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Serum CRP and Fibrinogen Levels as Inflammatory Biomarkers Before and After Oral Daily Tadalafil 5 mg Treatment in Patients with Erectile Dysfunction: Case-Control Study

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ABSTRACT

Background: Erectile dysfunction [ED] is the inability to obtain and maintain an erection appropriate for sexual activity. estimated one in ten adult males experience ED on a long-term basis.

Aim of the work: We aimed to assess endothelial biomarkers [C-reactive protein and fibrinogen] before and after Platelet-Rich Plasma versus daily Tadalafil 5 mg and evaluate the role of Platelet-Rich Plasma in vasculogenic erectile dysfunction.

Patients and Methods: This research had been conducted on 40 cases with vasculogenic ED and **10** normal healthy individuals as a control. Patients were divided into two groups; group 1 which included 20 ED patients who received daily Tadalafil 5 mg, and group 2 which included 20 ED patients who were injected with Platelet-Rich Plasma. CRP and Fibrinogen were collected from all patients before and after treatment.

Results: The findings in this study supported that Tadalafil has a higher value in treatment in male patients with ED. As regards the Peak systolic velocity [PSV], it significantly increased from 17±1.07 cm/s before tadalafil treatment to 27.37±1.24cm/s after it [P value = 0.04]. Also, it was significantly increased in the PRP group from 13±1.02 cm/s at the baseline to 25.37±1.33 cm/s after it [P value = 0.013]. The difference between the two groups at the baseline was significant statistically [P value = 0.03] [Table 2], however after treatment we found no statistically significant difference between the 2 groups [P value = 0.1].

Conclusion: According to our results, Tadalafil and PRP improve the inflammatory biomarkers such as CRP and Fibrinogen, although the increase of the biomarkers was more in Tadalafil, Tadalafil is more effective than PRP in the therapy of men with Erectile Dysfunction.

Keywords: Erectile dysfunction; Tadalafil; PRP; CRP; Fibrinogen.

INTRODUCTION

Definition of erectile dysfunction is the inability to obtain and sustain an erection strong enough to allow for satisfying sexual interaction [1]. Middle-aged and older adults frequently experience erectile dysfunction [ED], and its prevalence is rising steadily over the past few years [2].

The reasons for ED might be psychological, neurologic, hormonal, vascular, or drug-related. Worldwide, 23% of men between the ages of Forty and eighty have ED symptoms [3]. ED can have an organic, psychogenic, or mixed genetic cause. 89% of studied cases have organic reasons, which may be vascular, neurological, anatomical or endocrine [4].

Males with Diabetes mellites [DM] have a much higher prevalence of ED, they tend to develop the condition earlier than males in the general population [5]. Endothelial dysfunction, particularly vasculogenic ED, is thought to be a significant factor in the pathophysiology of ED [6]. Endothelial dysfunction is frequently linked to systemic atherosclerosis since it is a precursor to atherosclerosis. Recent research has shown that studied cases with athero-sclerotic cardiovascular disease have a significant prevalence of ED. On the other hand, it has been demonstrated that studied cases with ED have a high incidence of later CV illness [7].

Males with ED most usually use oral therapy with type 5 phosphodiesterase inhibitors, such as tadalafil, as their first-line treatment. PDE5I increases smooth muscle relaxation & penile artery blood flow by blocking the inactivation of cGMP [8]. Impacts of PDE-5 inhibitors include boosting or preserving vascular endothelial function and promoting hemodynamics, among others [9]. According to **Lee *et al.*** [10]'s study, hyperlipidemia had been thought to increase the risk of ED, and tadalafil, new generation-PDE-5, appeared to have a synergistic impact on studied cases hemodynamics.

In contrast to whole blood, platelet-rich plasma, autologous plasma fraction created by centrifuging whole blood, has Three to seven times greater mean platelet concentration [11]. Intracavernosal injections of PRP have recently gained popularity as effective angiogenic, vasculogenic and regenerative therapy options for ED [12].

