ORIGINAL ARTICLE

Administration of Testosterone and its Rationale in the Treatment of Erectile Dysfunction

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ABSTRACT

Background: Despite increasing use of testosterone in the management erectile dysfunction, debate remains regarding the selection of candidate for the hormonal treatment. The aim of this study is to find out the role of testosterone in erectile dysfunction (ED), the incidence of testosterone deficiency in the patient of ED and therapeutic response of testosterone in ED in common practice.

Material & Methods: This cross-sectional study had conducted among the patients with age above 30 years, complaining of erectile dysfunction treated with testosterone by self-medication or clinical practitioners. Total 103 cases interviewed, who attended the private chamber of Urologists and the Urology OPD, BIRDEM General Hospital between periods of April 2014 to September 2015.

Result: Of 103 cases, testosterone level was normal in 78.6% cases. All were treated with testosterone. Among the participants 47.57% were between 30-40 years and 9.09% were of the age between 60-70 years. Twenty-two patients having testosterone deficit were treated with testosterone supplement and marked improvement was observed (88.1%). In this study 49 patients having normal testosterone level received testosterone along with sildenafil or tadalafil, of these 47 cases (95%) had moderate to marked improvement. On the other hand 32 patients having normal testosterone level received testosterone monotherapy but there was no improvement in 87.5% cases.

Conclusion: The result of the study suggests that testosterone replacement therapy is beneficial in patient of ED due to hypogonadism. However, testosterone monotherapy in erectile dysfunction with normal testosterone level should be considered injudicious.

Key Words: erectile dysfunction, testosterone, sildenafil, tadalafil

Introduction

A study reported that there were about 152 million men with complaints of erectile problems in the whole world in 1995, and this number would rise to approximately 322 million in 2025[1]. Particularly in the early 1980s, significant advances in the knowledge and comprehension of erectile physiology were made; new knowledge regarding the importance of organic causes has led to the change of prevailing perception that most EDs have a psychogenic origin[2]. Since ED is a disease of the aging, it is quite difficult to determine an isolated single factor in its etiology, because in aged individuals, systemic diseases including diabetes mellitus (DM), renal insufficiency and cardiovascular diseases, hormonal changes, chronic use of medications, surgical interventions and aging of tissues become isolated or cumulative underlying factors. Recent studies have shown that testosterone (T) deficiency can lead to diseases with potential morbidity such as metabolic syndrome, osteoporosis, and coronary artery disease. Although the role of hormones in ED has not been fully clarified, some indicative data have been obtained.

Hormones that may be possibly related to ED are androgens (testosterone = T, dihydrotestosterone = DHT, androstenedione, dehydroepiandrosterone = DHEA and dehydroepiandrosterone-sulphate = DHEA SO4), estrogens (in particularly, estradiol = E2), insulin (cause of DM and consequently, an indirect cause of ED), thyroid hormones, prolactin (PRL), melatonin, leptin and growth hormone (GH). It has been demonstrated that hormones are responsible for about 5% of ED cases with organic causes. In particular, a serum T level of <300 ng/dLis found in 10-20% of ED patients[3,4].

The introduction of phosphodiesterase[5] (PDE5) inhibitors for treatment of ED was a major step forward due to their efficacy, safety and simple use. However, approximately one third of patients do not respond to PDE5 inhibitors.[5] Moreover, patients taking nitrates cannot take PDE5 inhibitors.[6-8] In addition, theseagents have no effect on libido,[5-8] an essential componentof sexual function. Although the role of testosterone inimproving libido is well known,its exact function inthe pathophysiology of erection is still ill defined. However, testosterone is widely prescribed by general practitioners for the treatment of ED.

Our aim was to see the effect of testosterone on ED and its judicious use among the patients of erectile dysfunction who were treated with testosterone by self-medication or practitioners.

