Observational Study

Medicine®

OPEN

Effect of daily tadalafil on reported outcomes in patients with erectile dysfunction and depressive symptoms

STROBE, a case–control study

Kyu Shik Kim, MD, PhD[a], Tae Yoong Jeong, MD, PhD[b], Hong Sang Moon, MD, PhD[a,*]

Abstract

Erectile dysfunction (ED) and depression are closely related. We sought to determine ED and depression were improved by tadalafil, a phosphodiesterase type 5 (PDE5) inhibitor, at 5 mg daily, in this case–control study.

Participants were men aged 20 to 65 years with ED for >3 months, International Index of Erectile Function-5 (IIEF) score <21 points, and Zung Self-Rating Depression Scale (SDS) survey result >50 points who were willing to participate.

On first visit (V1) and after 1 (V2) and 2 months (V3), clinical features were examined using IIEF-5 for diagnosing and evaluating ED, SDS for evaluating depression, and International Prostate Symptom Score and Quality of Life (IPSS/QoL) survey for examining lower urinary tract symptoms (LUTS). Tadalafil 5 mg was administered daily for 2 months.

A total of 60 participants were an average age of 58.68 ± 6.71 years. Patient overall average IIEF was 8.76 ± 5.98, showing mild ED symptoms, and total average IPSS 13.74 ± 7.55 showed moderate LUTS. Average overall SDS index was 58.93 ± 9.21, indicating moderate-to-severe findings. Average change in IIEF among all patients revealed significant improvement from V1 to V2 (−2.69 ± 1.22, $P = .03$) and V1 to V3 (−4.38 ± 1.20, $P < 0.01$). IPSS also significantly improved from V1 to V3 (3.48 ± 1.37, $P = .01$), as did SDS index (V1, V2: 4.69 ± 1.89, $P = 0.02$), (V1, V3: 5.43 ± 1.89, $P < .01$). Patients with severe IIEF scores (group 1, n = 27) experienced significantly greater improvement in IIEF from V1 to V2 and V1 and V3, compared to those with mild-to-moderate IIEF scores. Both groups improved in SDS index from V1 to V2 and V1 to V3, with the greatest improvement between V1 and V3 for group 1 and V1 and V2 for group 2.

Daily tadalafil 5 mg could be helpful for ED patients with depressive symptoms and improved LUTS and quality of life.

Abbreviations: ED = erectile dysfunction, IIEF = International Index of Erectile Function, IPSS/QoL = International Prostate Symptom Score and Quality of Life, LUTS = lower urinary tract symptoms, PDE5 = phosphodiesterase type 5, SDS = Zung Self-Rating Depression Scale.

Keywords: depression, erectile dysfunction, phosphodiesterase 5 inhibitors

Editor: Jae Young Park.

The study protocol was reviewed and approved by the Institutional Review Board of Hanyang University Guri Hospital (Reg. No. 2015-03-013-003). Informed consent was obtained from all participants when they enrolled.

We did not register our trial with any organizations.

Funding: This research was supported by Hanmi Pharmaceutical.

Disclosure: HSM is an adviser of the Hanmi Pharmaceutical Co. Ltd., Seoul, Korea, but that had no influence on this work in relation with the company or its products. Other authors have no potential conflicts of interest to disclose.

The authors report no conflicts of interest.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

[a] Department of Urology, Myongji Hospital, Hanyang University College of Medicine, Goyang, [b] Department of Urology, Hanyang University Hospital, Hanyang University College of Medicine, Seoul, Korea.

[*] Correspondence: Hong Sang Moon, Department of Urology, Hanyang University Guri Hospital, 249-1, Gyomun-dong, Guri 471-701, Korea (e-mail: bladerummer5@hanmail.net).

How to cite this article: Kim KS, Jeong TY, Moon HS. Effect of daily tadalafil on reported outcomes in patients with erectile dysfunction and depressive symptoms: STROBE, a case-control study. Medicine 2020;99:23(e20546).