The goal of this research had been to assess serum endothelial biomarkers [C-reactive protein and fibrinogen] before and after Platelet-Rich Plasma versus daily Tadalafil 5 mg and evaluate the role of Platelet-Rich Plasma in vasculogenic erectile dysfunction.

PATIENTS AND METHODS

This research had been conducted on 40 studied cases with vasculogenic ED and 10 normal healthy individuals as a control. Patients were divided into two groups; group 1 which included 20 ED patients who received daily Tadalafil 5 mg, and group 2 which included 20 ED patients who were injected with Platelet-Rich Plasma. All patients were recruited from Andrology Outpatient Clinics at Al-Azhar University, Cairo, Egypt. Our study was approved by the ethical committee of our institution, where we collected the cases. All patients and control signed informed consent before recruitment. We recruited the patients according to the following criteria: The inclusion criteria were Men with Vasculogenic Erectile Dysfunction. The exclusion criteria were 1] patients with other sexual disorders such as desire disorders, 2] other types of erectile dysfunction [psychogenic or neurogenic], 3] previous treatment for ED, 4] a history of active inflammation, or malignant neoplasm.

Data collection

All studied cases had been subjected to the following: Full history taking with special attention to the history of any inflammatory, neoplastic, or autoimmune disease, General physical examination, Estimation of height, and weight, calculation of Body Mass Index [BMI], and International Index of Erectile Function questionnaire. Examination of testes, epididymis, vas deferens, Penile Duplex, and hormonal Profile [FSH, LH, Prolactin] To exclude the endocrinal cause. CRP and Fibrinogen samples were collected from all patients before and after treatment.

Sample collection

Three ml of cavernous blood are collected; 1.8 ml is collected on potassium citrate 3.2% in a 1:9 ratio then plasma is separated for fibrinogen testing and 1 ml is collected on plain tube for CRP testing by turbidimetric method.

Intra-cavernosal PRP injection sessions

A 5 ml Blood sample was taken from the patient and put in a Blood centrifuge. Blood samples undergo 2 cycles in the centrifuge, the first one on 1500 in 10 minutes, while, the second one on 3000 in 5 minutes. Plasma was taken from

the sample and injected Intracavernosally in 3 sessions with 3 weeks in between.

Statistical analysis: With the aid of IBM SPSS software package version 20.0 [IBM Corp, Armonk, NY], data had been fed into the computer and evaluated. Numbers and percentages had been used to indicate qualitative data. The normality of distribution had been examined using the Shapiro-Wilk test. As our data were normally distributed, we presented it as mean ± SD, and the comparison between the two groups was done by the independent t-test. Paired data were analyzed using the paired t-test. At a P value of 0.05, the significance of outcomes had been determined.

RESULTS

Our research was conducted on 40 cases with vasculogenic ED and 10 normal individuals. All three study groups were comparable regarding the baseline data as age and BMI [P value = 0.26, and 0.87 respectively] [table 1].

As regards the PSV, it significantly increased from 17±1.07 cm/s before tadalafil treatment to 27.37±1.24cm/s after it [P value = 0.04]. Also, it was significantly increased in the PRP group from 13±1.02 cm/s at the baseline to 25.37±1.33 cm/s after it [P value = 0.013]. The difference between the two groups at the baseline was significant statistically [P value = 0.03] [Table 2], however after treatment we found no statistically significant difference between the 2 groups [P value = 0.1] [Table 3].

According to the EDV, it significantly decreased from 9.0 ± 1.6 cm/s before tadalafil treatment to 3.1 ± 1.2 cm/s after it [P value = 0.001]. Also, it was significantly decreased in the PRP group from 6.9 ± 1.3 cm/s at the baseline to 4.6 ± 1.7 cm/s after it [P value = 0.04]. The difference between the two groups was not significant either at the baseline [P = 0.07] or after the treatment [P = 0.7]. Also, we found no significant difference between the 2 groups before [P = 0.0.056] or after treatment [P value = 0.9] regarding the RI.

