Conservative Management of Erectile Dysfunction: A Literature Review

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ABSTRACT

Objective: Over the past couple decades the concept of erectile dysfunction (ED) has evolved, as well as treatment options for it. This article provides an overview of literature on the different types of treatment options available to men with ED. The treatments discussed are those that are most common, such as pharmacotherapy, and those that are fairly new. Studies were found to show each options efficacy in the treatment of ED along with any possible side effects.

Data Collection: Research was done using a Pub Med database search. The original search keyword of "erectile dysfunction" produced 13184 articles. A broader search of keyword "conservative treatment of erectile dysfunction" produced 75 articles. These articles brought another search of the keywords "yohimbe for erectile dysfunction", "hypnosis and erectile dysfunction", "acupuncture and erectile dysfunction", "nutrition and erectile dysfunction" on Pubmed. The selection of the articles was based on the subject topic of erectile dysfunction. This included topics of the management and treatment, both allopathic and holistic, and the use of yohimbe, acupuncture, hypnotherapy, internet therapy, pharmacotherapy, and other nutrition supplements in regards to erectile dysfunction. The date of the articles was taken into consideration, with preference to those dated in the late 1990's and after. The origin of the information was considered, taking preference toward those which were in accredited and established journals and the presence of the peer review.

Data Synthesis: ED, although mostly caused by organic factors, such as atheromatous arterial disease, venous insufficiency, endocrine disorders, neurological disorders, injury or operations has psychological factors as well. An understanding of the all these factors must come into play with a given patient and is crucial to determining proper treatment.

Conclusions: Emerging evidence suggests that psychological factors such as depression, anxiety, catastrophizing, fear avoidance, self-efficacy and coping style are important aspects which should be considered in the treatment of ED, particularly psychogenic ED. Treatment options aimed at combining a variety of approaches which address the both the organic and psychogenic factors involved should be considered. More research needs to be done with nutritional supplements effect on ED. There is also no research available with possible effects chiropractic may have on the management of ED.

Key Indexing Terms: erectile dysfunction, sildenafil, tadalafil, vardenafil, yohimbe, L-arginine, hypnotherapy, prosthesis, acupuncture, psychogenic erectile dysfunction

Introduction

Over the past couple decades the concept of erectile dysfunction has evolved. Once thought of as merely a disorder known as impotence and considered predominately psychogenic, ED is now a well-understood physiologic result of multiple risk factors which result in inadequate erectile function. (2, 5) The fist extensive epidemiologic study of male sexual behavior in the United States was carried out by Kinsey et.al in 1948. This study concluded that ED was prevalent in less than 1% of men age 30 or younger, less than 3% in men age 30-45, 6.7% in men age 45-55, 13.5% in those 55-65, 25% in those 65 and up, and 80% in those 80 years old and up. The downfall of this study was that its numbers for the men aged 55 and older were small and therefore insignificant. (5) It was not until the Massachusetts Aging study conducted in 1987-1989 and the national Health and Social Life Survey in 1992 that the prevalence of ED was accurately measured. (5) As stated in Cecil Textbook of Medicine, current estimates suggest that 10-15% of all American men suffer from ED, with the incidence progressively increased as men get older. Data from the Massachusetts Aging Study report that 52% of men 40-70 years of age experience some degree of ED. with the increasing prevalence of ED it is expected that ED will affect 322 million men by the 2025. (7)

The penis consists of three erectile bodies, the corpus spongiosum and the paired corpora cavernosa, and also the urethra. (1, 2) The urethra extends though the corpus spongiosum, and functions to excrete urine and semen. Each column is surrounded individually by connective tissue, the tunica albuginea. The penis is then enclosed by a thin layer of subcutaneous and connective tissue. This dual layer is freely moveable allowing for erection. (3)

The pudendal artery, a branch of the abdominal aorta, passes underneath the pelvic bone and terminates in the common penile artery. This artery can be compromised just by the sitting position inhibiting blood flow to this common penile artery. When this artery is damaged arterial insufficiency and subsequent ED can occur. A cavernosal artery supplies blood into each of the erectile bodies. (4)