Received: 12 August 2019 / Received in final form: 29 April 2020 / Accepted: 2 May 2020

http://dx.doi.org/10.1097/MD.0000000000020546

1. Introduction

Erectile dysfunction (ED), the state of being unable to maintain satisfactory sexual intercourse due to the lack of a consistent erection, may affect physical and mental health and decrease quality of life for affected patients and their partners.[1]

ED frequently occurs in middle-aged men after age 40; 18% to 45% of men in their 40 s to 70 s have experienced ED, and 52% of US men in their 40 s to 70 s report the disease.[2–4]

Several medical status are associated with ED. ED is a confirmed risk factor for cardiovascular and coronary artery disease.[5,6] When risk factors for cardiovascular disease are improved by medication and lifestyle changes, ED also sometimes improves.[7] Diabetes mellitus is related with changes in smooth muscle and endothelial dysfunction, all of which can contribute to ED.[8] Comorbid anxiety or depression may occur in up to one-third of men with ED. ED has a close relationship with depression. One study found that depression was 1.8 times higher in men with ED than without.[9–11] In depression, change in limbic neurotransmitters may lead decreased desire for sexual activity and premature ejaculation.[12] The frequency of depression is roughly 2% to 15%, with a lifetime incidence rate of 16.5% in the United States, where depression is expected to rank second for disease-related costs by 2020.[13,14]

Antidepressants are frequently used to treat depression, but may cause sexual dysfunction or worsen ED. Phosphodiesterase-5 (PDE-5) inhibitors have been used to effectively treat ED in patients with depression, including patients treated with antidepressant therapy.[15,16] Treatment of ED with PDE5 inhibitors, which is common, is associated with improvement in depression.[11]

Tadalafil can be dosed at 5, 10, and 20 mg and was developed to treat ED. Daily doses of 5 mg are effective for improving ED and it is prescribed to patients with ED based on long-term use at low-dose levels. Lower urinary tract symptoms (LUTS) also improve following tadalafil treatment.[17,18]

When ED is accompanied by depression, a serious decrease in quality of life may occur. Effective treatment of ED is expected to improve depression. In this study, we examined whether ED and depression improved with tadalafil, a PDE5 inhibitor, at 5 mg daily.

2. Materials and methods

2.1. Patients and study design

This multicenter prospective study was performed by contacting outpatients with ED complaining of depression from July 2016 to June 2017.

Men aged 20 to 65 years with ED for >3 months, International Index of Erectile Function-5 (IIEF) score <21 points, a result on the Korean version of the Zung Self-Rating Depression Scale (SDS) survey of >50 points, and a willingness to participate in clinical tests and questionnaires were included. Participants gave informed consent.

Patients with uncontrolled hypertension or hypotension, myocardial infarction experience, mental record of depression, or history of psychiatric treatment including medication due to depression or plans for such treatment; or who were taking nitrate-related medicine for cardiovascular disease, had a PDE5 inhibitor prescription for ED for the past 1 month, took medicine (cimetidine, ketoconazole, erythromycin-based medicine) capable of inhibiting or activating hepatic cytochrome P4503A4, had hypersensitivity to medicine, had serious hepatopathy (GOT, GPT over 100 IU/L) or nephropathy (creatinine over 3 mg/dL), or who were determined improper for clinical tests were excluded.

Included patients were surveyed. On visit 1 (V1), patients gave their medical history and received a physical examination. Patients were directed to prepare questionnaires for visits 1, 2 (V2: 1 month later), and 3 (V3: 2 months later). Tadalafil 5 mg was administered daily for 2 months starting after visit 1.

2.2. Ethics statement

The Institutional Review Board of Hanyang University Guri Hospital approved this study, and all patients provided written informed consent.

2.3. Questionnaires

On visits 1, 2, and 3, patients described clinical features by taking the IIEF-5[19] for diagnosing and evaluating ED, SDS questionnaire for evaluating depression,[20] and International Prostate Symptom Score and Quality of Life (IPSS/QoL) survey[21] for a LUTS scale.

2.4. Treatment outcomes

Surveys were given to patients with depression and ED before administering tadalafil 5 mg 1 tablet/day. Depression was monitored by SDS questionnaire, which has 20 questions and a maximum score of 100 points from converting the index score from a total of 20 to 80. The SDS index was derived by dividing the sum of the values (raw scores) from the 20 items by the maximum possible score of 80, and expressed in decimals. An index score of 5 to 49 (raw scores 20–40) was normal; 50 to 59 (raw scores 41–47) mild to moderate; 60 to 69 (raw scores 48–55) moderate to severe; and ≥70 (raw scores ≥56) severe. Patients were divided into 2 groups by IIEF severity: severe group 1 and mild-to-moderate group 2. IIEF, SDS, and IPSS/QOL questionnaires were reviewed on visits 1, 2, and 3.

