



Adequate Exercise Improves Inflammatory, Gonadal Markers and Sexual Function in Type 2 Diabetics

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NA, HA and WKBAO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors BBA and PPMD managed the analyses of the study. Authors BBA and OAM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Sexual dysfunction is strongly associated with metabolic syndrome and its components, obesity, androgens, endothelial function, oxidative stress and inflammatory markers, which are influenced positively by physical activity. Therefore, an increase in physical activity is expected to improve the sexual function of people with diabetes. The study seeks to find the association between daily routine exercise and sexual function in diabetic men.

Methods: Heterosexually active type II diabetic men were categorized based on whether they were engaged in some form of exercise or not. Sexual function and sexual quality were assessed using the GRISS-M and SQoL-M respectively, while blood samples for lipid profiling and testosterone estimation were obtained in the fasting state.

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Results: The levels of testosterone were significantly higher among those who were engaged in some form of exercise compared to those who were not engaged in any form of exercise. In effect, better lipid profile markers, sexual function and adiponectin levels were recorded among participants who engaged in some form of exercise over those who were not engaged in any form of exercise.

Conclusion: Exercise may be an interventional approach to improving lipid profile indices and sexual quality in type II diabetic men.

Keywords: Sexual dysfunction; diabetes; exercise; lipid profile; inflammatory markers.

1. INTRODUCTION

The importance of exercise on the general health of the individual is quite documented. Several types of research have established a strong association between the general wellbeing of the individual and physical activity levels, quality of life and the reduction in the frequency of disease. Diabetics have been reported to have increased risk of coronary disease, poorer health outcomes and sexual function [1,2]. However, until recently, few types of research have documented the role of physical activity and exercise on the sexual function of the individual.

The shear stress involved in physical activity has been reported to be associated with activation of endothelial nitric oxide (NO) synthase levels [3], which has the potential of making the increased availability of NO to the endothelial bed and thus enhancing the mechanisms involved in the erectile process. Additional experimental work have shown that the shear stress that is evoked in exercise has the potential to induce the up-regulation of the cytosolic superoxide dismutase which is a potent free-radical scavenger, thus preventing the inactivation of NO by vascular superoxide or other reactive oxygen species and thus making NO available at the endothelial bed to enhance the erectile process [4]. Further studies have revealed low levels of testosterone among diabetic men with metabolic syndrome compared to their non-diabetic counterparts [5].

Earlier studies that encouraged exercise among diabetics only sort to link exercise levels to improvements in dyslipidemic markers and overall wellbeing in the diabetic. Recently, sexual dysfunction, as well as erectile dysfunction, has been strongly linked to androgens, endothelial function, oxidative stress indicators, markers of inflammation as well as obesity and the metabolic syndrome [2,5-8]. If improvements in components of the metabolic syndrome, obesity [9,10], inflammatory [11], dyslipidemic indicators [12], as well as endothelial function [3,13], are

strongly linked to physical activity levels and exercise [3,10,13,14], it is only logical to expect that these improvements will ultimately result in improved endothelial function and consequently impact on the sexual function of diabetics.

This research, therefore, seeks to establish the association between daily routine exercise and sexual function in diabetics. Some evidence has been provided [15] regarding the beneficial role of exercise in improving obesity, erectile function [15-19] as well as risk factors. Others have reported improvements in sexual function, testosterone levels as well as weight and waist circumference (WC) with moderate aerobic exercise [20]. Adeniyi [21] and his colleagues have provided strong evidence of the impact of pelvic floor therapeutic exercise in improving sexual function among non-diabetics. Whether these findings can be related to people with diabetes is assumed but yet to be established.

2. METHODS

2.1 Participants

The study was conducted among 325 type II diabetic males visiting the diabetic clinic of the Maamobi General Hospital in the Greater Accra region of Ghana, between October 2013 and September 2014. The studied participants were consecutively recruited to partake in this study and were on various oral diabetic medications. Participants were required to be heterosexually active, and to have engaged in sexual activity for at least 2 years before enrolment into the study. All participants met the legal sexual consent age of 18 years before being enrolled into the study. Participation of the diabetic respondents in this study was voluntary and informed consent was obtained from each participant. Ethical approval for this study was sought from the Committee on Human Research Publication and Ethics (CHRPE) of the School of Medical Science and the Komfo Anokye Teaching Hospital (KATH), Kumasi.

