Effect of Tadalafil on Penile Duplex parameters in Erectile Dysfunction Patients

Ali Mohamed Younis[a], Mohamed Amer Ahmed Abdellatif [a]*, Mahmoud Ahmed Ali[a], Mohammed Abu El-Hamd Ali [b], Abdallah Mahmoud El-Ebidi[c], Salah Mohamed Ali Maklad[d], Essam El-Din Abdel-Aziz Nada[b], Moustafa Adam Ali El Taieb[a]

[a]Department of Dermatology, Venereology And Andrology, Faculty of Medicine, Aswan University, Aswan, Egypt.
[b]Department of Dermatology, Venereology And Andrology, Faculty of Medicine, Sohag University, Sohag, Egypt.
[c]Department of Medical Biochemistry, Faculty of Medicine, Aswan University, Aswan, Egypt.
[d]Department of Diagnostic Radiology, Faculty of Medicine, Aswan University, Aswan, Egypt.

Abstract

Background: Tadalafil is a PDE-5 (phosphodiesterase inhibitor) inhibitor that supports endogenous nitric oxide's vasodilatory actions and aids in erection maintenance. The penile duplex has proven to be very useful for imaging superficial structures and for determining the reasons of erectile dysfunction (ED).

Objectives: To assess the effect of daily oral tadalafil 5mg for 3 months on penile duplex parameters in erectile dysfunction patients.

Patients and Methods: A case control study involved 30 Egyptian patients ED. Appropriate clinical history and penile duplex examination before and after treatment with daily oral tadalafil mg for 3 months were performed.

Results: The mean age of the patients was 53.17 ± 7.8 years. We founded that there was significant ($p < 0.001$) improvement in the level of erection after treatment. The rate of erection E1 and E2 was decreased from 53.3% to 3.3%. Likewise, the rate of E3-E5 was increased from 46.7% to 96.7%. Moreover, the mean duration of erection was elongated from 24.7 ± 5.3 to become 37.4 ± 3.8 and this was statistically significant ($p < 0.001$). Also, the mean peak systolic volume (PSV) was significantly ($p = 0.001$) increased after treatment (38.4 ± 9.1 cm/s) compared with the pre-treatment levels (23.9 ± 6.1 cm/s). Unlikely, the mean end diastolic volume (EDV) was insignificantly ($p = 0.340$) lower in post-treatment (2.25 ± 0.5 mL) compared with pre-treatment levels (2.97 ± 0.4 mL). Likely, the mean resistant index (RI) showed insignificant difference ($p = 0.965$) after treatment (0.9 ± 0.02) compared with before treatment (0.9 ± 0.08). For penile artery diameter, there was significant ($p = 0.009$) increase in the diameter after treatment (0.9 ± 0.1 mm) compared with before treatment (0.8 ± 0.1 mm).

Conclusion: Oral daily tadalafil 5mg for 3 months is considered an effective treatment for ED according to penile duplex parameters.

Keywords: Tadalafil; Penile duplex; Erectile dysfunction

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***Correspondence:** mohammed.abdellatif@med.aswu.edu.eg

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Introduction

The inability to repeatedly achieve or sustain a penile erection strong enough to allow for satisfying sexual performance is known as erectile dysfunction (ED). Vascular variables predominate in the aetiology of ED, with psychogenic factors coming in second. **(Faselis et al., 2020).**

Incidence: The prevalence of ED was 1–10% in males under the age of 40 and 2%–9% in men between the ages of 40 and 49, according to data from the International Consultation Committee. The incidence of ED rises with age. It rises to 20–40% in males 60–69 years old and 50–100% in those over 70 years old. **(Lewis et al., 2010).**

With coronary disease, which it shares risk factors like obesity, smoking, dyslipidemia, and metabolic syndrome, ED can be a manifestation of peripheral atherosclerosis and a possible early sign of coronary disease. **(Gandaglia et al., 2014).**

Because endothelial cells play a crucial role in maintaining vascular homeostasis, a number of pathological diseases that impact blood vessels, such as atherosclerosis, can result in vasculogenic ED. **(Zamorano-Leon et al, 2018).**

Since submillimeter-scale anatomical structures and blood flow in tiny arteries can be examined in real time, penile duplex has proven to be extremely useful for imaging superficial structures as ultrasonography technology has advanced. **(Jung et al., 2018).**

The most reliable marker of arterial illness is peak systolic velocity (PSV). When the PSV is less than 25 cm/sec, 92% of the time, arterial insufficiency can be accurately identified. End diastolic volume (EDV) over 5 cm/sec was consistently present in veno-occlusive ED during all stages of erection. **(Gratzke et al., 2010).**

The first-line therapy for ED is oral (PDE-5) antagonists. **(Yuan et al., 2013).**

An erection must be induced by sexual stimulus, and the PDE-5 inhibitor aids in erection maintenance by amplifying endogenous nitric oxide's vasodilatory effects. The U.S. Food and Drug Administration (FDA) has recently authorised the use of four PDE-5 inhibitors for the treatment of ED, including avanafil, sildenafil, tadalafil, and vardenafil. These drugs have comparable efficacy and safety profiles. **(Ückert et al., 2013).** Our study's objective was to evaluate the impact of oral tadalafil 5 mg daily for three months on the penile duplex characteristics of ED patients.