2.5. Statistical analysis

Groups were compared using Student t tests and χ^2 tests. Data were analyzed using SPSS software v.22.0 (IBM SPSS version 22.0, IBM, Armonk, NY), and $P < .05$ was defined as statistically significant.

3. Results

A total of 60 patients participated, 9 were lost to follow-up and 1 decided to withdraw, so 50 patients were analyzed (Fig. 1). None dropped out due to side effects. Average age was 58.68 ± 6.71 years, mean testosterone level was 4.89 ± 1.97 ng/mL, and mean blood pressure was 108.00 ± 10.44 mmHg. Total average IIEF was 8.76 ± 5.98, indicating mild ED symptoms and mean total IPSS was 13.74 ± 7.55, demonstrating moderate LUTS. IPSS storage was an average of 4.88 ± 3.24 and mean IPSS voiding was 8.86 ± 5.21. Mean SDS index was 58.93 ± 9.21, indicating moderate-to-severe findings by SDS index (Table 1).

IIEF score was classified as severe (n = 27), moderate (n = 8), mild-to-moderate (n = 10), and mild (n = 5). Improvement in IIEF score was observed in all groups by V3 except those with a mild

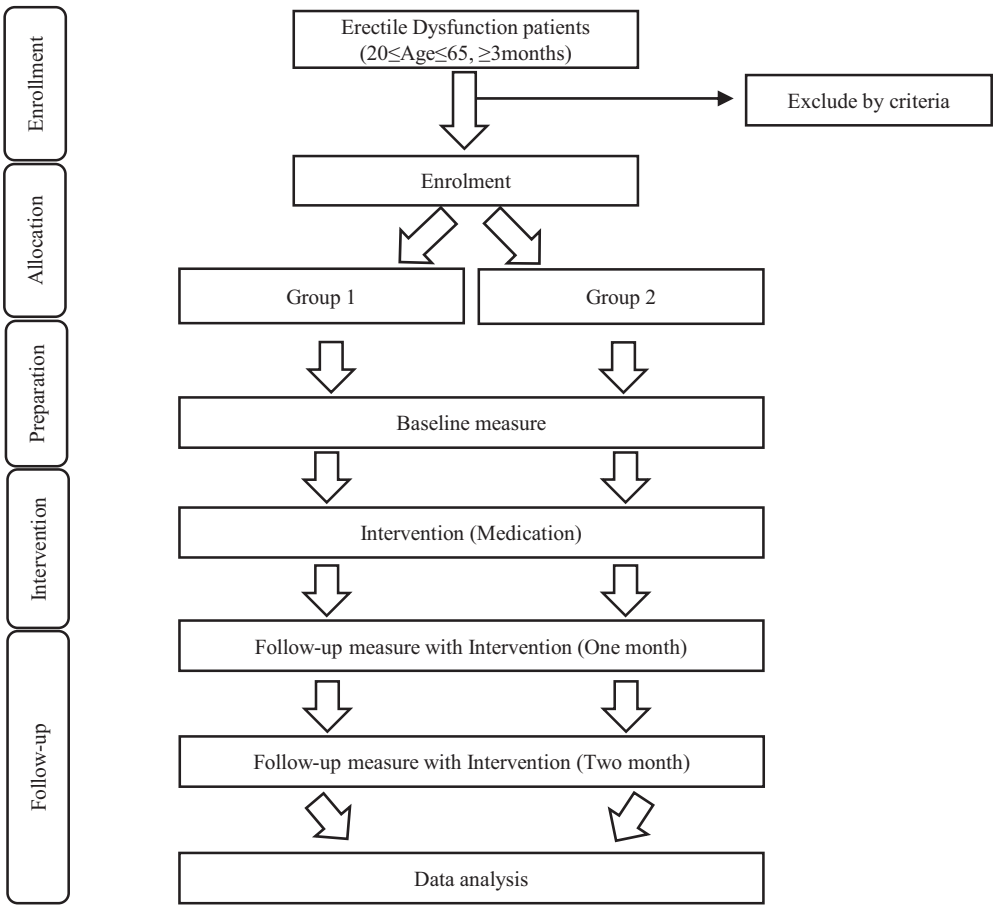

Figure 1. Flow diagram. *IIEF: International Index of Erectile Function.

score at V1. At V1, mean score was 20.60 ± 0.89 in patients with a mild IIEF score decreasing to 16.40 ± 7.57 at V2 followed by a slight increase to 16.80 ± 7.86 at V3. When V3 was compared with V1, SDS index score decreased and depression symptoms improved in all groups (Fig. 2).

