REVIEW ARTICLE

EFFECTS OF AEROBIC EXERCISE IN THE MANAGEMENT OF ERECTILE DYSFUNCTION: A META ANALYSIS STUDY ON RANDOMIZED CONTROLLED TRIALS

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ABSTRACT

BACKGROUND: Penile erection is a hemodynamic process involving increased arterial inflow and restricted venous outflow, coordinated with corpus cavernosum and penile arterial smooth muscle relaxation. Any problem in this mechanism results in Erectile Dysfunction and its etiology is generally multifactorial. This study is aimed at determining the objective outcome of aerobic training in the management of Erectile Dysfunction of arterogenic origin using Meta analysis.
METHODS: Relevant publications were searched up to November 2010 in the MEDLINE (PubMed) database. The citation lists of randomized controlled trials on the effect of aerobic training and Erectile Dysfunction management using the International Index of Erectile Function (IIEF) as treatment outcome measure. Studies on different operative techniques on the effects of aerobic training for men with Erectile Dysfunction due to arterogenic Erecile Dysfunction were selected. Data on participants' characteristics, study quality, population, intervention, treatment outcome were collected and analyzed.
RESULTS: There were 5 randomized controlled studies using the International Index of Erectile Function as measure of treatment outcome. A total of 385 subjects were involved in 5 studies; results indicated significant effect of aerobic training on Erecile Dysfunction (t=5.856, p= .000) at p< 0.05.
CONCLUSION: Subjects with arterogenic Erectile Dysfunction might benefit from aerobic training. More randomized controlled studies in this area are warranted
KEYWORDS: Erectile dysfunction; Impotence; Exercise; Index of erectile function

INTRODUCTION

Male erectile dysfunction (ED) has been defined as the persistent inability to attain and/or maintain an erection sufficient for sexual performance (1). ED is very common, and its prevalence as well as severity increases with age (2). It has been recognized that the major cause of ED is atherosclerosis affecting the pelvic vasculature (3). The presence of ED has been known to predict future cardiovascular disease, and early detection may allow timely modification of remediable risk factors, or lead to the diagnosis of occult cardiovascular disease (4, 5).

Penile erection is a hemodynamic process involving increased arterial inflow and restricted venous outflow, coordinated with corpus cavernosum and penile arterial smooth muscle relaxation. Any problem in this mechanism results in ED, and its etiology is generally multifactorial (6). Diabetes, hypertension, high serum cholesterol level, peripheral vascular disease and cardiac problems are significantly found together with ED (7). However, vascular reasons predominate in the etiology of ED and it frequently appears along with atherosclerosis (7). It is known that atherosclerotic lesions prevent blood flow into cavernosal tissues resulting in ED (8).

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The endothelium is vital to the maintenance of vascular health. It is a critical determinant of vascular tone and patency, reactivity, inflammation, vascular remodeling, and blood fluidity. (9, 10). Nitric oxide (NO) is the most potent vasodilator and is secreted by the endothelium. It is synthesized from Larginine by the endothelial enzyme NO synthase (eNOS). NO released in response to sexual stimulation relaxes penile vascular smooth muscle by increasing intracellular cyclic 3', 5'-guanosine monophosphate (cGMP) concentration. Vasodilatation of erectile tissues allows the sinusoidal spaces to fill with blood resulting in the attainment and maintenance of an erection (5).

Erection is a complex physiological process in which vascular factors play a pre-eminent role. Therapeutic options for men with arteriogenic erectile dysfunction (ED) are mainly administration of phosphodiesterase type 5 inhibitors, intracavernous injections of vasoactive agents (for example, prostaglandin El, papaverine/phentolamine, or triple drug), intraurethral administration of prostaglandin El, and administration of centrally acting drugs (11, 12). However, all of these methods circumvent the patient's problem temporarily, and patients are not cured of impotence, they will remain dependent on these treatments for the remainder of their sexually active lives. An effective treatment that cures the problem permanently is needed where penile revascularization and exercise remain treatment options for such patients. However, due to the complexity of penile revascularization such as cost ineffectiveness, unavailability of experts, side effects of surgery and high failure rates among the elderly (13) have left people with ED at the mercy of exercise.

Although there have been sufficient data on the relationship between ED and several well-recognized risk factors which including aging, coronary artery disease, atherosclerosis, diabetes mellitus, dyslipidemia, high blood pressure, and pelvic surgeries, little attention has been paid by the urologists to the role of lifestyle factors in ED. However, accumulating data from basic science and clinical studies have determined a link between the occurrence of ED and a number of lifestyle factors, such as smoking, obesity, alcohol consumption, and lack of physical activity. The application of findings from animal and human studies to the clinical practice regarding the modification of lifestyle factors could help to improve ED as well as reducing the risks of developing cardiovascular diseases (14).