The autonomic nervous system, through parasympathetic and sympathetic innervations, is involved in the creation of an erection, the maintenance of an erection, and ejaculation. The sensory nerves of the penis are supplied by the pudendal nerve which then carries input to the S2-S4 segment of the spinal cord. Most sensory fibers are located in the skin surrounding it with increased numbers on the glans penis. (1, 2, 4)

For an erection to occur there needs to first be some type of mental or erotic stimulation from the brain (psychogenic erection) or by some type of friction to the skin alone (reflexogenic erection). An erection also needs adequate function of the corporo-veno-occlusive mechanism in order to happen. Without this mechanism blood can prematurely leak from the penis resulting in erectile dysfunction known as venous leak. (4)

The causes of erectile dysfunction have traditionally been divided into two groups: organic and psychogenic. However, most cases of ED are multifactorial. Organic causes include pathologies that affect blood supply, nerve supply or desire. Psychogenic causes include difficulty in a relationship and negative body image, especially after a surgery or illness. (1, 2, 3) Risk factors of ED include smoking, alcohol consumption, vascular deficiency, hypertension, diabetes mellitus, and hyperlipidemia. If these pathologies alone do not cause ED the medications for them will. (1, 2)

In today's society there is an increasing demand for a more holistic approach to the care, treatment, and management of disease. In general people are finding that drugs and surgeries, which are supposed to help the problem, are actually doing the opposite. This trend can be seen in all aspects of health care, especially with problems of sexual dysfunction.

Erectile dysfunction (ED) poses a problem for men of all ages, cultural backgrounds, and ethnicity. The conventional treatment for this disorder consist of drug therapies and surgeries, which include the use of phosphodiesterase type 5 inhibitors (PDE5I's), Alprostadil pellets (MUSE), intracavernosal injections, vacuum devices, surgery, and psychosexual counseling (1). This literature review will present some conservative alternatives, such as the use of dietary

supplements, acupuncture, and different types of psychotherapy, for the treatment and management of ED. This literature review will also provide an overview of some of the current mainstream treatment options.

Discussion

The evaluation of men with ED has progressed from an extensive, invasive series of procedures to identify those patients who could be treated by injection therapy or surgery to identifying those at risk for ED, modifying their risk factors and subjecting them to oral therapy. (5) In 1998 sildenafil (Viagra), a phosphodiesterase 5 (PDE5) inhibitor, was approved by the food and drug administration as an oral treatment for those with ED. Since this time two more phosphodiesterase 5 inhibitors have been introduced to the market, vardenafil (Levitra) and tadalafil (Cialis). (5, 7, 8)These medications offer a more natural, non-invasive way to acquire an erection than injection and vacuum therapies and have become the more popular treatment option.

Medications

Sildenafil increases cGMP in the smooth muscle of the corpus cavernosum which results in prolonged vasodilatation and a firmer longer-lasting erection. (8) More than 20 million men have been treated with sildenafil since its inception and it has been shown to be effective in men that have ED due to diabetes, hypertension, coronary artery disease, peripheral vascular disease, and spinal cord injury, as well as after coronary artery bypass surgery, transurethral prostatectomy, and radical prostatectomy. (7) Patients are required to take their recommended dosage about 1 hour before engaging in sexual intercourse once daily and the effects could last anywhere for 30 min to 4-5 hours after administration. This medication needs to be taken on an empty stomach and the patient needs to take into account their diet because fatty foods slow the absorption rate. (8)

Vardenafil has much of the same characteristics as sildenafil as to duration of effects, maximum dosage, and dietary effects. However, it does have higher in

vitro potency which results in more rapid binding to PDE5 and it has a slower dissociation from this enzyme compared to both sildenafil and tadalafil.

Tadalafil has a different pharmokinetic profile than both sildenafil and vardenafil and can be taken with food and its efficacy can be maintained for at least 36 hours. However, unlike the other two this medication needs to be taken 2 hours before sexual intercourse. (7) All the PDE5's mentioned also require sexual stimulation prior to its use.