2.2 Socio-demographic Data

A self-designed, semi-structured questionnaire was administered to each consented participant for age, marital status, behavioral and lifestyle activities (exercise, smoking and alcohol consumption). Participants were asked to respond as to whether they did not engage in any exercise at all, engaged in exercise for not more than 2 days per week or engaged in exercise for 3 days or more per week. Participants who responded yes to at least 1 exercise per week were categorized as having been involved in some exercise. An exercise was defined as any activity causing light perspiration or a slight-to-moderate increase in breathing or heart rate for at least 30 min.

2.3 Sexual Function and Sexual Quality of Life

The Golombok Rust Inventory of Sexual Satisfaction for males (GRISS-M) was used to assess the sexual function of all the recruited diabetics. The GRISS-M has 28 items on a single sheet and is used for determining existence and severity of sexual problems in heterosexual couples or individuals who have a current heterosexual relationship. All the 28 questions are structured on a five-point (Likert type) scale which is converted into a stanine score with scores of 5 and above indicating sexual dysfunction. The GRISS-M allows for the subscales of the sexual function of subjects into subscales of impotence, premature ejaculation, in frequency, non-communication, dissatisfaction, non-sensuality and avoidance. The Sexual Quality of Life-Male (SQoL-M) was used in assessing the sexual quality of life of the participants.

2.4 Biochemical Assay

Samples were obtained from participants between the morning hours of 6:00 to 8:00 GMT in the fasting state and were used in assessing lipid profile, inflammatory marker as well as markers of gonadal function. Lipid profile was analyzed using the JAS Diagnostics® reagent kits on the BT 5000® Chemistry Analyzer (Biotechnica, Italy). AxSYM automated analyzer (Abbott Diagnostics, USA) was used in the estimation of free and total testosterone. The AxSYM automated analyzer uses Elabscience® reagent kits. Bioavailable testosterone was calculated according to the method of Sodergard et al. [22]. The Sandwich-ELISA method was used to assay the adiponectin levels using the

Elabscience® reagent kits on the AxSYM analyser (Abbott Diagnostics, USA).

2.5 Statistical Analysis

Data were analysed using Graph Pad Prism version 5.0 and presented as mean \pm SD for relevant variables. For comparison of categorical variables, the Chi-square test was used while for continuous variables, the unpaired t-test was employed. A p-value <0.05 was considered significant.

3. RESULTS

From this study, the age of the studied participants ranged from 29 - 89 years, with mean \pm SD being 63.04 ± 3.05 years. The age of the studied participants who were not engaged in exercise (64.13 ± 1.17 years) was not significantly different ($p = 0.5201$) from those who were engaged in some form of exercise (62.55 ± 1.31). However, those who were not engaged in exercise had significantly been diagnosed of diabetes much earlier (9.85 ± 0.74 years, $p = 0.0085$) compared to those who were engaged in some form of exercise (6.82 ± 0.85 years). The mean duration of diabetes of the studied population was 8.38 ± 1.01 years. Whereas none of the studied participants smoked cigarettes, about 20% consumed alcoholic beverages (70/325) and almost all the studied participants were married (313/325, that is, 96.3%).

When the studied participants were stratified based on exercise, those who were not involved in exercise had similar mean level of lipid profile markers, inflammatory markers as well as sexual dysfunction and its subscales as those who were involved in exercise (Table 1). Sexual quality of life was also not significantly affected. However, the mean level of markers of gonadal function were generally significantly higher ($p = 0.0304$, 0.0423 and 0.0066 for total, free and bioavailable testosterone respectively) among those who were engaged in some form of exercise (2.79 ± 0.89 , 0.09 ± 0.02 and 2.49 ± 0.77 for total, free and bioavailable testosterone respectively) as compared to those who were not engaged in any form of exercise (0.79 ± 0.39 , 0.03 ± 0.01 and 0.45 ± 0.05 for total, free and bioavailable testosterone respectively) (Table 1). Some form of exercise increased the markers of gonadal function by 71.7%, 66.7% and 81.9% for total, free and bioavailable testosterone respectively over those who did not engage in any form of exercise.

