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Platelet-rich plasma effects on erectile function

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Abstract
Aim: To evaluate the safety and feasibility of PRP injections in a subset of patients treated for ED.
Material and Method: The present prospective study was conducted among 28 subjects suffering from erectile dysfunction (ED) in the Department of Urology, Sawai Man Singh Hospital Jaipur. The study was approved by the Institutional Ethical Committee of the hospital. Data was prospectively collected and retrospectively reviewed for patients treated with PRP for ED by a single surgeon. Informed consent was obtained and patients were aware of off-label use. Demographic data, procedural details, outcomes data, and pre- and post-procedural International Index of Erectile Function (IIEF- 5) questionnaires (for male patients) were collected. Erectile function was evaluated using IIEF-5 scores (24 points in total). Scores below 21 points suggested ED. Each participant was injected with autologous PRP using a proprietary system.
Results: None of the subject had normal IIEF score before the treatment. Post treatment, normal IIEF score was found among 57.14% and 71.43% of the subjects at 1 and 3 month respectively. Mean IIEF-5 scores increased from 15 to 20 after the administration of the PRP at 3 month with statistically significant difference. Treatment with PRP leads to erection hardness and ability to engage in a successful intercourse among 75% and 71.43% of the subjects respectively.
Conclusion: The results of the current study were very promising regarding the function improvement of ED patients. After three months of follow-up, patients injected with PRP seemed to have better sexual life.

Keywords: PRP, ED, IIEF-5

Introduction

Epidemiologic studies have shown that erectile dysfunction (ED) is a highly prevalent condition, affecting more than 300 million men globally, and the use of regenerative medicine, such stem cells, to reverse ED is highly desired [1]. ED is defined as the chronic inability to achieve or sustain a penile erection. Indeed, regular and chronic ED increases with age from 35% of men aged 60 to 50% of men older than 70 being affected [2]. Many risk factors for ED exist including age, coronary artery disease, obesity, smoking, depression, hypertension, prior pelvic surgery, and spinal cord injuries as well as other psychological variables [3]. Sexual health and erectile quality are key components to not only an individual's quality of life but also their partner's mental, emotional, and physical well-being [4].

Intracavernosal injection of platelet-rich plasma (PRP) as a treatment for erectile dysfunction (ED) is an emerging practice that warrants awareness among primary care physicians and urologists alike. Platelets contain various growth factors such as platelet-derived growth factor (PDGF), IGF-I, and vascular endothelial growth factor (VEGF). When platelets are activated, they will release many kinds of growth differentiation factors and a few types have been found to facilitate nerve repair and regeneration [5]. In the current era of consumerism, increasing numbers of patients are demanding novel and innovative treatment options. There is a trend toward the global emergence of clinics offering PRP as a treatment for ED for many desperate and vulnerable men; however, despite the introduction and commercialization of this therapy, there remains little evidence to support its use and guide patient or clinician in the Decision-Making process [6].

One of the most well described platelet-based therapies is autologous platelet-rich plasma (PRP). PRP is derived from the centrifugation of whole blood with a separator gel to remove the red and white blood cells. The resulting supernatant has a greater than four-fold increase in platelets and other plasma proteins. Within urology, as with many other specialties, there are numerous conditions where tissue regeneration is desirable. In a prior rodent model, Wu et al performed intracavernosal injection of PRP after cavernous nerve crush injury and noted increased myelinated axons and improved recovery of erectile function [7]. Currently, there is scarce literature available on the efficacy of PRP for the treatment of urologic conditions in humans, and thus, no assessment of safety. The aim of this study was to evaluate the safety and feasibility of PRP injections in a subset of patients treated for ED.

