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Management of Erectile Dysfunction Using Platelet-Rich Plasma Cavernosal Injections

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ABSTRACT

Background: Among the most common medical conditions affecting middle-aged men, erectile dysfunction (ED) can have an impact on the well-being of the patient and his partner. Several medical specialties have made use of platelet-rich plasma (PRP) for decades.

Objective: To evaluation of the efficacy of platelet-rich plasma (PRP) cavernosal injections in the management of erectile dysfunction, and to study its safety and adverse effect in the treatment of erectile dysfunction.

Subjects and methods; This intervention clinical prospective study was conducted at multicenter including Badr University Hospital and AL Haram Hospital on 40 patients suffering from erectile dysfunction, using PRP cavernosal injection. Follow up of erectile function and penile hemodynamics involved evaluation of patients utilizing International Index of Erectile Function (IIEF-5) at 3, 6 months after initiation of therapy together with PCDUS.

Result: The mean ED duration was 18.62±4.9-month. There were 16 patients with mild ED (40%), 18 patients had mild to moderate ED (45%) and six patients had moderate ED severity (15%) according to IIEF grading. The mean IIEF-EF pre-treatment was 15.35±3.1, the mean IIEF-EF after 3rd month was 17.28±2.95, and the mean IIEF-EF after 6th month was 19.40±2.74, regarding follow up of IIEF-EF of the study population. Statistical analysis revealed that the groups under consideration differed significantly with respect to the IIEF-EF at baseline, the third month, and the sixth month.

Conclusion; A negative significant correlation was revealed between percentage of change and ED duration, which means less improvement in patients with longer duration of erectile dysfunction.

Keywords: Erectile Dysfunction, Platelet-Rich Plasma, Cavernosal Injections.

INTRODUCTION

The inability to achieve or maintain an erection strong enough to engage in sexual activity is known medically as erectile dysfunction. Factors that increase the risk of this syndrome include being older, being a smoker, and having vascular conditions like diabetes or hypertension. Keys to keeping an erection are healthy vascular and neurological processes. This happens because of the parasympathetic nervous system, which uses nitric oxide pathways to relax the smooth muscles of cavernosal veins and widen the penile arterioles [(1)].

As one of the most common medical issues affecting men in their middle years, erectile dysfunction (ED) can have a detrimental effect on the patient's and their partner's quality of life [(2)]. A potential precursor to cardiovascular disease, erectile dysfunction is influenced by hormonal, neurological, and vascular variables [(3)].

Erectile dysfunction treatment should aim to restore erections, increase sexual spontaneity, and improve quality of life. Regardless of the underlying etiology, phosphodiesterase 5 (PDE5) inhibitors are the first line of pharmaceutical treatment for ED [(4)]. Should the results of oral medication not be satisfactory. Penile prostheses, low-intensity shockwave therapy, suction devices, intracavernosal injections, and other methods are available to patients [(5)].

PRP, or platelet-rich plasma, is a type of autologous blood plasma with platelet concentrations three to seven times higher than what is considered physiologically normal. If the final cell product has platelet counts greater than 1,000,000 U/μL [(6)]. Vascular endothelial growth factor, epidermal growth factor, fibroblast growth factor, and insulin-like growth factor, as well as platelet-derived growth factor (PDGF) are just a few of the many growth factors found in PRP, which gives it the ability to regenerate damaged tissues by reestablishing blood flow and balancing the composition of extracellular matrix and smooth muscle cells [(7)].

For decades, PRP has found utility in a wide variety of medical fields. Multiple studies have shown that PRP therapy is helpful in the fields of cosmetics, ophthalmology, and neurology with few, if any, negative side effects [(8)], rehabilitative medicine, cardiovascular surgery, reconstructive surgery, aesthetic surgery, tissue engineering, and nerve and trunk restoration [(9)].

This study aimed to evaluate the efficacy of PRP cavernosal injections in the treatment of erectile dysfunction, and to study its safety and adverse effect in the treatment of erectile dysfunction.

PATIENTS AND METHODS

This intervention clinical prospective study was performed on 40 cases who had erectile dysfunction for more than 6 months, in multicenter including Badr University Hospital and AL Haram Hospital, for duration of one year from the actual start time (January 2023 to January 2024).

Inclusion criteria:

Age 30-50 years (middle age), patients who have been using PDE5 inhibitors and have reported a poor response to these drugs in the months leading up to

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screening, must have a history of erectile dysfunction that spans at least six months, decline to forego any treatment for erectile dysfunction while the trial is underway, and make a pact to have sexual relations four times a month.