Table 1. Lipids, inflammation, sexual function in diabetics with/without exercise

Parameters	Total (n=325)	With no EXX (n=170)	With EXX (n=155)	P value
Lipid profile parameters				
Cholesterol (mmol/l)	4.26±1.10	4.09±0.17	4.45±0.16	0.3405
Triglycerides (mmol/l)	0.92±0.06	0.93±0.06	0.92±0.07	0.8237
HDL-cholesterol (mmol/l)	1.39±0.06	1.38±0.06	1.40±0.07	0.8644
LDL-cholesterol (mmol/l)	2.71±0.96	2.82±0.12	2.58±0.12	0.1636
Inflammatory marker				
Adiponectin (ng/ml)	1.51±0.12	1.39±0.13	1.48±0.14	0.7884
Markers of hypogonadism				
Total testosterone	2.89 ± 0.33	0.79 ± 0.39	2.79 ± 0.89	0.0304
Free testosterone	0.12 ± 0.00	0.03 ± 0.01	0.09 ± 0.02	0.0423
Bioav. testosterone	2.75 ± 0.09	0.45 ± 0.05	2.49 ± 0.77	0.0066
sexual function				
Sexual dysfunction (sd)	5.10±0.23	5.65±0.22	4.39±0.24	0.4231
Impotence (ed)	4.87±1.17	4.82±0.19	4.50±0.27	0.3482
Premature ejaculation (pe)	4.75±1.12	4.71±0.19	4.61±0.25	0.7653
Non-sensuality (ns)	5.35±1.09	4.91±0.21	5.42±0.29	0.1573
Avoidance (av)	4.79±1.76	5.00±0.22	4.71±0.26	0.3932
Disatisfaction (dis)	4.91±1.15	5.25±0.23	4.382±0.26	0.2745
Non-communication (nc)	5.32±1.69	5.17±0.21	5.06±0.25	0.7354
Infrequency (if)	4.79±1.54	4.82±0.16	4.63±0.19	0.4556
SQOL	42.76±4.33	43.74±3.62	40.70±4.04	0.5750

Table 2 shows the comparison between the studied participants who were engaged in at least 3 days of exercise or more per week to those who do not engage in exercise at all. Markers of lipid abnormalities (total cholesterol, triglyceride and bad cholesterol (LDL-c)) were significantly ($p = 0.0429, 0.0032$ and 0.0179 respectively) lower among those who were engaged in at least 3 days of exercise per week as compared to those who were not engaged in

Table 2. Lipids, inflammation, sexual function in diabetics with (3-5x)/without exercise

Parameters	No EXX (n=170)	3 or more EXX/WEEK (n=90)	P value
Lipid profile parameters			
Cholesterol (mmol/l)	4.09±0.17	4.15±0.13	0.0429
Triglycerides (mmol/l)	0.93±0.06	0.67±0.03	0.0032
HDL-cholesterol (mmol/l)	1.38±0.06	1.45±0.06	0.0373
LDL-cholesterol (mmol/l)	2.82±0.12	2.38±0.09	0.0179
Inflammatory marker			
Adiponectin	1.39±0.13	1.57±0.18	0.0024
Markers of hypogonadism			
Total testosterone	0.79 ± 0.39	2.85 ± 0.09	0.0179
Free testosterone	0.03 ± 0.01	0.08 ± 0.00	0.0217
Bioav. testosterone	0.45 ± 0.05	2.79 ± 0.89	0.0041
Sexual function			
Sexual dysfunction (sd)	5.65±0.22	4.73±0.29	0.4301
Impotence (imp)	4.82±0.19	4.20±0.36	0.1053
Premature ejaculation (pe)	4.71±0.19	3.94±0.27	0.0253
Non-sensuality (ns)	4.91±0.21	4.86±0.35	0.9077
Avoidance (av)	5.00±0.22	4.25±0.35	0.0493
Disatisfaction (dis)	5.25±0.23	4.38±0.26	0.0241
Non-communication (nc)	5.17±0.21	5.06±0.34	0.7554
Infrequency (if)	4.82±0.16	4.08±0.22	0.0096
SQOL	43.74±3.62	51.48±5.17	0.0274

exercise at all. Mean good cholesterol level (HDL-c) was however significantly ($p = 0.0373$) higher when those who were engaged in at least 3 days of exercise per week (1.45 ± 0.06 , mmol/L) where compared to those who were not engaged in exercise at all (1.27 ± 0.05 , mmol/L) (Table 2).