3.1. Mean scores in enrolled patients

The change in average IIEF score for all patients showed a significant improvement from V1 to V2 (−2.69 ± 1.22, $P = .03$) and from V1 to V3 (−4.38 ± 1.20, $p < .01$). Average IIEF value changed from moderate (V1) to mild-to-moderate (V3). Change in IPSS also demonstrated a significant improvement from V1 to V3 (3.48 ± 1.37, $P = .01$). IPSS storage further showed a nonsignificant trend toward improvement, whereas IPSS voiding change significantly improved from V1 to V2 (1.92 ± 0.35, $P = .05$) and V1 to V3 (2.54 ± 0.93, $P < .01$). QoL was significantly different between V1 and V2 and between V1 and V3, as was SDS index (V1, V2: 4.69 ± 1.89, $P = .02$), (V1, V3: 5.43 ± 1.89, $P < .01$) (Table 2).

Table 1

Patient demographics.

	Total (n = 50)	Group 1(n = 27)	Group 2(n = 23)	P
Mean age, y	58.68 ± 6.71	60.89 ± 5.60	56.09 ± 7.08	.22
BMI, kg/m^2	24.64 ± 2.88	25.18 ± 3.37	24.00 ± 2.07	.03
Testosterone, ng/mL	4.89 ± 1.97	5.14 ± 2.28	4.59 ± 1.52	.09
Mean blood pressure, mmHg	108.00 ± 10.44	109.70	106.00	.50
IIEF	8.76 ± 5.98	4.26 ± 1.77	13.83 ± 4.24	<.01
Total IPSS	13.74 ± 7.55	13.07 ± 6.63	14.52 ± 8.59	.33
IPSS-storage	4.88 ± 3.24	4.81 ± 3.10	4.96 ± 3.46	.89
IPSS-voiding	8.86 ± 5.21	8.26 ± 4.55	9.57 ± 5.92	.10
QoL	3.56 ± 1.03	3.67 ± 1.04	3.43 ± 1.04	.90
SDS index	58.93 ± 9.21	58.80 ± 9.16	59.08 ± 9.46	.65

BMI = body mass index, IIEF = The International Index of Erectile Function, IPSS = International Prostate Symptom Score, IPSS-S = International Prostate Symptom Score Storage, IPSS-V = International Prostate Symptom Score Voiding, Group 1 = Severe erectile dysfunction in IIEF, Group 2 = mild to moderate erectile dysfunction in IIEF, QoL = quality of Life, SDS = Zung Self-Rating Depression Scale.

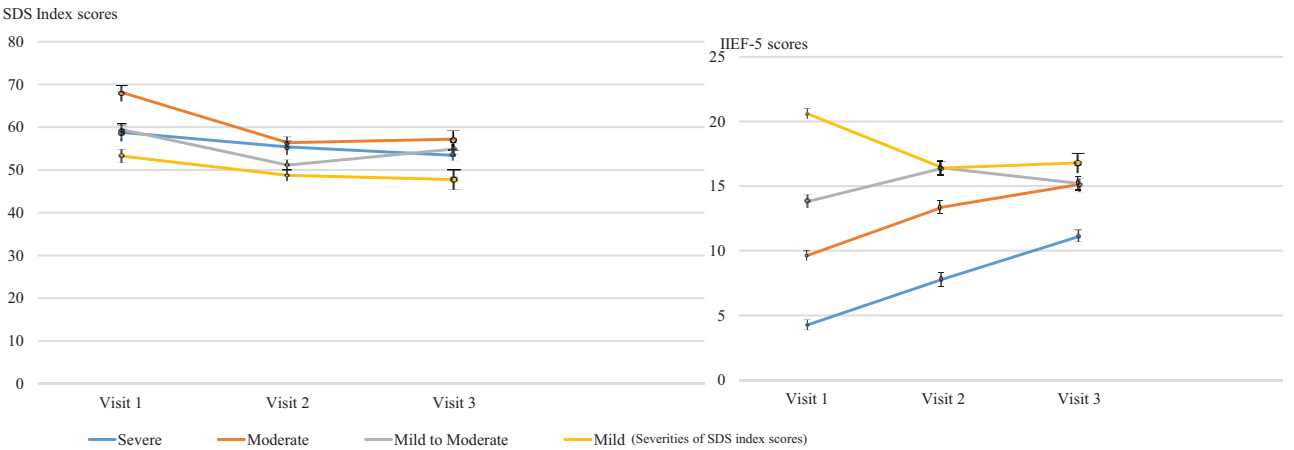

Figure 2. Comparison of IIEF and SDS mean scores by IIEF-5 severity. IIEF = The International Index of Erectile Function, SDS = Zung Self-Rating Depression Scale.