Several studies (15-17) have shown an inverse relationship between physical activity levels and biomarkers of inflammation in both the healthy individuals and subjects with cardiovascular condition. Studies (18-21) have also reported the role of exercise in the management of erectile dysfunction. The majority of these studies are subjective, retrospective case series and non randomized non controlled studies. However, randomized controlled trials (RCTs) are generally accepted as the most valid method for determining the efficacy of a therapeutic intervention, because the biases associated with other experimental designs can be avoided (22). Therefore, the purpose of the present Meta analysis study was to determine the role and effect of aerobic exercise in the management of erectile dysfunction in randomized controlled trials.

MATERIALS AND METHODS

Clinical trials were included if they met all of the following inclusion criteria: study population defined; Men with arteriogenic ED were considered; the present review was concerned with studies that used aerobic exercise on ED; only randomized controlled trials on this topic were selected for review; The main outcome measure was satisfactory intercourse without additional therapy using the International Index of Erectile Dysfunction (IIED) scores. The present review utilized studies that had successfully undergone rigorous peer review (i.e., published peer-reviewed journals), were included.

The Medline (Pubmed) electronic database was searched (from June 1972 to November 2010) for systematic reviews that evaluated the effects of therapeutic exercise on ED. The key words and search terms used to develop the search strategy for each of these databases included: exercise therapy, aerobic exercise, therapeutic exercise, rehabilitation exercise, impotence and erectile dysfunction. In addition, the electronic searches

were supplemented by checking the reference lists of any relevant identified articles.

MEDLINE is the U.S. National Library of Medicine's (NLM) premier bibliographic database that contains over 18 million references to journal articles in life sciences with a concentration on biomedicine. A distinctive feature of MEDLINE is that the records are indexed with NLM Medical Subject Headings (MeSH).The great majority of journals are selected for MEDLINE based on the recommendation of the Literature Selection Technical Review Committee (LSTRC), a National Institute of Health (NIH)-chartered advisory committee of external experts analogous to the committees that review NIH grant applications. MEDLINE is the primary component of PubMed, part of the entry series of databases provided by the NLM National Center for Biotechnology Information (NCBI). MEDLINE may also be searched via the NLM Gateway (23).

The literature search results were screened, and relevant articles were retrieved. Data was extracted from each identified paper and included information on study design, participants and outcome measures. The main outcome was the efficacy of treatment for ED compared with placebo, sham, or active control in improving ED IIED total scores.

In the statistical analysis, the difference between the pre-test and post-test values (changed score) for IIEF score was computed. Student *t*–test was used to compare the mean changed score values of IIEF. All statistical analysis was performed on an IBM compatible micro computer using SPSS for window version 15.0, (Chicago IL, USA). The probability level for all the above tests was set at 0.05 to indicate significance.

RESULTS

The search criteria identified 210 studies from 1972 to 2010; on inserting randomized controlled trials only 26 studies were identified out of which only 5 met the inclusion criteria and 21 studies did not meet the inclusion criteria, hence, were excluded. Five (18, 24-27) randomized controlled trials (RCTs) met the inclusion criteria; studies involved the use of aerobic exercise in the management of ED, the IIEF was the assessment tool for ED and also involved control groups. A total of 385 subjects were involved: Lamina et al (25), n=43; Lamina et al (26), n=43; Esposito et al (18), n= 110; Kalka et al (27), n= 129; Maio, Saraed and Marchiori (24), n= 60.

The mean± SD of base line erectile function as assessed by the IIEF for the interventions and control groups was 13.91±6.37 and 13.26±6.82, respectively. There was no group significant difference in base line values of EF (t= .158, p= .879) at p< 0.05. Detailed mean± SD for pre and post intervention are presented on table 1.

Table 1: Pre and posttest International Index of Erectile Function (IIEF) values (mean± SD), (N= 365).

	Exercise				**Control**			
	Pre		Post		Pre		Post	
Variable	mean	SD	mean	SD	mean	SD	mean	SD
IIEF	13.91	6.37	16.7440	5.93661	13.2560	6.82068	13.6160	6.50792

Table 2 showed significant mean effects in changed score values between exercise and control in all data pooled together (t= 5.856, p= .000) at p< 0.05.

Table 2: Effect of exercise on erectile dysfunction (mean± SD changed score values), N= 385

Variables	Exercise mean± SD	Control mean± SD	t-value	p-value
IIEF	2.8300±.83	.3600±.44917	5.856	.000

*significant, p< 0.05

DISCUSSION

Evidence from 5 randomized studies published in the years between 2004 and 2010, has demonstrated strong evidence that aerobic exercise can benefit people with arterogenic ED. These review results of this study build on and update the evidence from studies that concluded that concluded that exercise was beneficial for people with ED and cardiovascular disorders (25-27); on ED and obesity (18) and on normal subjects with ED (24). However, studies have shown common pathway for ED, cardiovascular (28 -30) and metabolic disorders (19, 31).