Markers of hypogonadism (total, free and bioavailable testosterone) together with adiponectin, a marker of inflammation were significantly higher ($p = 0.0179$, 0.0217 , 0.0041 and 0.0024 for total, free bioavailable testosterone and adiponectin, respectively) among participants who were engaged in at least 3 days of exercise per week (2.85 ± 0.09 , 0.08 ± 0.00 , 2.79 ± 0.89 and 1.57 ± 0.18 for total, free, bioavailable testosterone and adiponectin respectively) compared to those who were not engaged in exercise at all (0.79 ± 0.39 , 0.03 ± 0.01 , 0.45 ± 0.05 and 1.39 ± 0.13 for total, free, bioavailable testosterone and adiponectin respectively) (Table 2). At least 3 days of exercise per week also increased the markers of gonadal function by 84.2%, 75.0% and 85.7% for total, free and bioavailable testosterone respectively over those who did not engage in any form of exercise.

The mean stannine score for SD was similar between the participants who did not engage in any form of exercise and those who engaged in at least 3 times of exercise per week. However, mean stannine score for the subscales (premature ejaculation, avoidance, dissatisfaction and infrequency) were significantly ($p = 0.0253$, 0.0493 , 0.0241 and 0.0096 respectively) lower when participants who engaged in at least 3 times of exercise per week were compared to those who did not engage in any form of exercise (Table 2). Even though there was no difference in the SQoL when participants who did not engage in any form of exercise were compared to those who did some exercise (Table 1), participants who engaged in at least 3 times of exercise per week recorded significantly higher SQoL scores when they were compared to those who did not engage in any form of exercise (Table 2).

As shown in Table 3, exercise indicates a significant negative association with total cholesterol ($r = -0.18$; $p = 0.0435$). Free testosterone and bioavailable testosterone show significant positive correlation with exercise ($p = 0.0299$ and 0.0379 respectively). Exercise significantly improves sexual functioning ($r = -$

0.18 ; $p = 0.0428$), sexual satisfaction ($r = -0.21$; $p = 0.0190$) as well as the frequency of sexual activities ($r = -0.17$; $p = 0.0450$) from this study (Table 3).

Table 3. Correlation between exercise, lipid profile and sexual dysfunction and subscales

Variables	r	P Value
Lipid profile		
Total Cholesterol	-0.18	0.0435
Triglycerides	-0.06	0.4797
HDL-cholesterol	0.08	0.3738
LDL-cholesterol	-0.15	0.0818
Inflammatory marker		
Adiponectin	0.09	0.3311
Markers of Hypogonadism		
Total testosterone	0.18	0.0859
Free testosterone	0.19	0.0299
Bioavailable Testosterone	0.18	0.0379
Sexual function		
Sexual dysfunction	-0.18	0.0428
Impotence	-0.01	0.9173
Prem. Ejaculation	-0.01	0.9142
Non-sensuality	-0.13	0.1379
Dissatisfaction	-0.21	0.0190
Avoidance	-0.08	0.3693
Infrequency	-0.17	0.0450
Non-communication	0.01	0.8845
SQoL	0.00	0.9989

4. DISCUSSION

The benefits derived from exercise to an individual's health are phenomenal, thus justifying the need to further explore their significance under diseased states. Our study demonstrates the therapeutic advantage of regular exercise.

As predicted, the onset of diabetes was delayed among subjects who were engaged in some form of exercise compared to those who were not engaged in exercise. The role that exercise plays in reducing the risks of metabolic diseases cannot be over emphasized. It has been reported to contribute to the general wellbeing of an individual through various mechanism, which collectively inhibit the onset of cardiovascular diseases and diabetes [23].