3.2. Improvements of questionnaires comparing severity of ED

Patient demographics were similar between the IIEF severe group 1 (n = 27) and mild-to-moderate group 2 (n = 23), except for average body mass index and IIEF score (Table 1). Group 1 had a significant improvement in IIEF from V1 to V2 (-3.56 ± 0.92, $P < .01$), and an even greater improvement from V1 to V3 as the average IIEF score changed from severe to moderate (-6.85 ± 1.11, $P < .01$). Group 2 had some improvement between V1 and V2 or V3, but the differences were not significant. A significant improvement was observed in IPSS score between V1 and V3 for group 1. Scores improved for group 1 between V1 and V2 and for group 2 from V1 to V2 or V3, but not significantly.

A significant improvement was seen in IPSS storage and voiding in group 1 from V1 to V2 (2.19 ± 1.11, $P = .05$) and in IPSS voiding in group 2 from V1 and V3 (3.22 ± 1.49, $P = .04$). SDS index in group 1 improved from V1 to V2 and from V1 to V3, but only the latter was significant (5.37 ± 2.60, $P = .04$). Improvement in SDS index was noted in V1 to V2 and V1 to V3 in group 2, but only V1 to V2 was significantly different (6.52 ± 2.92, $P = .03$). QoL improved significantly between V1 and V3 for both groups (0.78 ± 0.31, $P = .02$ for group 1; 0.87 ± 0.35, $P = .02$ for group 2) (Table 3).

3.3. Side effects

Side effects from tadalafil during the study included nasal congestion (1 person) and voiding difficulty (2 persons: 1 narrow urine stream, 1 residual urine sense), but none caused the patients to drop out.

4. Discussion

In this study, tadalafil 5 mg was administered daily to patients with depression and ED for 2 months and outcomes were observed. ED, lower urinary tract symptoms, and QoL all improved. Depression also improved significantly with drug treatment. More severe levels of ED showed greater improvement after 2 months, but depression showed significant improvement without any difference in improvement of ED.

The frequency of ED and depression is high in older men, and ED is closely related to life satisfaction and depression.[22–25] However, no clear mechanism has linked ED and depression, and their relationship is complex. Psychogenic changes from depression increase the probability of ED, whereas the stress of ED creates depression. Major depression causes nocturnal ED and treatment of depression with antidepressants causes sexual disorder and ED.[26–28] In a meta-analysis for correlation between ED and depression, the risk of ED was 1.39 times higher in patients with depression than those without, and the risk of depression was 2.92 times higher in patients with ED.[29]

Biological and ethological hypotheses address depression as a risk factor for ED.[30] The ethological hypothesis is that in cases of depression, development of uneasiness due to patterns of negative thinking and a lack of self-confidence increase ED risk. The biological hypothesis is that depression causes the hypothalamic pituitary adrenocortical axis to discharge excessive

Table 2

Comparison of IIEF, IPSS, QoL, and SDS mean scores at V1, V2, and V3 in enrolled patients.

n = 50	Total visit 1	Total visit 2	Total visit 3	V1 vs V2 diff	*P*	V1 vs V3 diff	*P*
IIEF	8.76 ± 5.98	11.28 ± 6.16	13.14 ± 5.98	−2.69 ± 1.22	0.03	−4.38 ± 1.20	<.01
Total IPSS	13.74 ± 7.55	11.02 ± 5.83	10.28 ± 6.01	2.56 ± 1.35	0.06	3.48 ± 1.37	.01
IPSS-storage	4.88 ± 3.24	4.20 ± 2.35	3.88 ± 2.27	0.64 ± 0.57	0.26	0.98 ± 0.56	.08
IPSS-voiding	8.86 ± 5.21	6.82 ± 4.26	6.38 ± 3.97	1.92 ± 0.35	0.05	2.54 ± 0.93	<.01
QoL	3.56 ± 1.03	3.08 ± 1.43	2.74 ± 1.26	0.44 ± 0.25	0.08	0.86 ± 0.23	<.01
SDS index	58.93 ± 9.21	54.08 ± 9.58	53.75 ± 9.65	4.69 ± 1.89	0.02	5.43 ± 1.89	<.01

IIEF = The International Index of Erectile Function, IPSS = International Prostate Symptom Score, IPSS-S = International Prostate Symptom Score Storage, IPSS-V = International Prostate Symptom Score Voiding, QoL = quality of Life, SDS = Zung Self-Rating Depression Scale.