As with any medication there are contraindications of PDE5 inhibitor use and adverse side effects. One absolute contraindication is concomitant use of nitrates due to the fact that PDE5 inhibitors potentiate their hypotensive effects. Use of nonselective α- antagonists, doxazosin and terazosin, are another absolute contraindication. The most commonly reported adverse events include headache, facial flushing, dyspepsia, dizziness, and rhinitis. Abnormal vision is another adverse event reported with use of sildenafil, and slightly with vardenafil. Tadalafil users also report episodes of back pain and myalgia. (7, 8) Patients that use sildenafil that have ischemic heart disease and hypertension are associated with a higher incidence of adverse effects than those with diabetes (3.6%, 2.3%, and 1.9% respectively). (7) Also, safety concerns regarding the effects of tadalafil on sperm have been raised because it is also an inhibitor of PDE11. (7)

Nutritional Supplements

Due to the side effects with the traditional oral pharmacotherapy and the invasiveness of other treatments, patients have been looking for a more holistic approach to manage their ED. More nutritional supplements and herbs are being looked at to be helpful. In the literature collected the most popular herbal and nutritional supplements used have been yohimbine, L-arginine and ginko biloba. (9, 13, 28) Although these compounds lack adequate clinical trial to support their efficacy they do all have some degree of evidence that they may be helpful for ED. According to Mackay, improvements in the penile endothelial L-arginine-nitric oxide activity appear to be the unifying explanation for the actions of these

naturally occurring agents. (9) New research is also being done on the effects pomegranate juice may have on prevention and management of ED.

Yohimbine

One study done by Guay et.al attempted to better define the population of men responsive to yohimbine due to the fact tobacco was thought to affect the regimen of yohimbine more than the other risk factors. The study consisted of 18 nonsmoking men with erectile dysfunction. Guay et.al measured the nocturnal penile tumescence with the Rigiscan™ monitor, hormone profiles, answers to the Florida Sexual Health Questionnaire, and clinical responses at baseline and at two different doses of yohimbine. 50 % of the men were able to produce a successful erection for intercourse in more than 75% of the attempts. The yohimbine responders were found to have slightly higher serum testosterone levels, higher scores on the Florida Sexual Health Questionnaire, and improved increased rigidity on Rigiscan™ testing. They concluded by stating that yohimbine is an effective therapy to treat organic dysfunction in some men with ED. (12)

A meta-analysis of seven randomized trials with more than 400 particpants with ED with a variety of etiologies determined that yohimbine was better than a placebo for all forms of ED, especially with non-organic ED. However, patients need to be informed that the over-the-counter yohimbe supplement has questionable value and may not contain any of the active ingredients found in yohimbine. If interested the patients should be told to consult with their primary care physician to discuss if using the prescription form. (26, 27)

Even though yohimbine is a dietary supplement some side effects are possible. Such effects include palpitations, fine tremor, diastolic blood pressure elevation, anxiety, and nausea. (26)

L-arginine

L-arginine is an amino acid that functions as a precursor to the formation of nitric oxide, which mediates the relaxation of vascular and non-vascular smooth

muscle. L-arginine exist in a large concentration of our food supply such as legumes, whole grains, and nuts. These foods can provide several grams of L-arginine per day when consumed in moderate to large amounts. (26) The majority of L-arginine studies show positive treatment results. However, the data on the efficacy of L-arginine is mixed. In the review article written by Douglas MacKay MD, he discusses two different studies, one by Chen et al, the other by Zorgniotti and Lizza. The latter was a smaller, uncontrolled human clinical trial. The participants were given 2.8 g arginine per day for two weeks. 40 % of the patients in the treatment group reported significant improvement compared to those in the placebo group. The study by Chen et al was a larger, double blind trail in which 5g of L-arginine was given per day or matching placebo for six weeks. There was only 31% improvement rate subjectively. However those that did report improvement initially has low urinary nitric oxide output which doubled by the end of the study. (27)

Another study found by Kernohan et.al looked at the effect of NMI 861 on erectile function. NMI 861 is a combination of 7.7mg yohimbine tartrate and 6g L-arginine glutamate. NMI 861 was administered in 16 healthy male subjects and 12 healthy male subjects received a combination of NMI 861 with intravenous nitroglycerine (GTN). Systolic and diastolic blood pressures, pulse rates and adverse events were measured in each study. NMI was well tolerated by all subjects with no adverse events reported. There was no significant change in pulse or DBP between the placebo and the NMI 861. There was also no significant difference in the hypotensive response induced by GTN between the NMI 861 and the placebo groups. Kernohan et.al found that acute oral administration of NMI 861 was found to be well tolerated and bioavailable in healthy male subject. (11)