Exclusion criteria:

Extreme prostatectomy, radical cystectomy, or rectal surgery performed in the past, or pelvic trauma, that may have affected erection performance. Individuals who have undergone a TURP procedure in the past, as well as those who have had penile surgeries such as lengthening, malignancy, grafting, a history of priapism or penile fracture, radiation therapy to the pelvis, hormonal therapy for prostate cancer, whether used before or after the diagnosis, individuals suffering from neurological disorders, polyneuropathy, or any abnormality affecting the blood, a morning blood testosterone level below 300 ng/dl was considered abnormal and indicated untreated hypogonadism.

Prior to commencing PRP therapy, all patients were subjected to the following:

Full history taking including:

- **Personal history:** Name, age, marital status and number of children.
- **Medical history and operative history:** (i) Past medical conditions that could increase the likelihood of erectile dysfunction in example, conditions with the blood sugar, blood pressure, heart, liver, kidneys, or nervous system. (ii) Medical history that includes pelvic, genital, and surgical procedures. (iii) Dosage history, particularly for drugs that impair erection.
- **Sexual history:**
  - How long the illness lasts, how it starts, and where it starts.
  - The regularity, quality, and condition of morning erections.
  - When stimulated visually or manually, an erection always follows.
  - Sexual desire, frequency of sexual encounters, and duration of sexual coitus
  - In a relationship, the attitude and level of cooperation from one partner that affects the other.

Examination:

General examination: Checking the patient's vitals (blood pressure, temperature, and heart rate) and doing a thorough physical examination to look for gynecomastia and other secondary sexual characteristics.

Genital examination: (i) The penis was examined for its size and location of the urethral meatus during the penoscrotal examination. Any discomfort or plaques were felt during palpation. (ii) The genital exam measured the size of the testicles,

Neurological examination: Bulbocavernosus reflex, one hand's index finger was inserted into the perineum, which is located above the bulbocavernosus muscle at the penis's crus. Squeezing the glans penis briefly with the other hand to contract the bulbocavernosus muscle.

Laboratory investigations:

Evaluation of total cholesterol, triglycerides, HDL, LDL, total testosterone, and hemoglobin A1c. After a 12-hour fast, blood samples were taken in the morning, between 8 and 10 am.

Evaluation of erectile function (EF) using an abridged Arabic version of International Index of Erectile Function (IIEF-5).

Both before and after treatment, every patient participated in a structured interview to complete the IIEF-5 Arabic version of the questionnaire.

The IIEF-5 score is the sum of the ordinal responses to the 5 items: (1) From 22 to 25: Absent erectile dysfunction. (2) From 17 to 21: Mild degree of erectile dysfunction. (3) From 12 to16: Mild to moderate degree of erectile dysfunction. (4) From 8 to11: Moderate degree of erectile dysfunction. (5) From 5 to 7: Severest degree erectile dysfunction [(10)].

Patients were evaluated by penile color Doppler ultrasonography (PCDUS) before and 3 and 6 months after ICI therapy.

Measurements were taken from the proximal sections of the cavernosal arteries to determine their diameter, peak systolic and end diastolic velocities, and resistance index.

Interpretation of penile duplex parameters:

If the vascular function is satisfactory following sufficient pharmacologic stimulation, then the PSV should be 30 cm/s or above.

A normal cutoff value for the EDV is less than 5 cm/s and for the RI is larger than 0.8; these metrics evaluate the venoocclusion mechanism's integrity.

PRP preparation: A patient's blood sample was taken during therapy to obtain PRP.

Venipuncture performed in the clinic:

Twenty milliliters of whole blood was collected by venipuncture and placed in acid citrate dextrose (ACD) tubes to avoid activating the platelets before they were used. An autologous platelet separator that has been approved by the FDA was used to process the blood sample. After a 5-minute centrifugation run at 2000 RPMS (soft spin), the blood was collected. Next, the platelet-containing supernatant plasma was transferred to a separate sterile tube that did not include anticoagulant. In order to isolate platelets, the tube was spun at a higher speed of 4000 RPMS for 10 minutes. Between the two halves, PRP and platelet-poor plasma (PPP) were found. Platelet pellets were created at the base of the tube. After removing PPP, gently shaking the tube washed the platelet pellets into a minimum volume of plasma (2-4 mL).

