention paid to the impact of training on semen quality and the process of spermatogenesis [13], especially in men with hyperglycaemia and central obesity, this study aimed to investigate the effect of 14-week supervised aerobic exercise on sperm DFI, serum TT, and semen parameters in men with hyperglycaemia and central obesity (waist circumference [WC] > 102 cm).

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Received: 30.08.2020

Accepted: 29.12.2020

Citation: Ismail AMA, Abdelghany AI, Atef H. Response of testosterone and semen parameters to a 14-week aerobic training in sedentary obese men with hyperglycaemia. *Physiother Quart.* 2023;31(1):28–33; doi: <https://doi.org/10.5114/pq.2023.123525>.

Subjects and methods

Subjects

A total of 40 sedentary obese men aged 26–39 years, with BMI limited to 30–34.9 kg/m², fasting blood glucose (FBG) levels of 100–125 mg/dl, and WC > 102 cm were involved in this study. Semen assessment assumed the cut-off values of the World Health Organization of 2010 (semen volume: 1.5 ml, concentration: 15 million/ml, total motility: 40%, normal morphology: 4%) [14].

Men were excluded by an andrology physician if they presented with prostatitis, varicocele and/or a procedure of varicocele removal, previous surgery in the scrotal or groin areas, systemic diseases, infectious genital diseases, congenital testicular maldescent or absence, erectile dysfunction, leukocytospermia, previous administration of drugs (antioxidant/fertility supplements, male contraceptives, any drugs that might affect the fertility of men, and anabolic drugs), low testosterone levels (below 2.8 ng/ml), participation in any physical activity program in the previous 6 months, orthopaedic lower limb problem that hindered the completion of the designed training program; smokers and alcoholics were also excluded.

Randomization

With the aid of randomized blocks generated by a computer, the individuals were blinded to the methodology and treatment protocol of this study and randomly assigned to the study group or the control group (Figure 1).

Intervention

The study group (20 patients) received a 14-week supervised aerobic walking program on an electronic treadmill (Sprint Sports, AC, made in China), 3 times per week (day after day), in addition to a 1-hour home walking program out of the exercise program (home walking was conducted on the alternative days of the treadmill walking). Under the supervision of a qualified physical therapist, each treadmill session involved a 5-minute warm-up phase (in the form of treadmill walking at an intensity of 40% of maximum heart rate [HRmax]), 30-minute continuous moderate-intensity treadmill walking (at an intensity of 50–70% of HRmax), and a 5-minute cooling-down (intensity as in the warm-up phase). The control group (20 patients) received only general advice on maintaining increased physical activity.

Outcome measures

On the day previous to the first exercise session, BMI, FBG, and WC were assessed. An inelastic tape was used to measure WC at the midpoint between the lower rib and iliac crest. Semen samples were collected by masturbation to be subjected to computer-assisted semen analysis. The investigated semen parameters were volume, count, morphology, and motility (static and progressive).

Sperm chromatin dispersion test kits were used to assess sperm DFI. Serum TT was evaluated. All measurements were repeated after the trial end in all patients of both groups.