In terms of the CRP level, in the tadalafil group, it significantly decreased from 80.46 ± 15.61 mg/l to 9.13±3.35 mg/l after treatment [P value = 0.001]. Also, in the PRP group, it decreased from 103.46±16.12 mg/l to 15.03 ± 3.41 mg/l [P value = 0.001]. Although the level of CRP was significantly decreased in both groups, its level was significantly lower in the tadalafil group than in the PRP group [P = 0.001]. Also, the fibrinogen level was significantly decreased in each treatment group [P value = 0.001] and was lower in the tadalafil group than in the PRP group [P value = 0.001] [Tables 2, and 3].

Table [1]: Demographic data of the studied patients

	Tadalafil Group A [n = 20]	PRP Group B [n = 20]	Control Group C [n = 10]	P value
Age [Mean ± SD]	48±10	44±5	48±6.5	0.262
BMI [Mean ± SD]	22±3.1	21±2.8	20±4	0.875

Table [2]: Comparison between Tadalafil and PRP before administration

	Tadalafil Group A [n = 20]	PRP Group B [n = 20]	P value
PSV, cm/s [Mean ± SD]	17±1.07	13 ± 1.02	**0.033***
EDV, cm/second [Mean ± SD]	9.0 ± 1.6	6.9 ± 1.3	0.075
RI [Mean ± SD]	0.65 ± 0.2	0.62 ± 0.3	0.964
CRP, mg/L [Mean ± SD]	80.46 ± 15.61	103.46 ± 16.12	**<0.001**
Fibrinogen level[g/l] [Mean ± SD]	30.5 ± 4.15	29.45 ± 2.55	0.891

Table [3]: Comparison between Tadalafil and PRP after administration

	Tadalafil Group A [n = 20]	PRP Group B [n = 20]	P value
PSV, cm/s [Mean ± SD]	27.37±1.24	25.37±1.33	0.143
EDV, cm/second [Mean ± SD]	3.1 ± 1.2	4.6 ± 1.7	0.729
RI [Mean ± SD]	0.79 ± 0.36	0.70 ± 0.21	0.896
CRP, mg/L [Mean ± SD]	9.13±3.35	15.03±3.41	**<0.001***
Fibrinogen level [g/l] [Mean ± SD]	3.09± 0.43	10.42±0.72	**0.001***

DISCUSSION

Continuous inability to achieve or sustain a penile erection strong enough for acceptable sexual performance is known as erectile dysfunction. vascular component of the pathogenesis of erectile dysfunction predominates over psychogenic variables [13].

For clots to form, fibrinogen must be present in sufficient amounts in plasma. In cases of severe bleeding, fibrinogen is the first coagulation factor to reach critically low plasma concentration. Microvascular constriction results from fibrinogen binding to vascular endothelium intercellular adhesion molecule-1 [14, 15].

Because of their capacity to offer supra-physiologic levels of necessary growth factors to give regenerative stimulus that promotes repair in tissues with low healing potential, platelets with a high concentration in platelet-rich plasma have therapeutic potential [16]. Platelets in Platelet-rich Plasma, incubated with Endothelial cells in situ, induced a rise in membrane expression of Inter-cellular adhesion molecule-1 on Endothelial cells compared with autologous Platelet poor plasma [17].

Tadalafil is long-acting, selective PDEI that must be taken Thirty minutes before sexual activity because it has the longest period of action in its class & maximum period of seventy-two hours. It also has an onset time of twenty minutes [18]. Tadalafil 5 mg daily improves Erectile dysfunction and Ejaculation after 12 weeks and is more effective than the use of Tadalafil on demand [19].

In our study, we found the mean ± SD for age in group A was 49 ± 10, group B was 45 ± 5 and 47 ± 6.5 for group C. **Zaghloul *et al.*** [20] conducted a study on forty-eight patients complaining of ED non-responding to on-demand PDE5 inhibitors had been allocated into two equal groups, diabetics and non-diabetics with Mean ± SD for age 50.16 ± 6.89, 52.33 ± 5.17, respectively.