Materialand Methods

This cross-sectional study had conducted among the patients with age above 30 years, complaining of erectile dysfunction treated with testosterone by self-medication or clinical practitioners. Total 103 cases interviewed, who attended the private chamber of Urologists and the Urology OPD, BIRDEM General Hospital between periods of April 2014 to September 2015. All cases were invited to answer voluntarily the IIEF-5 questionnaire containing 15 questions. It discusses the following parameters of sexual function: erectile function, orgasmic function, sexual desire, satisfaction with relations and overall satisfaction. The relevant investigations done previously were also reviewed.

Data were collected, processed, analyzed, and evaluated statistically using Analysis of Variance (ANOVA) and the Student's t-test. Chi-square test was used for proportional data. An alpha of 5% ($P<0.05$) was considered for purposes of statistical significance.

Result

A total 103 patients of ED were included in this study based on inclusion & exclusion criteria. Age distribution of the study population is plotted in table 1 which shows that majority of the study population was in 30-40 years of age group (61.5% & 50% in no deficiency & testosterone deficiency groups respectively).

Age distribution Normal testosterone % Testosterone deficiency %

Table I: Age distribution of the study population

Age distribution	Normal testosterone	%	Testosterone deficiency	%
30-40	49	47.57	11	10.68
40-50	17	16.50	6	5.83
50-60	8	7.77	3	2.91
60-70	7	6.80	2	1.94
N	**81**	**78.64**	**22**	**21.36**
Mean ± SD (Years)	36 ± 1.9		38 ± 2.3	

Among the total number of 103 study population, testosterone was given in 103 patients (59.5%). 78.6% (81) patients out of 103 patients of testosterone therapy had normal testosterone level where as 22 (21.4%) patients had testosterone deficit. Table 3 reflects that patients with low testosterone responded quite well (88.1%) to testosterone therapy with improvement of libido and erectile performance. On the contrary, patients with normal testosterone level 32 patients (39.5%) who treated with testosterone therapy alone does not show satisfactory change in erectile performance and the patient with normal testosterone group who are treated with sildenafil or tadalafil along with testosterone (49 patients 60.5%), shows satisfactory improvement in erectile function. P-value was quite significant here (<0.01) (Table 2). Analysis of this finding can be inferred, as patients of erectile dysfunction having normal testosterone level do not show further improvement in testosterone treatment.

Table II: Modalities of treatment and their response

Category	Treatment options	Treatment response for ED			*P* value
		Marked improvement	Moderate improvement	Poor improvement	
Testosterone Deficiency *(n=22, 21.4%)*	Testosterone **22 (100%)**	20 (88.1%)	00	02 (11.09%)	<0.01
	Testosterone + Sildenafil / Tadalafil **0 (0%)**	00	00	00	
Normal Testosterone *(n=81, 78.6%)*	Testosterone **32 (39.5%)**	00	04 (12.5%)	28 (87.5%)	<0.01
	Testosterone + Sildenafil / Tadalafil **49 (60.5%)**	00	47 (95%)	02 (5%)	

Discussion

This study was conducted to see the rationality of use of testosterone among the patient complaining of erectile dysfunction. Experimental animal studies have demonstrated the relationship between testosterone and ED[9]. In patients for whom testosterone replacement therapy (TRT) has been planned, the complaints and symptoms related to erectile dysfunction can be nonspecific. Although there is no definite evaluation method for the diagnosis, in the first examination, questionnaires such as the IIEF (international index of erectile dysfunction), ADAM (androgen decline in the aging male) and AMS (aging male survey) should be used. Investigation of the serum Testosterone level is recommended when there are high symptom scores accompanied by ED, lack of libido, loss of muscle mass, metabolic syndrome and diabetes mellitus type 2[10]. The first choice of therapy in ED is PDE-5 inhibitors, but this therapy results in no response in 30-50% of the patients. When TRT is added to the therapy of non-responders, the outcome is positive[11].