Procedure:

Under sterile conditions, with the exception of a few patients who underwent local anesthetic, the entire process was executed painlessly. In order to minimize the danger of infection, the skin was sterilized with alcohol prior to injection. An insulin syringe needle (½ inch in diameter) was used to replace the needle during the intracavernosal injection, which was administered using a 10 ml syringe. The penis was held in an upright posture and the needle was inserted into the cavernous body through the skin and subcutaneous tissue in a smooth and continuous manner. After carefully and smoothly injecting 3 ml of PRP into each corpora cavernosa, pressing the injection site for 1–2 minutes, and massaging the penis for 2-3 minutes, the contents of the syringe were distributed throughout the penis. After the surgery, patients were monitored in the clinic for about fifteen to twenty minutes to identify any difficulties or side effects. Over the course of three months, patients attended six sessions, which were spaced two weeks apart.

Follow up:

Evaluation of patients using IIEF-5 at 3, 6 months following therapy commencement in conjunction with PCDUS was part of the follow-up for erectile function and penile hemodynamics.

Ethical approval:

The study was authorized by Helwan University's Faculty of Medicine Ethics Committee. Each participant received a full summary of the study's aims prior to completing an informed consent form. The Helsinki Declaration was observed at all stages of the study.

Statistical analysis

All data were collected, tabulated, and analyzed using Windows version 26.0 of SPSS Inc.'s software, which is based in Chicago, Illinois, USA. Qualitative data were represented by absolute frequencies (number) and relative frequencies (%), but quantitative data were shown by the mean plus or minus the standard deviation and median. The Pearson correlation coefficient was used to assess the connection between the various study variables. A significant p-value was considered when it is equal or less than 0.05.

RESULTS

Table (1) shows the demographic data of the studied patients.

Table (1): Presentation of demographic data of the study population

Variable		Studied group (n=40)	
		mean	**SD**
Age		42.3	5.9
BMI (kg/m^2)		26.1	1.7
		N	**%**
Residence	Urban	21	52.5
	Rural	19	47.5
Special habit	Smoking	23	57.5
	Non-smoking	17	42.5

Table (2) shows that (40%) were diabetic and dyslipidemia was reported in (37.5%) of patients. The mean testosterone (ng/dl) was 523.1 ±47.3, regarding base line characters of the study population.

Table (2): Medical history of the studied group

Variable	Studied group (n=40)	
	N	**%**
Diabetes	16	40
HTN	13	32.5
Dyslipidemia	15	37.5
Coronary heart disease (CHD)	7	17.5
	Mean	**SD**
Testosterone (ng/dl)	523.1	47.3

Table (3) shows that mean ED duration was 18.62±4.9 month. Mean IIEF score pre intervention was 15.35±3.1. There were 18 patients with mild to moderate ED (45%).

Table (3): Baseline erectile dysfunction of studied population

Variable	Studied group (n=40)	
	Mean	SD
ED duration (month)	18.62	4.9
IIEF score pre intervention	15.35	3.1
ED severity pre-treatment (IIEF grade)	**N**	**%**
Mild	16	40
Mild to moderate	18	45
Moderate	6	15

Table (4) shows that the mean IIEF-EF pre-treatment was 15.35±3.1. The mean % of change was 28.37±13.12 with median 25 regarding baseline and last follow up of IIEF among the studied population.

Table (4): IIEF scores at different intervals in the study population

Variable	Studied group (n=40)	
	Mean	SD
Pre-treatment	15.35	3.1
3rd month	17.28	2.95
6th month	19.40	2.74
Percentage of change (baseline vs 6 month)	28.37	13.12

Table (5) illustrates that in terms of baseline, third month, and sixth month of IIEF-EF, the groups that were part of the study showed statistically significant differences.

Table (5): Evaluation of IIEF-EF in the study population baseline, after 3, 6 months

Variable	Studied group (n=40)			
	Mean	**SD**	**t test**	**P value**
Pre-treatment	15.35	3.1	-8.16	P1<0.001*
3rd month	17.28	2.95	-18.36	P2<0.001*
6th month	19.40	2.74	-11.83	P3<0.001*

P1= pre-treatment vs 3 months follow up, P2= pre-treatment vs 6 months follow up, P3=3 months follow up vs 6 months follow up.

Table (6) shows that in terms of baseline, third month, and sixth month of IIEF-EF, the groups that were part of the study showed statistically significant differences.

Table (6): IIEF grades at different intervals in the study population.

Grade	Baseline		3 months		6 months		test	P value
	N	%	N	%	N	%		
Normal	0	0	3	7.5	7	17.5	3.7	P1<0.001*
Mild	16	40	20	50	21	52.5	5.3	P2<0.001*
Mild to moderate	18	45	13	32.5	10	25	7.1	P3<0.001*
Moderate	6	15	4	10	2	5		

P1= pre-treatment vs 3 months follow up, P2= pre-treatment vs 6 months follow up, P3=3 months follow up vs 6 months follow up.