Material and Method

The present prospective study was conducted among 28 subjects suffering from erectile dysfunction (ED) in the Department of Urology, Sawai Man Singh Hospital Jaipur. The study was approved by the Institutional Ethical Committee of the hospital. Data was prospectively collected and retrospectively reviewed for patients treated with PRP for ED by a single surgeon. Informed consent was obtained and patients were aware of off-label use. Demographic data, procedural details, outcomes data, and pre- and post-procedural International Index of Erectile Function (IIEF- 5)

questionnaires (for male patients) were collected. Erectile function was evaluated using IIEF-5 scores (24 points in total). Scores below 21 points suggested ED. Each participant was injected with autologous PRP using a proprietary system [8]. The subjects were selected according to the inclusion and exclusion criteria as mentioned below:

Inclusion Criteria

1. Adult male Patients ≥ 40 years old
2. Patients who have IIEF-5 score ≤ 21

Exclusion Criteria

1. Patients that are critically ill who required medical treatment
2. Patients who are unwilling to participate in the survey
3. Patients who are diagnosed with psychiatry illness or mentally challenged.
4. Patients who underwent surgical treatment for ED
5. Patients who are admitted and required intervention in hospital
6. Patients who received non-pharmacological local therapy (herbal medications)
7. Patients who received hormone therapy for ED (hypogonadism)
8. Immunocompromised patients (HIV, AIDS and cancer patients)

PRP process and preparation

PRP is prepared by a process known as differential centrifugation. In differential centrifugation, acceleration force is adjusted to sediment certain cellular constituents based on different specific gravity. In the PRP method, an initial centrifugation to separate red blood cells (RBC) is followed by a second centrifugation to concentrate platelets, which are suspended in the smallest final plasma volume. WB (whole blood) is initially collected in tubes that contain anticoagulants. The first spin step is performed at constant acceleration to separate RBCs from the remaining WB volume. After the first spin step, the WB separates into three layers: an upper layer that contains mostly platelets and WBC, an intermediate thin layer that is known as the buffy coat and that is rich in WBCs, and a bottom layer that consists mostly of RBCs. For the production of pure PRP (P-PRP), upper layer and superficial buffy coat are transferred to an empty sterile tube. For the production of leucocyte rich PRP (L-PRP), the entire layer of buffy coat and few RBCs are transferred. The second spin step is then performed. 'g' for second spin should be just adequate to aid in formation of soft pellets (erythrocyte-platelet) at the bottom of the tube. The upper portion of the volume that is composed mostly of PPP (platelet-poor plasma) is removed. Pellets are homogenized in lower 1/3rd (5 ml of plasma) to create the PRP (Platelet-Rich Plasma).

In the present study, PRP was obtained from a sample of patients' blood drawn at the time of treatment. Blood was centrifuged at 4000 rpm for 15 min. A 30 cc venous blood draw will yield 3-5 cc of PRP depending on the baseline platelet count of an individual, the device used, and the technique employed. The blood draw occurs with the addition of an anticoagulant, such as citrate dextrose A to prevent platelet activation prior to its use. The steps followed were as follows:

1. WB was obtained by venipuncture in acid citrate dextrose (ACD) tubes,
2. Blood was not chilled at any time before or during platelet separation,
3. Blood was centrifuged using a 'soft' spin,
4. Transfer of supernatant plasma containing platelets into another sterile tube (without anticoagulant),
5. Tubes were centrifuged at a higher speed (a hard spin) to obtain a platelet concentrate.
6. The lower 1/3rd is PRP and upper 2/3rd is platelet poor plasma (PPP). At the bottom of the tube, platelet pellets are formed.
7. Remove PPP and suspend the platelet pellets in a minimum quantity of plasma (2-4 mL) by gently shaking the tube.

PRP injection Process

Between 4 and 9 mL of PRP was injected per treatment session. Intra-cavernosal injection was performed for ED. Patients were observed in the clinic for 20–30 minutes post-procedurally for potential complications or side effects. Clinical information, safety related questions, survey data, and IIEF-5 questionnaires were collected at the time of clinical follow-up and telephone calls were used to evaluate for possible adverse events for which no medical attention was sought.

Recording of data

The severity of ED was measured using the International Index of Erectile Function-5 (IIEF-5) which is a self-evaluation questionnaire used for the assessment of male sexual function including screening and diagnosis of severity of ED (Pastuszak, 2014). Participants were asked to rate their ability to achieve and maintain an erection that is good enough for a satisfactory sexual intercourse without any treatment for the past 6 months. Response options ranged from very low, low, moderate, high and very high. Among the questions asked were as follow:

- How do you rate your confidence that you could get and keep an erection?
- When you had erections with sexual stimulation, how often were your erections hard enough for penetration?
- During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?
- During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?
- When you attempted sexual intercourse, how often was it satisfactory for you?