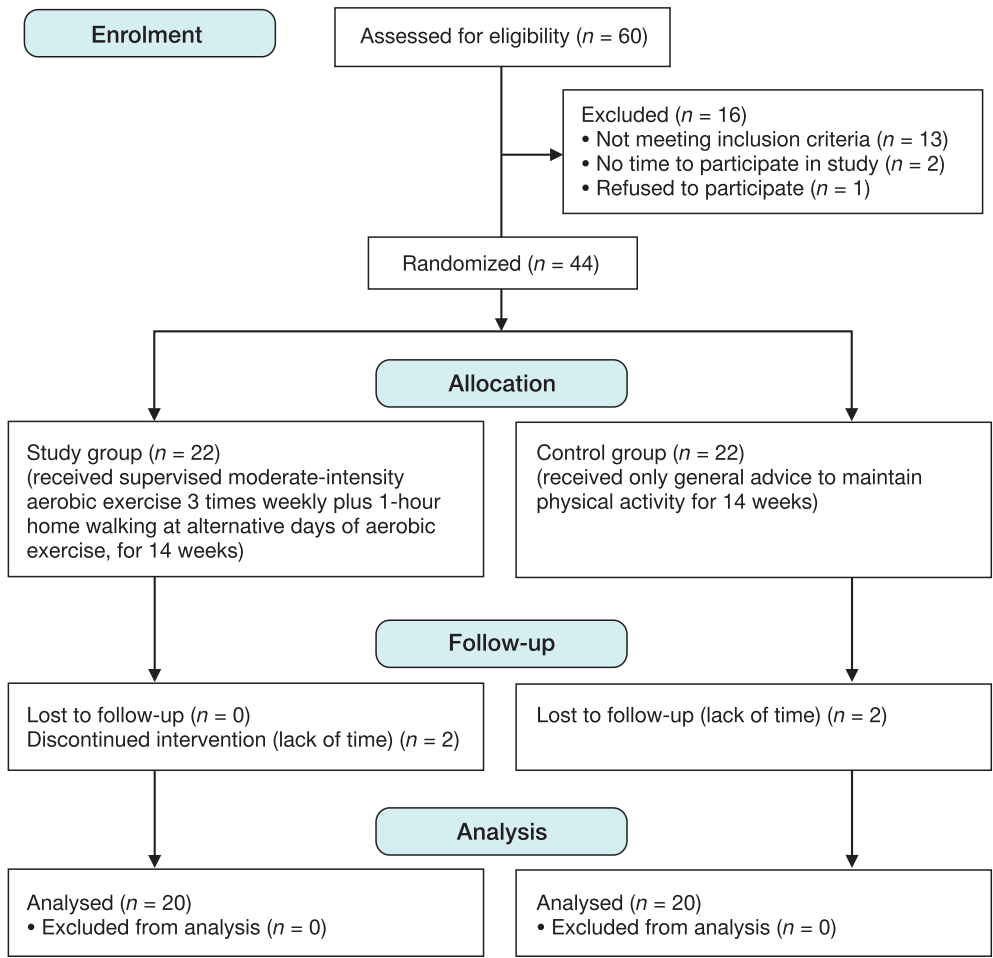


Figure 1. CONSORT flow diagram of the study

Statistical analysis

All outcome measures were exposed to a normality test (Shapiro-Wilk test) by using the SPSS software, version 23 (IBM Corp., New York, USA). The outcomes were BMI, WC, FBG, abstinence duration, TT, and semen parameters (volume, count, static motility, progressive motility, morphology, DFI). All outcomes were normally distributed so all variables were analysed with parametric tests. The baseline characteristic of patients (age, BMI, WC, abstinence) were analysed by an unpaired *t*-test. Mixed model multivariate analysis of variance (MANOVA) was used to detect the difference in time and treatments between the groups at outcome measures. The level of significance was set at 0.05. A level of *p* < 0.05 was applied to assess the significance.

The sample size was estimated by using version 3.1.9.2 of the G*Power software (Franz Faul, Universität Kiel, Germany). The *t*-test type I error rate was set at 5% (alpha-level of 0.05), and a 0.89 effect size of the main key parameter (TT) resulted from a pilot study conducted in 10 men; type II error rate was at 85% power. The proper sample size for this study was 38 men.

Ethical approval

The research related to human use has complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the Institutional Review Board of Faculty of Physical Therapy, Cairo University (approval No.: P.T.REC/012/002899).

Informed consent

Informed consent has been obtained from all individuals included in this study.

Results

Regarding the baseline characteristics, the unpaired *t*-test presented no significant difference between the 2 groups in age, BMI, WC, or abstinence (*p* > 0.05), as shown in Table 1.

In the study group analysis, multiple pairwise comparisons revealed that there was a significant difference between pre- and post-treatment BMI, WC, FBG, TT (Table 2), and all semen parameters except for volume and count of semen (Table 3). In the control group analysis, there was no significant difference between pre- and post-treatment values of any outcome measure (Tables 2, 3).

According to data analysis, there were outcome improvements in both groups but a superiority of the experimental group was observed (Tables 2, 3).