Three of the randomized studies (25-27) that contributed to the present study data indicated the positive role of both interval and continuous aerobic training in the dual management of both ED and cardiovascular disorders (hypertension and ischemic heart disease ,respectively); this is not surprising because of the arterogenic inter-relationship between ED and several cardiovascular disorders. The physiological basis for the therapeutic role of continuous exercise in the management of both ED and some cardiovascular disorders as reported in the present study, could be related to the biochemical, neural and hormonal changes in the blood vessel walls that induce an acute and long-term blood vessel relaxation. The blood vessels might relax after each exercise session because of body warming effects; local production of certain chemicals, such lactic acid and NO; decreases in nerve activity; and changes in certain hormones and their receptors (32, 33). Over time, as the exercise is repeated, there appears to be a growing evidence of a prolonged effect. Thus, chronic (regular, long-term) physical training might reduce basal concentrations of inflammatory markers.

Esposito et al (18), in their randomized study investigated the effect of physical activities on 110 obese subjects. They reported significant effect of physical activities on both body mass index and EF. The physiological rationales underlying this hypothesis are that healthy lifestyle factors are associated with maintenance of good erectile function in men (19); obesity has been positively associated with endothelial dysfunction and increased serum concentrations of vascular inflammatory markers (34, 35); and both endothelial and erectile dysfunction may share some common metabolic and vascular pathways that may be influenced by behavioral-related pathways (19, 36). Obese men with erectile dysfunction had evidence of abnormal endothelial function, which was indicated by reduced blood pressure and platelet aggregation responses to L-arginine and elevated serum concentrations of markers of low-grade inflammation, such as IL-6, IL-8, and CRP. It has been shown that there are significant associations between IEEF score and proxy indicators of elevated body fat, the vascular response to L-arginine, and circulating IL-8 and CRP levels. The association we found between IEEF score and indices of endothelial dysfunction supports the presence of common vascular pathways underlying both conditions in obese men. A disturbance in nitric oxide activity linked to reduced nitric oxide availability could provide a unifying explanation for this association. In particular, in isolated corpus cavernosum strips from patients with erectile dysfunction both neurogenic and endothelium-dependent relaxation is impaired (37).

Obesity is a state of chronic oxidative stress and inflammation (38). The increased oxidative stress associated with obesity may increase free radical formation, which could quench and deactivate nitric oxide, reducing its availability for target cells. Weight loss programs with dietary modifications and increased physical activity may lead to reduced oxidative stress associated with

improved nitric oxide availability (39). As impaired nitric oxide activity appears to play an important role in the pathogenesis of erectile dysfunction (40), improved nitric oxide availability associated with weight loss may be implicated in the amelioration of erectile function in our series of obese men. A reduced CRP level due to sustained lifestyle changes may have contributed to amelioration of erectile function after treatment. Levels of CRP correlate significantly with reduced nitric oxide availability (41) and increasing severity of penile vascular disease as measured by penile Doppler (42). Moreover, consistent findings support a predictive role of CRP and IL-6 for cardiovascular events in different populations (43), while IL-8 is a potent chemoattractant (44).

Many studies have been conducted on this topic; their results have been challenged by lack of controlled groups and non-randomization. Randomized controlled trials (RCTs) are generally accepted as the most valid method for determining the efficacy of a therapeutic intervention, because the biases associated with other experimental designs can be avoided.Non-randomized controlled trials, can detect associations between an intervention and an outcome. But they cannot rule out the possibility that the association was caused by a third factor linked to both intervention and outcome. Random allocation ensures no systematic differences between intervention groups in factors, known and unknown, that may affect outcome. Randomized controlled trials are the most rigorous way of determining whether a cause-effect relation exists between treatment and outcome and for assessing the cost effectiveness of a treatment (45, 22).

In conclusion, aerobic training can successfully treat ED in selected patients with arterogenic ED. However, there are very few high-quality randomized trials regarding aerobic training and ED. Practitioners should bear in mind that aerobic training and other risk factors modification is associated with higher rates of ED management success.Since these results are based on small studies, the evidence would be stronger if confirmed by large trials. Effectiveness data were limited; however, the effectiveness of ED is largely determined by the patient health status and associated condition. In addition, work is needed in the standardization of follow-up protocols, evaluation of ED management success and failure, patient selection, and statistical analysis. More randomized studies that compare various exercise techniques are warranted. These studies should evaluate efficacy, complications, quality of life, cost implications, and long-term outcomes of ED management compare to other therapeutic modalities available. Also more database search is also warranted to further broaden the data search on the topic.

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