Table 3

Comparison of IIEF, IPSS, QoL, and SDS mean scores at V1, V2, and V3 between groups 1 and 2.

	Group 1 (n = 27)							Group 2 (n = 23)						
	V1	V2	V3	V1 vs V2 diff	*P*	V1 vs V3 diff	*P*	V1	V2	V3	V1 vs V2 diff	*P*	V1 vs V3 diff	*P*
IIEF	4.26 ± 1.77	7.81 ± 4.45	11.11 ± 5.49	−3.56 ± 0.92	<.01	−6.85 ± 1.11	<.01	13.83 ± 4.24	15.35 ± 5.39	15.52 ± 5.76	−1.52 ± 1.43	.29	−1.70 ± 1.49	.26
IPSS	13.07 ± 6.63	10.52 ± 4.88	10.07 ± 6.01	2.56 ± 1.59	.11	3.00 ± 1.72	.09	14.52 ± 8.59	11.61 ± 6.85	10.52 ± 6.14	2.91 ± 2.29	.21	4.00 ± 2.20	.07
IPSS-S	4.81 ± 3.10	4.44 ± 2.17	4.04 ± 2.56	0.37 ± 0.73	.61	0.78 ± 0.77	.32	4.96 ± 3.46	3.91 ± 2.56	3.70 ± 1.89	1.04 ± 0.90	.25	1.26 ± 0.82	.13
IPSS-V	8.26 ± 4.55	6.07 ± 3.50	6.41 ± 4.03	2.19 ± 1.11	.05	0.19 ± 1.17	.12	9.57 ± 5.92	7.70 ± 4.95	6.35 ± 4.00	1.87 ± 1.61	.25	3.22 ± 1.49	.04
SDS index	58.80 ± 9.16	55.37 ± 8.90	53.43 ± 9.91	3.43 ± 2.46	.17	5.37 ± 2.60	.04	59.08 ± 9.46	52.55 ± 10.31	54.13 ± 9.55	6.52 ± 2.92	.03	4.95 ± 2.80	.09
QoL	3.67 ± 1.04	3.37 ± 1.31	2.89 ± 1.22	0.30 ± 0.32	.36	0.78 ± 0.31	.02	3.43 ± 1.04	2.74 ± 1.51	2.57 ± 1.31	0.70 ± 0.38	.08	0.87 ± 0.35	.02

Group 1 = Severe erectile dysfunction in IIEF, IIEF = The International Index of Erectile Function, IPSS = International Prostate Symptom Score, IPSS-S = International Prostate Symptom Score Storage, IPSS-V = International Prostate Symptom Score Voiding, Group 2 = mild to Moderate erectile dysfunction in IIEF, QoL = quality of Life, SDS = Zung Self-Rating Depression Scale.

catecholamine, leading to poor cavernosal muscle relaxation and ED.[31]

In general, improvement in ED increases life satisfaction and improves self-confidence and life quality. When ED and depression are concomitant, treatment of ED first improves depression. Following administration of sildenafil (a PDE 5 inhibitor) in patients with both depression and ED, depression improved.[32,33] In addition, sildenafil treatment of patients with ED who were also taking serotonin reuptake inhibitors for depression yielded improvement in ED.[16] Treatment of ED patients with vardenafil, another selective PDE 5 inhibitor, also led to improvement of both ED and depression,[11] and depression was improved following treatment of ED with penile prosthesis implantation in patients with Peyronie disease and ED.[34] Treatment of ED with tadalafil 5 mg daily improved ED and depressive symptoms in our study. Doctors should consider physical symptoms of ED and patient psychologic status before and after treatment.