Wilks' lambda test within mixed MANOVA reported a significant effect of time (*p* = 0.0001 and *f* = 19.10). Also, there

Table 1. Baseline characteristics of the study and control groups

Characteristics	Study group (mean ± SD)	Control group (mean ± SD)	<i>T</i>	<i>p</i>	Sig.
Age (years)	33.60 ± 4.14	34.05 ± 4	−0.35	0.73	NS
BMI (kg/m²)	32.55 ± 1.75	32.84 ± 1.37	−0.56	0.57	NS
WC (cm)	110.80 ± 8.35	111.40 ± 5.99	−0.26	0.79	NS
Abstinence (days)	3.85 ± 1.56	3.95 ± 1.56	−0.19	0.84	NS

Sig. – significance, NS – non-significant, BMI – body mass index, WC – waist circumference

Table 2. Within- and between-group analysis of BMI, WC, FBG, and TT

Variables	Study group (mean ± SD)	Control group (mean ± SD)	<i>p</i>
BMI (kg/m²)			
Pre-treatment	32.55 ± 1.74	32.84 ± 1.37	0.57 ^a
Post-treatment	30.99 ± 1.95	33.03 ± 1.18	0.001 ^b
Within-group <i>p</i>	0.0001 ^b	0.19 ^a	
% of improvement	4.8	0.57	
WC (cm)			
Pre-treatment	110.80 ± 8.35	111.40 ± 5.99	0.79 ^a
Post-treatment	107.80 ± 7.87	112.70 ± 6.10	0.03 ^b
Within-group <i>p</i>	0.0001 ^b	0.08 ^a	
% of improvement	2.7	1.16	
FBG (mg/dl)			
Pre-treatment	109.90 ± 7.36	110.65 ± 7.52	0.75 ^a
Post-treatment	105.15 ± 5.98	111.30 ± 7.96	0.009 ^b
Within-group <i>p</i>	0.0001 ^b	0.32 ^a	
% of improvement	4.3	0.58	
TT (ng/ml)			
Pre-treatment	4.03 ± 0.98	4.10 ± 0.59	
Post-treatment	4.74 ± 0.33	3.91 ± 0.29	
Within-group <i>p</i>	0.02 ^b	0.36 ^a	
% of improvement	17.6	4.6	

BMI – body mass index, WC – waist circumference, FBG – fasting blood glucose, TT – total testosterone
^a non-significant difference, ^b significant difference

Table 3. Within- and between-group analysis of semen parameters

Variables	Study group (mean ± SD)	Control group (mean ± SD)	<i>p</i>
Volume of semen (ml)			
Pre-treatment	2.55 ± 0.35	2.59 ± 0.26	0.90 ^a
Post-treatment	2.61 ± 0.24	2.58 ± 0.24	0.78 ^a
Within-group <i>p</i>	0.10 ^a	0.97 ^a	
% of improvement	2.3	0.38	
Count of semen (ml)			
Pre-treatment	35.90 ± 5.61	36.70 ± 5.30	0.64 ^a
Post-treatment	37.10 ± 6.64	36.40 ± 5.35	0.71 ^a
Within-group <i>p</i>	0.07 ^a	0.65 ^a	
% of improvement	3.34	0.81	
Progressive motility (%)			
Pre-treatment	29.35 ± 4.36	29.20 ± 3.25	0.98 ^a
Post-treatment	39.70 ± 4.12	28.80 ± 2.36	0.004 ^b
Within-group <i>p</i>	0.0001 ^b	0.72 ^a	
% of improvement	35	1.36	
Morphology (%)			
Pre-treatment	8.80 ± 1.23	8.70 ± 1.35	0.93 ^a
Post-treatment	9.40 ± 0.98	8.80 ± 1.25	0.10 ^a
Within-group <i>p</i>	0.03 ^b	0.98 ^a	
% of improvement	7	1.1	
DFI (%)			
Pre-treatment	21.30 ± 2.35	21.90 ± 3.25	0.82 ^a
Post-treatment	18.25 ± 1.27	21.32 ± 3.89	0.001 ^b
Within-group <i>p</i>	0.001 ^b	0.76 ^a	
% of improvement	14.3	2.6	
Static motility (%)			
Pre-treatment	53.75 ± 8.75	54.10 ± 7.85	0.95 ^a
Post-treatment	40.55 ± 5.69	54.60 ± 8.12	0.02 ^b
Within-group <i>p</i>	0.0001 ^b	0.74 ^a	
% of improvement	24.5	0.9	

DFI – deoxyribonucleic acid fragmentation index
^a non-significant difference, ^b significant difference

was a significant effect of interaction between time and treatment ($p = 0.0001$ and $f = 32.34$). Finally, a significant difference of treatment effect was noted ($p = 0.004$ and $f = 3.54$).