Table (7) shows that when it came to baseline, third-month, and sixth-month penile Doppler ultrasound, the groups under study did not vary significantly.

Table (7): Evaluation of penile Doppler u/s in the study population baseline, 3, 6 months after intervention

Variable	**Studied group** (n=40)				
	Baseline	**3rd month**	**6th month**	**t test**	**P value**
	Mean ± SD				
RT Cav. a. diameter (mm)	**0.93±0.39**	**0.99±0.41**	**0.99±0.42**	**-1.9 -2 -1.18**	**P1=0.062 P2=0.052 P3=0.244**
LT Cav. a. diameter (mm)	**0.93±0.47**	**0.98±0.44**	**0.98±0.44**	**-1.7 -1.69 0.5**	**P1=0.094 P2=0.098 P3=0.759**
RT PSV (cm/sec)	**26.28±1.88**	**26.78±2.11**	**27.3±1.86**	**-2.52 -4.4 -3.25**	**P1=0.058 P2=0.061 P3=0.067**
LT PSV (cm/sec)	**26.23±1.87**	**27.03±1.82**	**27.3±1.8**	**-2.75 -4.51 -3.24**	**P1=0.070 P2=0.059 P3=0.066**
RT EDV (cm/sec)	**7.75±1.55**	**7.43±1.66**	**7.2±1.57**	**3.34 6.11 4.52**	**P1=0.072 P2=0.069 P3=0.055**
LT EDV (cm/sec)	**7.58±1.43**	**7.33±1.44**	**7.23±1.46**	**3.6 4.15 1.43**	**P1=0.062 P2=0.077 P3=0.060**

P1= pre-treatment vs 3 months follow up, P2= pre-treatment vs 6 months follow up, P3=3 months follow up vs 6 months follow up.

Table (8) shows that the percent of change in IIEF was significantly correlated ED duration only.

Table (8): Correlation between percentage of change in IIEF and different parameters

Variables		**Percentage of change**
Age	**r**	**0.047**
	p	**0.773**
BMI	**r**	**-0.198**
	p	**0.222**
Testosterone (ng/dl)	**r**	**-0.119**
	p	**0.465**
ED duration (month)	**r**	**-0.521**
	p	**0.001***

DISCUSSION

Rather than tackling the underlying pathophysiologic causes, most therapies for erectile dysfunction concentrate on enhancing penile hemodynamics. Autologous PRP is three to seven times more concentrated in platelets than whole blood [(11)]. Injectable PRP has become a standard treatment option across many medical fields because of the growth factors it contains in high concentrations [(12)].

An exciting new regenerative, angiogenic, and vasculogenic method for treating erectile dysfunction is PRP injections into the vernosal canal. According to ten animal studies, PRP injections may alleviate erectile dysfunction (ED) by reducing inflammation, repairing damaged tissue, protecting neurons, and enhancing neurogenesis [(13)].

The current study showed that the mean age was 42.3±5.9, there were 15 population had diabetes (40%), there were 13 population had HTN (32.5%), there were 15 population had dyslipidemia were (37.5%), there were seven population had CHD, (`17.5%), the mean testosterone (ng/dl) was 523.1 ±47.3, regarding base line characters of the study population.

Our results are consistent with **Poulios *et al.*** [(14)] who planned to perform the first ever randomized, controlled trial of platelet-rich plasma injections for moderate to mild erectile dysfunction: Subjects with mild to moderate erectile dysfunction who were sexually active were randomly randomized to receive 10 mL of PRP (n = 30) or a placebo (n = 30) intracavernosal injections two times, separated by one month. Their study included 60 participants, with a median age of 58 and 59 years, who were randomly assigned to receive either PRP injections (n = 30) or placebo injections (n = 30).

Our results are consistent with **Poulios *et al.*** [(14)] who showed that both the PRP and placebo groups had EDs for an average of 78 months (IQR: 48, 120) compared to 60 months (IQR: 39, 117) for the placebo group. Twenty patients registered mild erectile dysfunction (PRP=13, placebo=7), thirty-two mild to moderate erectile dysfunction (PRP=14, placebo=18), and eight moderate erectile dysfunction (PRP=3, placebo= 5). When comparing the two groups' baseline characteristics, no statistically significant differences were found.