Lei *et al.* [21] aimed to analyze the impact and clinical importance of tadalafil and atorvastatin in middle-aged and elderly studied cases with hyperlipidemia complicated by erectile dysfunction on hemodynamics and sexual function. They found the mean ± SD for age 60.32 ± 3.50 in the experimental group and 59.25 ± 3.36 for the control group.

According to IIEF-5 scores, our results revealed that most cases were mild [53.3%], moderate cases were [33.3%] and severe cases were 13.3% for group A. In group B, we found mild cases were [63.3%], moderate cases were [26.7%] and severe cases were [10%]. There is no variation between the two groups. After treatment, were significant differences before and after Tadalafil and PRP [p-value = 0.001].

In agreement with us, the research of **Zaghloul *et al.*** [20], sought to determine if platelet-rich plasma and daily oral tadalafil intake would be beneficial for treating erectile dysfunction in diabetic studied cases who had not responded to PDE5 inhibitors. Both the diabetes group's mean total IIEF-5 score [8.04 vs. 12.1, p = 0.003] and the non-diabetic group's [10.2 vs. 14.8, p = 0.001] showed a substantial increase. **Gallo *et al.*** [22] reported the same results as ours. They found that the mean IIEF-EF score rises from 22.1 ± 2.2 to 27.8 ± 2 in group B [P < .001] in the tadalafil group, the rise in mean IIEF score had been 5.7.

Rajfer *et al.* [8], conducted a 24-week, multi-center study in which males with erectile dysfunction were given 2.5 and five milligrams of tadalafil or placebo. 238 of 287 men who began protocol completed it [83%]. In tadalafil 2.5 and five mg arms, for instance, the mean IIEF-EF domain score increased by 6.1 & 7.0 points, proving that tadalafil had been superior to the placebo across all primary efficacy end objectives, while the placebo group only saw a 1.2-point increase. According to the worldwide erectile functioning questionnaire, tadalafil use significantly reduced the quality of sexual encounters, sexual desire, and overall sexual life satisfaction.

Similar to our findings, **Lei *et al.*** [21], found that the Mean ± SD of the IIEF-5 score was 15.16 ± 3.02 in PRP experimental group and 14.84 ± 2.44 in the control group. After therapy, when compared to the control group, the experimental group's sexual function considerably improved, as evidenced by superior IIEF-5 scores, longer nocturnal penile erection times, longer total erection durations, and longer penile root hardness > 60% maintenance periods.

Our results were supported by **Matz *et al.*** [23] who studied cases with Pyronine's illness and were both given ICI of platelet-rich fibrin matrix, and both groups experienced objective improvements in their IIEF-5 scores for rigidity and satisfaction.

Confirming our findings, **Taş *et al.*** [24] showed that cavernous PRP therapy in ED cases is dependable, however, despite a considerable rise in mean

IIEF-EF scores, ED grades remained the same. **Porst *et al.*** [25] found that there is a difference regarding IIEF-EF scores compared to placebo [LS mean change: 4.2; 5.4] [p< 0.01]. Improvements in IIEF-EF LS mean scores were seen after taking tadalafil 2.5 mg & Five mg, respectively [a minimal clinically important difference].

In the present research, we showed that there is a difference among our three groups Cavernosal CRP before and after intervention and fibrinogen level [g/l], PSV, and EDV after intervention [p< 0.05]. Our results show statistical variation before and after the administration of Tadalafil regarding PSV, EDV, RI, CRP, Fibrinogen, and IIEEF. Our results show statistical variation before and after the administration of PRP regarding CRP, IIEEF, and fibrinogen.

In agreement with us, **Lei *et al.*** [21] findings of our investigation demonstrate that following treatment, CRP in the experimental group was substantially lower than that in the control group [p=0.00]. After therapy, the experimental group's hemodynamic markers, including HSV, LSV, PSV, HCT and ESR, greatly outperformed those in the control group, with variation [p=0.00].