Discussion

Increased aromatase production caused by excessive accumulation of visceral adipose tissue elevates the rate of TT conversion to oestrogen via the direct stimulation of the hypothalamic-pituitary-gonadal axis (HPGA) in the brain. Also, low TT levels – induced by visceral adiposity – increase the accumulation of FFA extracted from diet and low lipolytic process (TT plays an important role in lipolytic metabolism) [4]. In addition to the decreased concentrations of reproductive/sex hormones [15] and quality of spermatogenesis, IR may originate from the above-mentioned causal-effect relationship between obesity and low TT levels, especially with sedentary lifestyle [4].

The present study revealed that a 14-week aerobic training produced a significant improvement in BMI, WC, FBG, semen parameters (except for semen volume and count), and TT in men with hyperglycaemia and central obesity.

Besides the protective role against the negative mental and psychological aspects of sedentarism [16], moderate-intensity aerobic exercise (MIAE) prevents the apoptosis – induced by hyperglycaemia – of testicular cells and increases the synthesis of TT from these cells. Suppression of chronic hyperglycaemia – augmented by regular training – promotes the synthesis of TT, which improves spermatogenesis, integrity of sperm DNA, condensed sperm chromatin, and semen quality [17].

Improved semen parameters after MIAE may be caused by the repetitive stimulation of HPGA, which promotes the function and/or number of testicular Sertoli and Leydig cells (these cells produce TT in response to the increased secretion of the luteinizing hormone and follicle-stimulating hormone after exercise) [18].

The mechanism explaining the changes of sex hormones – including TT – after programs of weight loss is scarcely described in the published literature [19]. Increased TT after training may be related to the improvement of IR, leptin levels, lipid profile, systemic inflammatory markers, and central obesity – the source of increased aromatase production (low aromatase levels decrease the rate of TT conversion to oestrogen) [20]. Insulin levels – commonly known to be decreased after lifestyle modification protocols – are strongly associated with stimulation of TT synthesis, especially after prolonged training [21].

Experimental studies revealed reduced implantation and/or normal pregnancy, development of embryo (weight and length), rates of live birth in female rats with normal weight when mated to obese males. However, lifestyle modifications (diet and exercise) counteract these issues by the gained correction of metabolic status of paternal obesity after exercise [22].

In a cohort study, Håkonsen et al. [23] observed significantly improved sex hormone levels, including serum TT, and semen parameters (despite improvement, DFI showed non-significant changes) after a weight loss strategy applied for 14 weeks in obese men ($n = 43$) with a BMI $> 33 \text{ kg/m}^2$.

In line with the results of this study, despite a non-significant increase of semen volume and count, a strategy of weight loss (diet with nearly 14-week daily exercise) in overweight and obese men resulted in a significant improvement in motility (progressive and static), DFI, and morphology of sperms in addition to a significant BMI decrease [24].

In agreement with the gained improvements in the present study, when compared with the non-exercised group, continuous MIAE on a treadmill significantly improved BMI, WC, DFI of sperms, and semen parameters (progressive motility and morphology) in the exercised male group. Opposite to the present study results, the increase of semen count and concentration that reached the significance level may be due to the longer duration of training (24 weeks) [25].

Again, besides a significant decrease of WC and increase of serum TT, 14-week MIAE significantly increased the morphology, count, and motility of sperms in sedentary obese men [26].

Moreover, 12-week regular aerobic activity significantly improved BMI, FBG, and serum TT in overweight and obese men with IR [27]. In turn, 5-week MIAE increased serum TT concentration in healthy young males [28].

Aerobic training at 55–70% of HRmax for 12 weeks (3 times weekly) produced a significant decrease in body weight and BMI. The selected exercise intensity was the main cause of the significant increase of serum TT in obese men aged 35.2 ± 3.1 years [29].

A significant increase of serum TT was related to a significant improvement of FBG, insulin, and WC in men with abdominal adiposity after high-volume MIAE > 200 minutes weekly [20].