It was interesting to note a significant effect of exercise on the improvement of sexual function, where individuals who engaged in some form of exercise were observed to have higher levels of total, free and bioavailable testosterone levels

compared to those who were not engaged in any form of exercise. Testosterone is considered to be a hormone that promotes sexual urge and desire [24,25] and thus, dramatic increase in their levels due to exercise is a positive indication that regular exercise can support the treatment of SD among type II diabetic males. Exercise was shown to negatively correlate with SD, where there was increased sexual satisfaction and increased sexual frequency among the subjects who were engaged in exercise compared to those who were not. SD is usually described as the inability to participate in a sexual relationship as one would wish and has multifactorial causes, including medical and psychological complications, of which diabetes is implicated [26,27]. Once an individual with SD begins to experience an increase in sexual satisfaction and an increased frequency for sex, then the path to the recovery from SD has been ensued.

In a recent study [5] where we explored the inter-relational effect of metabolic syndrome and SD on hypogonadism in type II diabetic men, we recorded low testosterone levels among diabetic men with metabolic syndrome, suggesting that metabolic syndrome and its components played a role in the manifestation of SD in this group of individuals. In view of this, this study further explored whether regular and consistent exercise had a significant benefit on the sexual function of diabetic men. It was exciting to note that regular and consistent exercise improved sexual function in these diabetic men, signaling that diabetic men experiencing SD when encouraged to undertake regular and consistent exercise alongside therapy will experience an improved sexual function. Adequate exercise has been reported to reduce the availability of free fatty acids on the endothelial bed and improve on the levels of anti-inflammatory hormones like adiponectin [3]. This has the potential to reduce the rate of formation of atherosclerotic lesions, thereby improving on endothelial function and vascular blood flow and thus making increased availability of NO for the effective mediation of the erectile process. The shear stress involved in exercise may improve the expression of endothelial nitric oxide synthase which have been documented [3] in cell culture experiments. Thus, the increased availability of NO on the endothelial bed will enhance the mechanism involved in the erectile process.

There was no difference in lipid parameters or sexual function when participants who did not engage in any exercise were compared to those

who engaged in some level of exercise. However, significant differences were recorded when the same group was compared to participants who engaged in exercise at least thrice per week. Thus, for exercise to have a significant positive impact on lipid levels as well as sexual function, participants should be engaged in exercise at least thrice per week. Our study further revealed a negative correlation between exercise and SD. These findings are supported by several studies where regular exercise was shown to improve lipid parameters [12,13,28] and sexual function [10,15,20,21].

It is interesting to find in this study that adiponectin levels were improved in the participants who engaged in exercise at least thrice per week but not in those who did just some exercise, thus exercise per se might not improve anti-inflammatory markers or lipid profile indices if it is not adequate. Adequate exercise was shown in this study to improve on premature ejaculation, reduce avoidance of sexual activity, improve the level of dissatisfaction and infrequency in sexual activity as well as improve the SQoL. Thus, the importance of exercise as an intervening tool in improving and salvaging the sexual function of patients in general cannot be overemphasized. This finding supports recent reports that have shown improved sexual function with exercise regimens as well as treatment of dyslipidemia and aggressive improvements in anti-inflammatory markers [15,20]. However most of these reports did not indicate the adequate number of days of exercise needed in order to record significantly beneficial improvements in lipid parameters as well as sexual function.

This study however provides evidence of a strong association between daily exercise routines performed at least thrice a week and significant improvements in sexual function, inflammatory markers as well as in serum lipid profile levels. Thus, a patient will require at least 3 days of normal exercise per week to translate into improvements in lipid profile parameters and sexual function. Clinicians and Dieticians treating diabetics and non-diabetics alike should therefore encourage their patients to engage in at least three times of routine daily exercise per week and to encourage those engaged in only weekend routine exercise to add an additional working day in other to translate exercise into a beneficial tool for the improvement of lipid profile levels, sexual function and the SQoL of their patients.

5. CONCLUSION

Adequate exercise has beneficial effects on improving lipid profile parameters, inflammatory markers as well as sexual function in diabetic patients. Adequate exercise also helps improve the sexual quality of life of the diabetic patient, At least normal daily exercise thrice a week is needed to translate exercise into a beneficial tool to improve on lipid profile indices as well as sexual function in diabetics.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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