Ginko Biloba

Ginko Biloba is one of the more commonly used nutritional supplements used to manage ED. Ginko biloba facilitates microvascular circulation that may lead to an improvement in sexual function. A study by Paick and Lee found evidence

that ginko extract may directly elucidate smooth muscle relaxation. (27, 28) A placebo controlled, double blind randomized trial used 240mg daily of ginko extract for twenty four weeks versus placebo for vasculogenic ED. No significant difference was shown between either group. This emphasizes the need for future quality research. When compared to papverine injections, after 6-8 weeks increased blood supply was detected in some of the patients given the ginko extract by ultrasound techniques. After 6 months, 50% of these patients regained erectile function. Even though there is minimal evidence supporting the use of ginko biloba alone for the treatment of ED, it may improve overall vascular perfusion by increasing nitric oxide availability, thus having a place in "whole patient" care. Also, in the few studies that were conducted using ginko there we very few adverse side effects reported, the worst being headaches. (26, 27, 28)

Pomegranate Juice

Pomegranate juice has been used as folk medicine in many cultures. It is a rich source of potent polyphenolic, flavonoid antioxidants (anthocyanins), which have been shown to possess anti-atherogenic properties. Dietary consumption of flavonoids has been shown to be inversely related to morbidity and mortality from coronary artery disease. Consumption of pomegranate juice by humans has shown reductions in systemic blood pressure and slows the progression of atherosclerosis. (21, 22) In a study done by Ignarro et al these findings were consistent in what they found. Their findings proved that pomegranate juice showed antioxidant activity that is sufficient to protect nitric oxide against oxidative destruction and thereby enhance the biological actions of nitric oxide. (21)

Due to the fact that erectile tumescence and rigidity require significant dilation of the penile arteries, nitric oxide deficiency may manifest as ED. This can be considered the fist manifestation of atherosclerotic disease. Pomegranate juice has potential benefit for ED due to its ability to decrease fibrosis, increase nitric oxide bioavailability and reduce atherosclerotic plaque. (21, 22) Forest et al examined the efficacy of pomegranate juice versus a placebo. 53 subects with

mild to moderate ED completed the study. However no statistical significance was found, a trend was demonstrated toward benefit of erectile dysfunction. Few adverse effects were reported, however none serious. The most commonly reported were upper respiratory infections and pharyngitis (8%), and then diarrhea and flatulence (2%). (22) Further studies on this topic need to be done to clarify the role pomegranate juice may have on ED. (21, 22)

Other Alternatives

In addition to recent advances in the medications for erectile dysfunction alternative therapies such as therapy, hypnosis and acupuncture have become increasingly popular. Most men are shying away from conventional therapies due to concerns about side effects and lack of efficacy. In 1990, 427 million visited alternative medicine practitioners. This number increased to 629 million by 1997, a 47.3% increase. (18)

Acupuncture

Acupuncture is mostly known for its role in pain reduction. However, there is significant clinical evidence to suggest that acupuncture has a regulatory effect on the nervous, circulatory and endocrine systems. A popular hypothesis for this statement is that acupuncture stimulates nerve receptors at point locations, transmitting signals to specific areas of the central nervous system, which initiate physiological changes in the body. (18)

A study was done by Kho et al evaluate the effect of acupuncture as a mono-therapy in patients with ED. The study was comprised of 13 patients, 9 with psychogenic ED and 4 with organic. Though the study was limited due to it was able to demonstrate a positive effect of acupuncture as a monotherapy. After treatment was completed 2 patients had a better erection, and 4 had increase in sexual activity. Two months after the initial treatments 5 patients still experienced improvements in sexual activity and quality of erection. The overall improvement rate of the study was 54%, or 7 out of 13. (19) This percentage was lower than other acupuncture studies which showed about 70% improvement.