To date, no clinical studies have investigated depression symptom improvement following treatment with tadalafil, a long-acting PDE 5 inhibitor. In a tadalafil study using rats with depression symptoms, depression was reported to improve. At the time of rat maternal separation, depression-like symptoms and memory decline take place as apoptotic cell death occurs in the hippocampal dentate gyrus. Injection with tadalafil reduced apoptotic cell death and led to cell proliferation in the dentate gyrus. Memory recovery and depression-like symptom improvement were observed as maternal separation rate.[35] We also observed improvement in depressive symptoms after administering tadalafil, but whether this was related to improvements in erection or a cerebral biological etiology requires further study. Tadalafil causes erection of the genital organ during sexual stimulation through the nitric oxide-cyclic guanosine monophosphate pathway, and its half-life of 36 hours is longer than other similar drugs.[36] Many studies have demonstrated the efficacy and safety of daily low-dose tadalafil, which allows sexual intercourse at any time without the need to take the drug before sexual intercourse.[37] In addition, tadalafil improves ED and LUTS and could solve both problems for middle-aged men. In this study, the QoL of patients improved as LUTS improved with tadalafil treatment.

The main limitation of this study was the small number of patients. The relationship between ED treatment and depression needs to be clarified through large-scale, randomized, double-blind, placebo-controlled trials. In addition, we were not able to clearly determine the level of improvement in depression based on ED severity level. Further long-term research would help resolve these interactions. Finally, we used questionnaires for ED symptoms, which may be subjective. Measurement of ED on an erection scale using Doppler ultrasonography or Rigi-Scan is a possible alternative.

5. Conclusion

ED decreases life quality and causes depression. Low-dose tadalafil improved both depressive symptoms and ED. Patients with ED should be checked for symptoms of depression. With treatment for ED, improvements of depressive symptom should be considered. Daily prescription of tadalafil 5 mg to patients with ED and depressive symptoms could be significantly helpful.

Author contributions

Conceptualization: Tae Yoong Jeong, Hong Sang Moon.
Data curation: Kyu Shik Kim.
Formal analysis: Kyu Shik Kim.
Funding acquisition: Hong Sang Moon.
Investigation: Tae Yoong Jeong.
Methodology: Hong Sang Moon.
Project administration: Tae Yoong Jeong.
Resources: Hong Sang Moon.
Software: Kyu Shik Kim.
Supervision: Hong Sang Moon.
Validation: Kyu Shik Kim.
Visualization: Kyu Shik Kim.
Writing – original draft: Kyu Shik Kim.
Writing – review & editing: Hong Sang Moon.

References

[1] NIH Consensus Conference. ImpotenceNIH Consensus Development Panel on Impotence. JAMA 1993;270:83–90.
[2] Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychological correlates: results of the Massachusetts male aging study. J Urol 1994;151:54–61.
[3] Nicolosi A, Moreira ED, Shirai M. Epidemiology of erectile dysfunction in four countires: cross-national study of the prevalence and correlates of erectile dysfunction. Urology 2003;61:201–6.
[4] Shiri R, Koskimaki L. Prevalence and severity of erectile dysfunction in 50-75-year-old Finnish men. J Urol 2003;170:2342–4.
[5] Vicenzini E, Altieri M, Michetti PM, et al. Cerebral vasomotor reactivity is reduced in patients with erectile dysfunction. Eur Neurol 2008;60:85–8.
[6] Wenbin Guo MM, Cun Liao MM, Zou Y, et al. Erectile dysfunction and risk of clinical cardiovascular events: a meta-analysis of seven cohort studies. J Sex Med 2010;7:2805–16.
[7] Gupta BP, Murad MH, Clifton MM, et al. The effect of lifestyle modification and cardiovascular risk factor reduction on erectile dysfunction: a systematic review and meta-analysis. Arch Intern Med 2011;171:1797–803.
[8] Marumo K, Nakashima J, Murai M. Age-related prevalence of erectile dysfunction in Japan: assessment by the International Index of Erectile Function. Int J Urol 2001;8:53–9.