Bansal *et al.* [26] reported that Lower hs-CRP at baseline [median 1.5 mg/L vs. 2.0 mg/L; P = 0.034]] and proportionately higher decrease in its level were associated with improvement with tadalafil. **Lee *et al.*** [27] researchers investigated the relative significance of high-sensitivity C-reactive protein levels in studied cases with diabetes and erectile dysfunction. They discovered that median hs-CRP values in non-responders and responders had been 0.31 ± 0.15 [0.18 to 0.63] & 0.14 mg/dL [0.09 to 0.40 mg/dL] [p=0.028].

Brock *et al.* [28], reported that Tadalafil, Little doses used orally once per day are safer and more efficient than high doses when required, particularly in people with diabetes, hypertension, hyperlipidemia and alcohol use.

In agreement with us, **Zaghloul *et al.*** [20], revealed that pharmaco-penile duplex readings found substantial improvement in mean PSV and EDV after PRP therapy in improved cases in both diabetic and non-diabetic groups. This improvement had been related to pharmaco-penile duplex readings.

Abdel-Kader [29], aimed to Identify the efficacy of five mg of tadalafil per day in treating erectile dysfunction in diabetic males. When compared to baseline PSV, they demonstrated significant increases in PSV after twelve weeks. When comparing the Twelve-week IIEF score to the baseline IIEF score, we discovered a significant rise. In the comparison of tadalafil, sildenafil, and vardenafil, **Jannini *et al.*** [30], found that for PSV and RI, mean baseline values had been 38 [33.5-42.6] and 0.87 [0.81-0.92] in sildenafil 50 mg group, 39.8 [38.6-45.8] and 0.86 [0.80-0.92] in sildenafil 100 mg group, 35.4 [30.9-39.9] and 0.87 [0.82-0.91] in tadalafil group, and 36.9 [39.3-43.5] and 0.85 [0.82 - 0.88] in vardenafil group, for PSV & RI values.

Conclusion: Tadalafil and PRP improve the inflammatory biomarkers such as CRP and fibrinogen, although the increase of the biomarkers was more in Tadalafil, we can say that Tadalafil is more effective than PRP in the treatment of men with Erectile Dysfunction. We recommend further studies on a larger sample of participants to prove or disprove our assumption. Further research is necessary to investigate a possible therapeutic role for Tadalafil in ED-studied cases.

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REFERENCES

1. Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, et al. Erectile Dysfunction: AUA Guideline. J Urol. 2018 Sep;200[3]:633-641. doi: 10.1016/j.juro.2018.05.004.
2. Ibrahim A, Ali M, Kiernan TJ, Stack AG. Erectile Dysfunction and Ischaemic Heart Disease. Eur Cardiol. 2018 Dec;13[2]:98-103. doi: 10.15420/ecr.2017.21.3.
3. Laumann EO, Glasser DB, Neves RC, Moreira ED Jr; GSSAB Investigators' Group. A population-based survey of sexual activity, sexual problems and associated help-seeking behavior patterns in mature adults in the United States of America. Int J Impot Res. 2009 May-Jun;21[3]:171-8. doi: 10.1038/ijir.2009.7.
4. Dick B, Reddy A, Gabrielson AT, Hellstrom WJ. Organic and psychogenic causes of sexual dysfunction in young men. Int J Med Rev. 2017 Dec 25;4[4]:102-11. doi: 10.29252/ijmr-040404.
5. Goldstein I, Jones LA, Belkoff LH, Karlin GS, Bowden CH, Peterson CA, Trask BA, Day WW. Avanafil for the treatment of erectile dysfunction: a multicenter, randomized, double-blind study in men with diabetes mellitus. Mayo Clin Proc. 2012 Sep;87[9]:843-52. doi: 10.1016/j.mayocp.2012.06.016.
6. Kirby M, Jackson G, Simonsen U. Endothelial dysfunction links erectile dysfunction to heart disease. Int J Clin Pract. 2005 Feb;59[2]:225-9. doi: 10.1111/j.1742-1241.2005.00453.x.
7. Ioakeimidis N, Vlachopoulos C, Rokkas K, Kratiras Z, Angelis A, Samentzas A, Fassoulakis C, Tousoulis D. Dynamic penile peak systolic velocity predicts major adverse cardiovascular events in hypertensive patients

with erectile dysfunction. J Hypertens. 2016 May;34 [5]:860-8. doi: 10.1097/HJH.0000000000000877.