The authors attributed this to not individualizing the treatment given to the subjects as well as not all the subjects had psychogenic ED compared to previous studies. (19)

Another study conducted by Engelhradt et al, where all the subjects were suffering from psychogenic ED, indicated that acupuncture can be effective as a treatment option in more than two-thirds of patients with psychogenic ED. In 13 out of 19 patients (68.4%) acupuncture was effective and no further therapy became necessary. This study was also the first attempt to conduct a randomized, prospective trail, where acupuncture was tested against a valid placebo. In the placebo group acupuncture points that were not specifically recommended for ED but those points chosen for chronic pain were used. (20)

Side effects form acupuncture has been minimal in the hands of a well trained practitioner. Forgotten needles and transient hypotension were the most commonly reported problems. However, when performed by a person who has not received any or improper training severe side effects, such as pneumothorax and infection form an aseptic procedure, are possible. (18, 19, 20)

Hypnosis

The literature on the effects of hypnosis on ED has been researched since the 1970s. Most patients suffering form ED are reluctant to bring their sexual problems to the attention of their physician, and if they do are not completely honest. This type of therapy, unlike conventional sex therapy, works primarily with the patients' unconscious processes in order to influence them in the desired direction of health and welfare. (14,15,16) According to an article by James A. Hall, MD (1978), in jungian psychoanalytic theory, the unconscious mind continually presses for a healthy ego, particularly in dreams, and seems to welcome suggestions for healthy functioning unless there is a severe neurotic conflict involving competing ego-images. This is the goal of hypnosis, building up in the patient's unconscious mind the ego-model of normal, healthy sexual function. (14) During a hypnotic state the trained physician can use uncovering techniques such as word-association, dream analysis, and age-regression.

These techniques are used to help the patient work through the dynamics of his problem. Age- regression specifically may result in memory recall or revivification which is usually accompanied by considerable effect. Ego-building and the breaking of maladaptive patterns are made possible following the uncovering of repressed and suppressed predisposing factors which make the therapeutic effect much more dynamic.(14, 15)

Hypnosis is found to have a great effect on ED that is psychogenic in nature. Patients that have organic ED found some benefit to hypnotherapy due to the fact that sexual failure is linked to self-esteem and feelings of adequacy before or after the onset of symptoms. In an article entitled *Hypnotic Techniques for Smoking Control and psychogenic Impotence (1990)* by Harold Crasilneck, out of the 2,892 patients that he treated for impotence he had a success rate of 88% in those with psychogenic ED. Crasilneck also achieved a reasonably good response in 45% of his patients that had organic causes of ED. (16)

In a more recent study done by Aydin et al, the efficacy of testosterone, trazodone and hypnotic suggestion for the treatment of ED was compared. The results for hypnosis saw an 80% improvement, which were similar to those of Crasilneck. (14, 17) Aydin et al concluded that hypnosis was the more promising treatment for non-organic male sexual dysfunction compared to that of testosterone and trazodone. (17)

Aydin et al have recently compared acupuncture vs. hypnosis vs. oral placebo vs. placebo needle therapy in 29 patients. They proved that acupuncture and hypnosis were successful in 60 and 70% respectively. (20)

As with any treatment there are precautions to those who wish to utilize hypnotherapy. For example, the patient should be free of psychosis, suicidal thoughts or excessive anxiety regarding hypnosis. The patient should have a clear understanding that hypnotherapy is a cooperative effort of the therapist and the patient to mobilize the healthy aspects of the patients' unconscious mind to aid in solving their problem. Hypnotherapy should only be used by professionals that are qualified to treat the same problems without hypnosis. (14, 15, 16, 17)

Psychosocial Therapy

Sex therapists are trained to remotivate patients in whom other type of treatments have failed as well as dealing with issues, such as the patients perception that their current treatment is temporary or that the patient has unrealistic expectations. The integration of psychosexual therapy and pharmacotherapy may be required in some cases due to the fact that many psychosocial factors adversely influence the efficacy of sildenafil and result in non-compliance with treatment. (24) A meta-analysis revealed that there is evidence that group therapy improves ED. Specifically focused group therapy showed greater efficacy than the control group. Also, men receiving both psychotherapy and sildenafil showed significant improvement in their ED and were less likely to drop out of care than those just taking the medication. (30)