Also, **Panunzio *et al.*** [(11)] aimed to compile the most recent findings regarding the effectiveness of intravenous injections of PRP in males suffering from primary organic ED. Following 1 month of follow-up, 299 patients showed a pooled mean difference (95% confidence interval) of 2.99 (1.86, 4.13), 204 patients showed a pooled mean difference of 2.85 (1.61, 4.09), and 199 patients showed a pooled mean difference of 3.21 (1.82, 4.60) on the International Index of Erectile Function (erectile function domain) compared to placebo-treated patients. The study found that PRP intracavernosal injections helped men with primary organic erectile dysfunction either noticeably enhance their erectile function or showed some improvement.

We found that the mean IIEF-EF before treatment was 15.35±3.1, after the third month it was 17.28±2.95, and after the sixth month it was 19.40±2.74. The mean % of change was 28.37±13.12 with median 25 regarding baseline and last follow up of IIEF among the studied population.

Moreover, **Shaher *et al.*** [(15)] who showed that the duplex parameters, SEP Q2, and 3, as well as the International Index of Erectile Function-Erectile Function (IIEF-EF), improved. Compared to the saline group, which exhibited an improvement of 18% at 1-month post-treatment, 76% of patients in the PRP group achieved a minimally clinically meaningful difference in IIEF-EF. Three months after treatment, 72% of patients in the PRP group and 16% in the saline group had achieved a minimally clinically relevant change; by six months after treatment, that number had reduced to 70% in the PRP group and 16% in the saline group.

Our study showed that there was statistically significant difference in the studied group regarding baseline, 3rd month and 6th month of IIEF-EF and there was no statistically significant difference in the studied group regarding baseline, 3rd month and 6th month of penile Doppler ultrasound.

Our follow up by IIEF-5 questionnaire showed that at 3rd month post intervention there were 3 participants had good sexual function (7.5%), half of population with mild ED severity (50%), 13 patients with mild to moderate ED severity (32.5%) and 4 populations with moderate ED severity (10%). At six months after treatment sexual follow up of study population showed that, there were 7 participants had good sexual function (17.5%), more than half of population with mild ED severity (52.5%), ten patients with mild to moderate ED severity (25%) and only two participants with moderate ED severity (5%).

Our results are consistent with **Poulios *et al.*** [(14)] who completed the final injections and then assessed ED severity three times (1, 3, and 6 months later) using the IIEF and the Sexual Encounter Profile (SEP). Improvements in IIEF and SEP scores were statistically significant across all follow-up time periods, and no serious adverse events were observed to be associated with the treatment. In comparison to placebo results of 25% (P <0.001), 39% (P =0.018), and 27% (P <0.001) during the same time periods, patients at 1 month, 3 months, and 6 months attained an MCID of 76%, 69%, and 27%, respectively.

Also, we intended to assess the security and effectiveness of injecting PRP as a treatment for moderate erectile dysfunction. Our results were supported by **Shaher *et al.*** [(15)]. One hundred instances of mild to severe erectile dysfunction were studied in a placebo-controlled fashion. In one group, participants had three injections of PRP (3 mL each corpus) spaced fifteen days apart, while in the other group, known as

the placebo (Saline) group, participants received six milliliters of saline administered intravenously. Six months followed the injection. Researchers came to the conclusion that PRP injections are a safe and effective way to treat moderate erectile dysfunction.

Epifanova *et al.* [16] discovered that the use of PRP enhanced IIEF-5 in erectile dysfunction patients. Due to the lack of side effects, the authors concluded that PRP is a dependable procedure and that it includes enough growth factors to have a therapeutic impact. **Taş *et al.*** [17] concluded that autologous PRP application provides short-term improvement in erectile function.

As well, **Masterson *et al.*** [13] based on their findings, it is safe to administer two injections of intracavernosal platelet-rich plasma to men with mild to moderate erectile dysfunction at one-month intervals. However, they did not find any significant difference in the effectiveness of the two therapies.

Clinical trials assessing PRP's efficacy in treating erectile dysfunction have yielded conflicting findings, despite **Fazekas *et al.*'s** [18] demonstration that the treatment is safe. **Scott *et al.*** [19] who was to assess the available data on platelet-rich plasma (PRP) treatment for erectile dysfunction (ED) and identify the most recent developments in this field. Based on their findings, PRP is a safe and effective treatment for erectile dysfunction.

CONCLUSION

While the research group did find a statistically significant difference in the IIEF-EF at baseline, 3 months, and 6 months, they did not find a statistically significant difference in the penile Doppler ultrasound at baseline, 3 months, or 6 months. Less improvement in individuals with longer duration of erectile dysfunction was observed in the study, as there was a negative significant link between percentage of change and ED duration.

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