Severity of ED is further categorised based on the IIEF scores: severe (5-7), moderate (8-11), mild to moderate (12-16), mild (17-21), and no ED (22-25). For analysis purposes, a binary variable was created based on IIEF-5 where scores from 12-21 is considered "less severe (Mild to Mild/Moderate)" and 5–11 is considered as "moderate to severe" ED[8]. IIEF score was recoded before the intervention and after the intervention at 1 & 3 months,

Statistical analysis: Data so collected was tabulated in an excel sheet, under the guidance of statistician. Data was analyzed using IBM SPSS. Statistics Windows, Version 22.0. (Armonk, NY: IBM Corp) for the generation of descriptive and inferential statistics. The statistical significant difference among the continuous and categorical variables was determined by the Chi square and anova test

respectively.

Results

The mean age of study subject was 44.6±8.79 years with minimum and maximum of 41 and 54 years respectively (table 1).

None of the subject had normal IIEF score before the treatment. Post treatment, normal IIEF score was found among 57.14% and 71.43% of the subjects at 1 and 3 month respectively. Moderate to severe IIEF score reduced from 28.57% of subjects to 7.14% of the subjects after 3 months. When IIEF scores was compared statistically at different time intervals, it was found to be statistically significant as $p<0.05$ (table 2). Mean IIEF-5 scores increased from 15 to 20 after the administration of the PRP at 3 month with statistically significant difference (table 3).

Treatment with PRP leads to erection hardness and ability to engage in a successful intercourse among 75% and 71.43% of the subjects respectively (table 4).

Discussion

ED globally affects a large number of adult men and significantly reduces their quality of life. Current treatments involved the use of PDE5-I, which induces mild side effects in 70% of patients. Moreover, the use of PDE5-I is limited in patients with cardiovascular disease and diabetes mellitus. Second line treatments for ED involved the use of vacuum devices and intrecavernosal injections with PDE5-I. To date, all these approaches have only temporal effects in patients suffering from ED[9]. Recently platelet-rich plasma (PRP) injections have recently been marketed as a form of autologous cell therapy under the banner of regenerative medicine despite limited scientific evidence on its use for treating erectile dysfunction (ED). As there is lack of strong clinical evidence supporting the efficacy of PRP in treating ED, hence the present study was planned to assess platelet-rich plasma effects on Erectile Function.

The mean age of study subject was 44.6±8.79 years in the present study. None of the subject had normal IIEF score before the treatment. Post treatment, normal IIEF score was found among 57.14% and 71.43% of the subjects at 1 and 3 month respectively. Moderate to severe IIEF score reduced from 28.57% of subjects to 7.14% of the subjects after 3 months. Mean IIEF-5 scores increased from 15 to 20 after the administration of the PRP at 3 month with statistically significant difference in the present study. Similar results were revealed by Matz et al[10]. Matz et al[10] found that platelet rich fibrin matrix injection is a well-tolerated, safe, and feasible treatment modality in patients with ED, Peyronie's disease (PD), and stress urinary incontinence. They reported an improvement in International Index of Erectile Function score by an average of 4.14 points after platelet-rich fibrin matrix injections. A randomized controlled trial in human subjects reported by Epifanova et al[11] found increased concentrations of growth factors, such as FGF, PDGF, and VEGF, in control and ED groups on evaluation with the flow cytometry-based xMAP system (Luminex, Austin, TX). These findings confirm that these growth factors are responsible for the recovery of erectile function. Treatment with PRP leads to erection hardness and ability to engage in a successful intercourse among 75% and 71.43% of the subjects respectively in the present study. Alkhayal S[12] reported similar results i.e. 35 out of 40 patients (85%) felt that the treatment improved their erection hardness and in 29 patients (72%) improved their ability to engage in a successful intercourse.

This study was also characterized by several limitations in its performance. This study lacks the control group and had small sample size.

Conclusion

The results of the current study were very promising regarding the function improvement of ED patients. After three months of follow-up, patients injected with PRP seemed to have better sexual life. The future goal of this study is to enroll a higher number of patients who will be evaluated for their erectile function over a longer time period of time. ED compromise a wide socioeconomic burden, affecting a great number of men, and any possible therapeutic strategy without the adverse effects of previous treatments may be very promising.

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