8. Sharma R. Novel phosphodiesterase-5 inhibitors: current indications and future directions. Indian J Med Sci. 2007 Dec;61[12]:667-79.
9. Lee U, Kwon MH, Kang HE. Pharmacokinetic alterations in poloxamer 407-induced hyperlipidemic rats. Xenobiotica. 2019 May;49[5]:611-625. doi: 10.1080/00498254.2018. 1466212.
10. Hesseler MJ, Shyam N. Platelet-rich plasma and its utility in medical dermatology: A systematic review. J Am Acad Dermatol. 2019 Sep;81[3]:834-846. doi: 10. 1016/j.jaad.2019.04.037.
11. Epifanova MV, Gvasalia BR, Durashov MA, Artemenko SA. Platelet-Rich Plasma Therapy for Male Sexual Dysfunction: Myth or Reality? Sex Med Rev. 2020 Jan;8[1]:106-113. doi: 10.1016/j.sxmr.
12. Bolat MS, Cinar O, Akdeniz E, Aşcı R. Low dose daily versus on-demand high dose tadalafil in diabetic patients with erectile and ejaculatory dysfunction. Int J Impot Res. 2018 Jun;30[3]:102-107. doi: 10.1038/s41443-018-0019-5.
13. Elshahid ARM, Shahein IM, Mohammed YF, Ismail NF, Zakarria HBAE, GamalEl Din SF. Folic acid supplementation improves erectile function in patients with idiopathic vasculogenic erectile dysfunction by lowering peripheral and penile homocysteine plasma levels: a case-control study. Andrology. 2020 Jan;8[1]: 148-153. doi: 10.1111/andr.12672
14. Gong B, Ma M, Xie W, Yang X, Huang Y, Sun T, Luo Y, Huang J. Direct comparison of tadalafil with sildenafil for the treatment of erectile dysfunction: a systematic review and meta-analysis. Int Urol Nephrol. 2017 Oct;49[10]:1731-1740. doi: 10.1007/s11255-017-1644-5.
15. Sidiropoulou S, Papadaki S, Tsouka AN, Koutsaliaris IK, Chantzichristos VG, Pantazi D, et al. The Effect of Platelet-Rich Plasma on Endothelial Progenitor Cell Functionality. Angiology. 2021 Sep;72[8]:776-786. doi: 10.1177/0003319721998895.
16. Grottke O, Mallaiah S, Karkouti K, Saner F, Haas T. Fibrinogen Supplementation and Its Indications. Semin Thromb Hemost. 2020 Feb;46[1]:38-49. doi: 10.1055/ s-0039-1696946.
17. Hein TW, Singh U, Vasquez-Vivar J, Devaraj S, Kuo L, Jialal I. Human C-reactive protein induces endothelial dysfunction and uncoupling of eNOS in vivo. Atherosclerosis. 2009 Sep;206[1]:61-8. doi: 10.1016/j. atherosclerosis.2009.02.002.
18. Wu PI, Diaz R, Borg-Stein J. Platelet-Rich Plasma. Phys Med Rehabil Clin N Am. 2016 Nov;27[4]:825-853. doi: 10.1016/j.pmr.2016.06.002.
19. Sen U, Tyagi N, Patibandla PK, Dean WL, Tyagi SC, Roberts AM, Lominadze D. Fibrinogen-induced endothelin-1 production from endothelial cells. Am J Physiol Cell Physiol. 2009 Apr;296[4]:C840-7. doi: 10.1152/ajpcell.00515.2008.
20. Zaghloul AS, El-Nashaar AM, Said SZ, Osman IA, Mostafa T. Assessment of the intracavernosal injection platelet-rich plasma in addition to daily oral tadalafil intake in diabetic patients with erectile dysfunction non-responding to on-demand oral PDE5 inhibitors. Andrologia. 2022 Jul;54[6]:e14421. doi: 10.1111/and. 14421. Epub 2022 Mar 17.