Patients and methods

After the approval of our ethical committee and written informed consent from all participants, the study included 30 patients complaining from ED who attending the Outpatient clinic of Dermatology, Venereology and Andrology, Aswan University Hospital, Aswan University, during the period from April 2018 and Marsh 2021. After taking detailed history from each participant in our study, complete clinical examination was done.

Penile duplex examination for all patients before and after treatment.

Inclusion criteria: Patients with ED

Exclusion criteria: Patients with history of pelvic trauma or pelvic surgical intervention, Patients with hypogonadism,

hyperprolactinemia, chronic liver disease, cardiovascular system diseases, chronic intake of central nervous system, anti androgen drugs or other drugs as tramadol, smokers and any blood diseases as hemophilia, purpura and anemia.

All patients were assessed by:

- Detailed history of medical diseases as renal, hepatic and cardiac diseases and history of previous surgical operations, family history and sexual history.
- Consent from the patient.
- Medical examination included general and local examination.
- Penile duplex examination before and after treatment.

Treatment protocols: Each patient treated with daily oral 5mg tadalafil for 3 months. Each patient was assessed by penile duplex before and after treatment.

Ethical considerations: Approval for this study was obtained from Institutional review board (IRB) of Faculty of Medicine-Aswan University prior to study execution. In addition, all participants received a written consent form.

Statistical analysis

The statistical analysis was done via statistical package for social sciences (SPSS) version 22 (SPSS Inc, Chicago, USA). For qualitative data, frequency and percent distributions was calculated.

Results

The current study included 30 patients with history of ED with mean age 53.17 ± 7.8 years.The results of current study showed significant ($p < 0.001$) improvement in the level of erection after treatment. The rate of E1 and E2 was decreased from 53.3% to 3.3%. Likewise, the rate of E3-E5 was increased from 46.7% to 96.7%, **(Table 1)**.

Table 1. Effect of treatment on degree of erection

Parameter (n=30)	Pre-treatment	Post-treatment	P-value*
Erection degree			
E1	3 (10%)	0 (0%)	**< 0.001**
E2	13 (43.3%)	1(3.3%)	
E3	11 (36.7%)	8 (26.7%)	
E4	3 (10%)	20 (66.7%)	
E5	0 (0%)	1 (3.3%)	

Moreover, the mean duration of erection was elongated from 24.7 ± 5.3 to become 37.4 ± 3.8 and this was statistically significant ($p < 0.001$) **(Table 2, Fig. 1)**.

Table 2. Effect of treatment on duration of erection and penile artery diameter.

Parameter (n=30)	Pre-treatment	Post-treatment	P-value*
Duration of erection	24.66 ± 5.3	37.41 ± 3.8	**< 0.001**
Penile artery diameter/cm	0.08 ± 0.01	0.09 ± 0.01	**= 0.009**

On the other hand, and for the penile artery diameter, there was significant ($p = 0.009$) increase in the diameter after treatment (0.9 ± 0.1 mm) compared with before treatment (0.8 ± 0.1 mm) **(Table 2,Fig. 2).**