Over the past decade the use of the internet has had a profound effect on health-care delivery. More and more patients are using health-related websites as a first source of information and support for their mental and/or physical problems. Before they consult a health care practitioner more and more people are visiting the worldwide web to search for possible causes and treatments for their complaints. In the case of those with erectile dysfunction, the internet offers them a safe place to research their problem without being judged or embarrassed. Van Diest et al examined the effects on internet therapy on sexual dysfunction in heterosexual men in a subjects-as-own-control design with pre-, post- and follow-up measurements using validated questionnaires. Two thirds of the participants utilizing the website reported significant improvement of their sexual functioning after receiving the therapy via internet. At the follow up 50% still reported improvement in their sexual functioning. This type of treatment appears to replicate the efficacy of face-to-face therapy for men with erectile problems. (29)

Chiropractic

There was a lack of literature to define chiropractics role in ED. It can be hypothesized that chiropractic can be beneficial in combination with other

therapies given the anatomy involved in the male erection. According to the article by Wagner and de Tejada, the penile blood vessels and trabecular smooth muscle have both motor sympathetic and parasympathetic innervation from fibers arising in the thoracolumbar and lumbosacral regions. The striated muscles outside the tunica albuginea are innervated by lumbosacral somatic nerves. Sympathetic, parasympathetic, and somatic systems act in a coordinated way and an interruption of any of these pathways may preclude normal erections. (25)

Prosthesis and Surgery

More invasive therapies such as intracorporeal injections, intraurethral injections, vacuum devices, and penile prosthesis are also options. However, patients prefer to start with the oral pharmacotherapy and use these options as a last resort. (1)

Surgery

If ED is caused by a veno-occlusive dysfunction, removal and/or ligation of the offending veins is an option. This surgical procedure gives cure in 40 to 60% of the cases with some degree of improvement in the rest. However due to its lack of durability it is being abandoned in many centers. One upside to this treatment option is the young patient is spared the prospect of an inevitable penile implant. (23)

Prosthesis

In most patients with ED, for example the older patient with diabetes or blood pressure/heart problems, penile prosthesis is usually the only guarantee of restoring erection. The overall success rate of these devices is about 90%, but sensation, ejaculation and orgasm are not affected. Three main types of prosthesis exist: the semi-rigid, self-contained inflatable and the multi-component inflatable. The multi component inflatable gives the most natural results. Penile prosthetics have long term mechanical reliability and patient satisfaction rates of

more than 85%. However one has to keep in mind that these devices are susceptible to mechanical failure which may require revisional surgery, which may carry significant morbidity. Also, if surgery fails the patient is left with a penis permanently incapable of erections. (23, 24)

Conclusions

This literature review was done to present an understanding of the traditional treatments offered as well as how nutritional and herbal supplements, along with possible acupuncture, hypnosis, and sex therapy have been used and can be used to help treat and manage ED. Although the ideal treatment for ED has yet to be found this review outlines some of the treatment options that are currently available. One thing that is consistent in the literature is the reluctance to bring up the disease by both the physician and the patient due to its awkward nature. Improvement in training of the management of sexual dysfunctions at both the undergraduate and postgraduate level could help alleviate this problem on the clinical side. The public also requires better information about the availability of treatment.

ED, even though mostly caused by an organic factor, such as a systemic disease like diabetes, etc, often has psychogenic factors associated. When faced with ED, whether organic in nature, purely psychogenic, or mix of both, the patient will often become depressed, have increased anxiety, lower self-esteem, or inability to function psychologically in desired sexual situations. In the literature several studies noted that even though the newer pharmacotherapy's like sildenafil are effective there is greater efficacy if combined with some type of therapy.

Further research needs to be done on nutritional effects on ED. The few studies that were found that pertained to yohimbe, L-arginine, and ginko biloba were small and had mixed data concerning efficacy. More randomized trials are needed so that dietary supplements can have the opportunity to become part of the mainstream. However this would indicate a need for further funding. Most of the current research is funded by pharmaceutical companies. When researching

for alternative treatments it was surprising to find no research done on the effects chiropractic may have on erectile dysfunction, if any. It could be believed due to the neuroanatomy involved that chiropractic may be a powerful adjunct to most of the treatments discussed in this review.

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