[9] Araujo AB, Durante R. The relationship between depressive symptoms and male erectile dysfunction: cross-sectional results from the Massachusetts male aging study. Psychosom Med 1998;60:458–65.
[10] Rosen RC, Marin H. Prevalence of antidepressant-associated erectile dysfunction. J Clin Psychiatry 2003;64:5–10.
[11] Rosen R, Shabsigh R, Berber M. Efficacy and tolerability of vardenafil in men with mild depression and erectile dysfunction. Am J Psychiatry 2006;163:79–87.
[12] Rajkumar RP, Kumaran AK. Depression and anxiety in men with sexual dysfunction: a retrospective study. Compr Psychiatry 2015;60:114–8.
[13] Ayuso-Mateos JL, Vazquez-Barquero JL, Dowrick C. Depressive disorders in Europe: prevalence ures from the ODIN study. Br J Psychiatry 2001;11:4–18.
[14] Kessler RC, Berglund P, Demler O. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. Arch Gen Psychiatry 2005;62:593–602.
[15] Phosphodiesterase-5 (PDE-5) inhibitors have been used to effectively and safely treat erectile dysfunction in patients with depression, including patients treated with antidepressant therapy. Am J Psychiatry 2001;158: 1623–30.
[16] Nurnberg HG, Gelenberg A, Hargreave TB, et al. Efficacy of sildenafil citrate for the treatment of erectile dysfunction in men taking serotonin reuptake inhibitors. Am J Psychiatry 2001;158:1926–8.
[17] Gacci M, Salvi M, Oelke M. The use of single daily dose of tadalafil to treat signs and symptoms of benign prostatic hyperplasia and erectile dysfunction. Res Rep Urol 2013;5:99–111.
[18] Carson CC. Tadalafil—a therapeutic option in the management of BPH-LUTS. Int J Clin Pract 2014;68:94–103.
[19] Cappelleri JC, Siegel RL, Glasser DB, et al. Relationship between patient self-assessment of erectile dysfunction and the sexual health inventory for men. Clin Ther 2001;23:1707–19.
[20] Dunstan DA, Scott N, Todd AK. Screening for anxiety and depression: reassessing the utility of the Zung scales. BMC Psychiatry 2017;17:329.
[21] Choi HR, Chung WS, Shim BS, et al. Translation validity and reliability of I-PSS Korean version. Korean J Urol 1996;37:659–65.
[22] Shabsigh R, Klein LT, Seidman S, et al. Increased incidence of depressive symptoms in men with erectile dysfunction. Urology 1998;52:848–52.
[23] Althof SE. Quality of life and erectile dysfunction. Urology 2002;59:803–10.
[24] Seidman SN. Exploring the relationship between depression and erectile dysfunction in aging men. J Clin Psychiatry 2002;63(suppl 5):5–12.
[25] Seidman SN, Roose SP. Sexual dysfunction and depression. Curr Psychiatry Rep 2001;3:202–8.
[26] Roose SP, Glassman AH, Walsh BT, et al. Reversible loss of nocturnal penile tumescence during depression: a preliminary report. Neuropsychobiology 1982;8:284–8.
[27] Nofzinger EA, Thase ME, Reynolds CF, et al. Sexual function in depressed men: assessment by self-report, behavioral, and nocturnal penile tumescence measures before and after treatment with cognitive behavior therapy. Arch Gen Psychiatry 1993;50:24–30.
[28] Seidman SN, Shabsigh R, Roose SP. Dunner DL. Pharmacologic treatments of sexual dysfunction. Psychiatric Clinics of North America Annual of Drug Therapy. Philadelphia: WB Saunders; 1999;21–33.
[29] Liu Q, Zhang Y, Wang J, et al. Erectile dysfunction and depression: a systematic review and meta-analysis. J Sex Med 2018;15:1073–82.
[30] Makhlouf A, Kparker A, Niederberger CS. Depression and erectile dysfunction. Urol Clin North Am 2007;34:565–74.
[31] Goldstein I. The mutually reinforcing triad of depressive symptoms, cardiovascular disease, and erectile dysfunction. Am J Cardiol 2000;86:41–5.
[32] Seidman SN, Roose SP, Menza MA, et al. Treatment of erectile dysfunction in men with depressive symptoms: results of a placebo-controlled trial with sildenafil citrate. Am J Psychiatry 2001;158: 1623–30.
[33] Nurnberg HG, Hensley PL. Sildenafil citrate for the management of antidepressant-associated erectile dysfunction. J Clin Psychiatry 2003;64 (suppl 10):20–5.
[34] Khera M, Bella A, Karpman E, et al. Penile prosthesis implantation in patients with Peyronie's disease: results of the PROPPER study demonstrates a decrease in patient-reported depression. J Sex Med 2018;15:786–8.
[35] Baek SB, Bahn G, Moon SJ, et al. The phosphodiesterase type-5 inhibitor, tadalafil, improves depressive symptoms, ameliorates memory impairment, as well as suppresses apoptosis and enhances cell proliferation in the hippocampus of maternal-separated rat pups. Neurosci Lett 2011;488:26–30.
[36] Brock GB, McMahon CG, Chen KK, et al. Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses. J Urol 2002;168:1332–6.
[37] Masson P, Lambert SM, Brown M, et al. PDE 5 inhibitors: current status and future trends. Urol Clin North Am 2005;32:511–25.