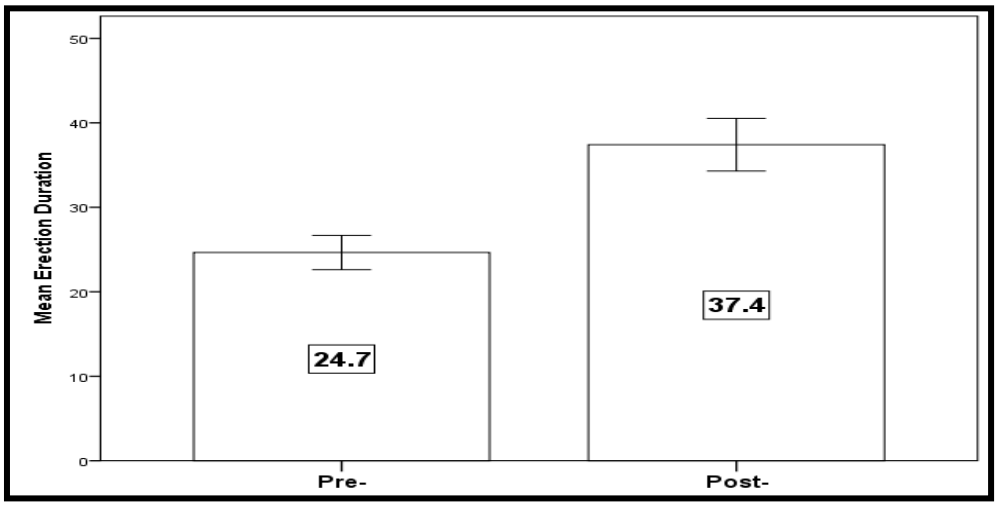

Fig. 1. Effect of treatment on erection duration among patients

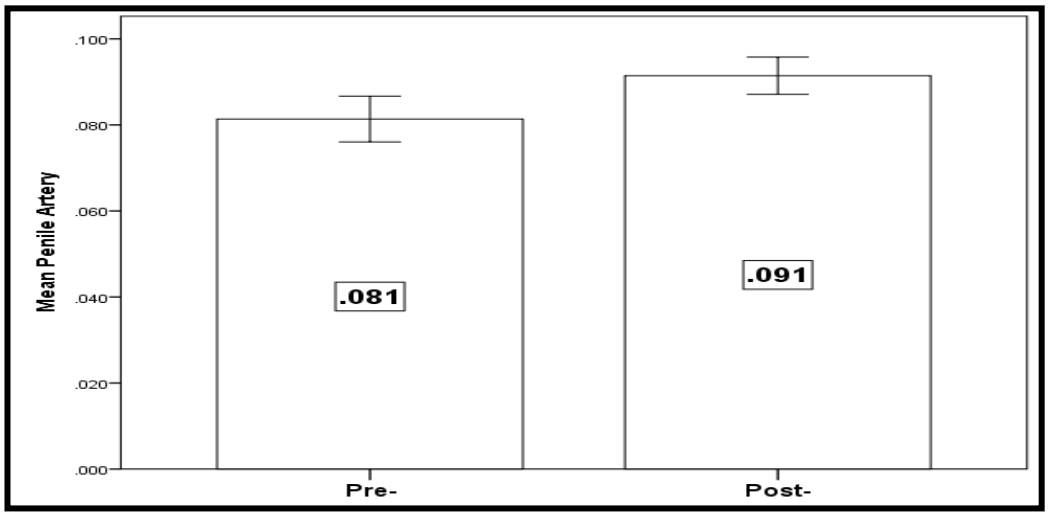

Fig. 2. Effect of treatment on the penile artery diameter among patients

Also, the mean peak systolic volume (PSV) was significantly (p = 0.001) increased after treatment (38.4 ± 9.1 cm/s) compared with the pre-treatment levels (23.9 ± 6.1 cm/s) **(Table 3, Fig. 3).**

Unlikely, the mean end diastolic volume (EDV) was insignificantly (p = 0.340) lower in post-treatment (2.25 ± 0.5 mL) compared with pre-treatment levels (2.97 ± 0.4 mL). Likely, the mean resistant index (RI) showed insignificant difference (p = 0.965) after treatment (0.9 ± 0.02) compared with before treatment (0.9 ± 0.08) **(Table 3).**

Table 3. Effect of treatment on penile duplex parameters.

Parameter (n=30)	Pre-treatment	Post-treatment	P-value*
PSV	23.86 ± 6.1	38.35 ± 9.1	**= 0.001**
EDV	2.97 ± 0.4	2.25 ± 0.5	= 0.340
RI	0.90 ± 0.08	0.90 ± 0.02	= 0.965