21. Du L, Jia JH, Xue WY, Qi JC. Effect of tadalafil combined with atorvastatin on hemodynamics and sexual function in middle-aged and elderly patients with hyperlipidemia complicated with erectile dysfunction. Pak J Med Sci. 2021 Nov-Dec;37[7]:1965-1971. doi: 10.12669/pjms.37.7.4257.
22. Gallo L, Pecoraro S, Sarnacchiaro P, Silvani M, Antonini G. The Daily Therapy With L-Arginine 2,500 mg and Tadalafil 5 mg in Combination and in Monotherapy for the Treatment of Erectile Dysfunction: A Prospective, Randomized Multicentre Study. Sex Med. 2020;8[2]:178-185. doi: 10.1016/j.esxm.2020. 02.003.
23. Matz EL, Pearlman AM, Terlecki RP. Safety and feasibility of platelet rich fibrin matrix injections for treatment of common urologic conditions. Investig Clin Urol. 2018 Jan;59[1]:61-65. doi: 10.4111/icu. 2018.59.1.61.
24. Taş T, Çakıroğlu B, Arda E, Onuk Ö, Nuhoğlu B. Early Clinical Results of the Tolerability, Safety, and Efficacy of Autologous Platelet-Rich Plasma Administration in Erectile Dysfunction. Sex Med. 2021;9[2]:100313. doi: 10.1016/j.esxm.2020.100313.
25. Porst H, Gacci M, Büttner H, Henneges C, Boess F. Tadalafil once daily in men with erectile dysfunction: an integrated analysis of data obtained from 1913 patients from six randomized, double-blind, placebo-controlled, clinical studies. Eur Urol. 2014 Feb;65[2]: 455-64. doi: 10.1016/j.eururo.2013.09.037.
26. Jamaluddin, Bansal M, Srivastava GK, Gupta NP. Role of Serum High-Sensitivity C-Reactive Protein as a Predictor of Therapeutic Response to Tadalafil in Patients With Erectile Dysfunction: A Prospective Observational Study. J Sex Med. 2019 Dec;16[12]: 1912-1921. doi: 10.1016/j.jsxm.2019.09.006.
27. Lee JW, Park HJ, Park NC. Serum High-Sensitivity C-Reactive Protein Levels and Response to 5 mg Tadalafil Once Daily in Patients With Erectile Dysfunction and Diabetes. Korean J Urol. 2013 Dec; 54[12]:858-64. doi: 10.4111/kju.2013.54.12.858.
28. Brock G, Heiselman D, Maggi M, Kim SW, Rodríguez Vallejo JM, Behre HM, et al. Effect of Testosterone Solution 2% on Testosterone Concentration, Sex Drive and Energy in Hypogonadal Men: Results of a Placebo Controlled Study. J Urol. 2016 Mar;195[3]:699-705. doi: 10.1016/j.juro.2015.10.083.
29. Abdel-Kader MS, Ali AF, Ali MM, Alsagheer GA. The Outcome of Daily Low Dose of Tadalafil in Diabetic Men with Erectile Dysfunction. Egypt J Hosp Med. 2022 Oct 1;89[1]:4495-9.
30. Jannini EA, Isidori AM, Gravina GL, Aversa A, Balercia G, Bocchio M, et al.; Endotrial Study Group. The ENDOTRIAL study: a spontaneous, open-label, randomized, multicenter, crossover study on the efficacy of sildenafil, tadalafil, and vardenafil in the treatment of erectile dysfunction. J Sex Med. 2009 Sep;6[9]: 2547-60. doi: 10.1111/j.1743-6109.2009.01375.x.

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