The data in this study do not refiect the ED prevalence in this region. The participants, however, sought medical care for ED. Moreover, the population studied did not consist only of the aged, and also did not include subjects who were being followed up for some andrological problem. The interest in researching the erectile function was only revealed at the time of the interview, and the patients were not previously aware of the objective of the study. The questionnaire used in this study as a diagnostic tool is currently the only one recommended by the National Institute of Health (1993) to evaluate penile erectile function[12]. Furthermore, it allows a grading of ED severity. The direct relationship between ED and aging is well established, by data from several studies[12,13]. In our study most of the patient receiving treatment for ED is young. An interesting socio-cultural influence is well exhibited in the result i.e decline of incidence of taking treatment in advanced age group seems due to acceptance of reduced sexual activity in older age in our country.

In our study, testosterone deficit was noted in 22 cases and they were treated with testosterone replacement therapy showed marked improvement (88.1%) of erectile performance with improvement of libido.

Various studies show the same result. In a study by MoraleyA et al showed testosterone replacement therapy was associated with significant efficacy in the treatment of hypogonadism and ED, with improvement in sexual attitudes and performance in 61% of patients[14]. A meta-analysis indicated 57% efficacy for testosterone replacement therapy in patients with ED and hypogonadism, ranging from 64% for primary hypogonadism to 44% for secondary hypogonadism[15]. In another study, testosterone monotherapy improved erectile function and penile vascular abnormalities in 36% and 42% of cases respectively[16]. In general, testosterone monotherapy for the treatment of ED is efficacious in men when the sole cause of ED is hypogonadism. But it is often not efficacious in other pathophysiologies such as vascular disease and neuropathy.

In this study, 49 patient who had normal testosterone level but received testosterone along with sildenafil or tadalafil. Of these 47 cases (95%) had moderate improvement of erectile performance. Other studies have confirmed the beneficial effects of combination therapy. The combination of testosterone and sildenafil were shown to improve erectile function in eugonadal men[17]. This improvement was superior to sildenafil or testosterone alone[17]. Chaterjee et al showed administration of intramuscular testosterone and sildenafil was efficacious in eugonadal man[18]. Oral testosterone was reported to reverse ED

associated with type 2 diabetes in patients failing on sildenafil therapy alone[18]. In a recent study, a total of 49 hypogonadal men with ED received T-gel for 6 months. Sildenafil was added at 3 months to those with no efficacy of T-gel alone. A total of 31 patients reported significant improvement in the sexual desire and erectile function with testosterone alone. In spite of normalization of total and bioavailable testosterone values, and significant improvement of sexual desire, the erectile function of 17 men did not improve[19]. These men received combined T-gel and sildenafil, after which all reported improvement in erectile function. A prospective study included hypogonadal men failing to respond to sildenafil or partially responding to sildenafil. Men receiving both sildenafil plus testosterone replacement therapy showed significant improvement in erectile function[20].

However, the patient with normal testosterone treated with only testosterone supplement for erectile dysfunction does not show satisfactory change in erectile performance (12.5%). Other study support our study. At present, there is no basis for large-scale testosterone replacement therapy in older men, unless they have symptomatic androgen deficiency[21,22]. Testosterone levels needed for normal sexual function vary among individuals. Some men may have normal sexual function even if their testosterone levels fall into the ageadjusted lower normal range[22]. However, in patients with sexual dysfunction, testosterone testing is advised to screen for hypogonadism[23], and testosterone replacement therapy is appropriate when clinical symptoms and biochemical evidence of hypogonadism exist[21,23]. Hypogonadal men with specific sexual dysfunctions such as ED, diminished libido, or both, are candidates for testosterone replacement therapy[21,23]. Testosterone monotherapy may correct sexual dysfunction caused by hypogonadism, but absence of an adequate response may require further evaluation to exclude associated comorbidities, such as those causing vasculogenic or neurogenic ED[23].

Conclusion

This study corroborates the data from the literature as regard as the relationship between ED and testosterone. Testosterone replacement therapy is clearly indicated in hypogonadism patients and is beneficial in patient with ED and hypogonadism. However, testosterone monotherapy for erectile dysfunction without identified hypogonadismis being prescribed by the practitioners are ineffective and therefore can be opined as injudicious. Adult ED cases can be effectively treated with PDE5 inhibitors or other vasodilators in most of the cases.

Conflict of interest: Authors declared that they have no conflict of interest.

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