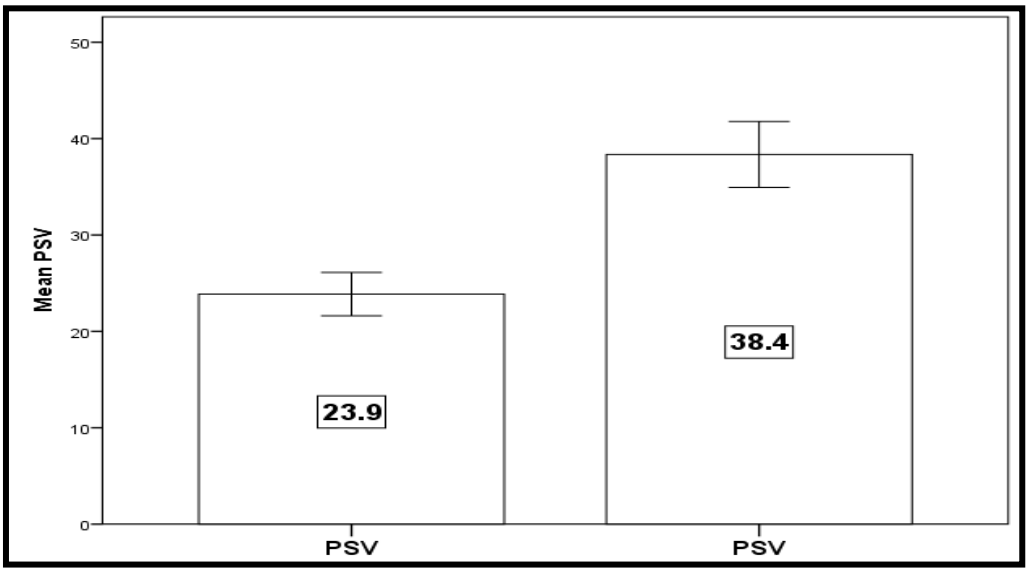

Fig. 3. Effect of treatment on the PSV among patients.

The rate of improvement of the studied parameters after treatment among cases showed that PSV absolute change was 14.1 m/s representing 69% increase, EDV absolute change was -1 m/s representing 2.8% decrease, RI absolute change was 0.01 m/s representing 1.3% increase, Penile artery diameter absolute change was 0.009 mm representing 15% increase **(Table 4).**

Side effects for daily oral tadalafil 5mg noticed by the patients included: headaches in 26.6 %, nausea in 10%, facial flushing in 20%, stuffy nose in 30%, muscle aches in 13.3% and indigestion in 23.3% of patients.

Recurrence rate after 3 month treatment with low dose of daily oral tadalafil 5mg in this stud was 30%.

Table 4. Rate of improvement of the studied parameters after treatment among patients

Parameter (n=30)	Improvement percentage	
	Absolute Change	**Relative%**
• **Erection duration**	12.9 ± 1.6	58 ± 9
• **PSV**	14.1 ± 1.9	69 ± 12
• **EDV**	-1 ± 0.7	2.8 ± 1.1
• **RI**	0.01 ± 0.01	1.3 ± 0.2
• **Penile artery diameter**	0.009 ± 0.003	15 ± 5

Discussion

The current study aimed to assess effect of treatment with daily tadalafil 5mg for 3 months on penile duplex parameters of ED.

In our study there was a significant increase in penile erection degree after ICI with 1ml psotaglandin E2. The rate of E1 and E2 was decreased from 53.3% to 3.3%. Likewise, the rate of E3-E5 was increased from 46.7% to 96.7%. There was a significant increase in duration of erection after treatment.

Regarding penile duplex findings there was a significant increase in PSV, insignificant decrease in EDV, insignificant decrease in RI, and significant increase in penile artery diameter/cm after treatment.

Yang et al. (2011) founded that mean PSV was 36.06 cm/sec, mean EDV was -2.306cm/sec and mean RI was 1.054 however these result measured after oral intake of 20mg tadalafil before penile duplex which closely matching our results In PSV and not matching our results in EDV and RI. This mismatching between two studies may be due to different treatment protocols, different sample sizes, and different mean age.

Aversa et al. (2007) compared the effect of oral tadalafil on penile duplex in two groups, first group with oral tadalafil 20mg on alternate days for four weeks and second group with oral tadalafil 20 mg on demand before penile duplex and showed significant increase in PSV from 9.570.4cm/s pre-treatment to 13.270.1 cm/s post-treatment with oral tadalafil 20mg on alternate days for four weeks and significant increase in PSV from 9.370.3 cm/s to 10.470.9 cm/s after oral tadalafil 20 on demand before penile duplex (P-value 0.05 in both groups).

In comparison with our results **Aversa et al.(2007)** founded a significant increase in PSV after both alternate day therapies with tadalafil 20mg and on demand oral tadalafil intake before penile duplex with more response with alternate days treatment, however these values are different due to the different treatment strategies.

Aversa et al.(2007) concluded that, chronic on demand therapy with PDE5i tadalafil improves endothelial function in men with several ED etiologies. This may sometimes represent the preferred therapeutic scheme in up to 42% of treated patients in multicenter studies comparing different regimes **(Mirone et al., 2005).** Moreover, current available data suggest that also a once-a-day 5 or 10mg dosing may be well tolerated and significantly improves erectile function in men with ED **(Porst et al., 2006).**

Recurrence rate after 3 month treatment with low dose of daily oral tadalafil 5mg in this stud was 30%, this was attributed to associated other Comorbidities as cardiovascular diseases, obesity, hypertension, dyslipidemia, glucose intolerance, venous leakage, hypogonadism or hyperprolactinemia which need further investigations and specific treatment to improve erectile function.

Conclusion

Penile duplex parameters in ED patients were significantly increased after daily treatment with oral tadalafil 5mg for 3 months.

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