Maintained normal integrity of HPGA function is controlled by normal metabolism of insulin and glucose [30]. Du Plessis et al. [31] related an increase in male fertility after MIAE to the noted enhancement of body composition, blood glucose, endocrine hormones, and oxidative stress mediators. Decreased adiposity index and gonadal fat – induced by MIAE – may improve the reproductive functions and sperm quality in obese rats.

When compared with a sedentary control group, trained rats with DM induced for 10 weeks revealed a significant improvement in semen viability, count, morphology, and motility owing to the decrease of blood glucose [32].

In comparison with a diabetic sedentary group, a 10-week endurance training significantly improved viability and motility of sperms, perhaps because of the significant increase of serum TT in diabetic trained rats [33].

Again, an 8-week not intensive endurance training produced a significant improvement of serum TT and sperm function in diabetic rats, possibly as a result of decreased lipid peroxidation, especially when the exercise was conducted with supplementation administered for muscle mass increase [13].

Improved DNA damage, morphology, motility, oxidative stress, mitochondrial membrane potential of sperms after exercise and diet interventions are caused by normalization of plasma levels of glucose, insulin, FFA, lipids (triglycerides and cholesterol) in rats with obesity induced by high fat diet [34].

Effect of exercise on HPGA is dependent on the selected exercise parameters (type, duration, and intensity). For example, high-intensity exercise negatively affects spermatogenesis and quality of sperms in addition to the sex hormones, including TT [18].

Regarding the type, opposite to the use of treadmill in the present study, bicycling for > 150 hours weekly lowered the motility and count of sperms. Long-term exposure to bicycling reduces semen quality by inducing repeated trauma and minor inflammatory processes, and by increasing testicle temperature owing to the various saddle-shaped designs of bicycles used in training [35].

As for the intensity of exercise, opposite to the selection of MIAE in the present study, exercise stress (vigorous inten-

sity) may lower gonadal functions via increased production of corticotropin-releasing hormone and catecholamines, which inhibit the production of gonadotropin-releasing hormone (GnRH). Lower levels of GnRH inhibit the synthesis of sex hormones, including TT [36].

With reference to the duration of exercise, in contradiction to the results of this study and besides the non-significant weight loss, too many different intensities (1, 2, and 3 hours) of a 5-day aerobic swimming exercise per week for 4 successive weeks decreased the testicular functions of rats, including sperm parameters, because of the raised testicular oxidative stress – related to the production of large amounts of reactive oxygen species – and the lowered synthesis of anti-oxidative enzymes [37].

Against the results of this study, besides the lower pregnancy rate and quality of sperms, DNA fragmentation increased after 10-week running (5 days weekly) in a male rat model, perhaps owing to the intensive or vigorous nature of training that increased oxidative stress in semen in addition to the administration of anabolic-androgenic steroidal drugs, which caused subfertility by under-stabilization of sperm chromatin [38].

In controversy to the results of this study, moderate-intensity bicycling for 12 weeks showed a non-significant difference in serum TT of sedentary young men (aged 21 ± 2 years, with normal BMI), possibly because of the lower frequency of exercise sessions (50-minute exercise session, 1 time weekly) [39]. Also, males with normal weight or BMI presented a non-significant change of serum TT after 12-week MIAE as a result of the lower response of TT synthesis to exercise in aged men due to the attenuating or inhibiting effect of aging on testicular functions [27].

Limitations

DM was not ruled out by tests other than a 2-hour glucose tolerance test, so there is a need to assess the differences between patients with pre-diabetes and DM, as more severe glucose disturbances can have a different (irreversible) impact on the measured parameters.

Lack of long-term follow-up, small number of participants, and lack of follow-up of the female partners' pregnancy rate (non-pregnant females after 1-year marriage with no obvious diagnosed medical problem that may prevent pregnancy) are the main limitations of this study that can be faced in future research.

Conclusions

The deteriorating effect of central adiposity, hyperglycemia, and sedentarism on semen quality and nuclear damage of sperms (assessed by DFI) is prevented or counteracted by increased exercise-induced TT production resulting from decreased BMI, FBG, and WC.

Acknowledgments

Those who participated in this study are appreciated by the authors.

Disclosure statement

No author has any financial interest or received any financial benefit from this research.

Conflict of interest

The authors state no conflict of interest.

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