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Efficacy and Reliability of Matrix PRP in Erectile Dysfunction Therapy: Experience of the Regenerative Medicine Center at CHEIKH KHALIFA University Hospital, Morocco

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Platelet-rich plasma is defined as a plasma fraction derived from autologous blood with a platelet concentration above the normal range. It constitutes a reservoir of bioactive proteins, mainly growth factors, which are essential for initiating and accelerating tissue repair and regeneration. Biological stimulation of damaged tissue with platelet concentrates (PRP) involves harnessing the tissue's regenerative potential by recruiting local stem cells.

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Methods: This is a retrospective study spread over 12 months (March 2021 to March 2022) involving a sample of 40 patients with erectile dysfunction with an age ranging from 34 to 71 years and an average of 52.5 years. Initial assessment and follow-up of patients was based on the International Index of Erectile Function (IIEF5) with a score of (5-10) indicating severe erectile dysfunction, (11-15) moderate, (16-20) mild, (21-25) no erectile dysfunction.
Results: All in all, a significant improvement in IEF5 was demonstrated in all patients, with the mean IEF5 of all patients rising uniformly after each dose, plateauing at months 3 and 6.
Conclusion: The IEF5 of 55% of patients improved after the 1st dose, with 70% of patients showing improvement after the 2nd dose, then stagnating at 80% after the3rd dose.

Keywords: Platelet-rich plasma; autologous blood; growth factors; regeneration; erectile dysfunction.

1. INTRODUCTION

Erectile dysfunction is defined as the inability to initiate or maintain a satisfying sexual relationship [1]. It is a very common pathology throughout the world, with the main risk factors being metabolic syndrome, diabetes and smoking. Apart from its pure pathophysiological side as much as its organic disease, erectile dysfunction causes a significant psychological burden on the sufferer, which is very poorly tolerated in conservative Eastern societies, as well as dissatisfaction in the partner, threatening the stability of the conjugal relationship on an ongoing basis [2,3].

The advent of IPDE5s at the end of the 90s certainly revolutionized the management of ED, but patient dissatisfaction remains fairly common. Not to mention the considerable percentage of side effects, the limits imposed by contraindications, and the fairly high cost of a complete therapeutic regiment hat remains inaccessible to a large segment of the population in an emerging country like ours [4,5].

Platelet-rich plasma is defined as a plasma fraction derived from autologous blood with a platelet concentration above the normal range. It constitutes a reservoir of bioactive proteins, mainly growth factors, which are essential for initiating and accelerating tissue repair and regeneration. Biological stimulation of damaged tissue with platelet concentrates (PRP) involves harnessing the tissue's regenerative potential by recruiting local stem cells [6,7,8].

In terms of erectile dysfunction, PRP injection seems to be experimentally effective, never the less clinical studies remain rare and timid in this direction, we report in this article the experience of the International Center of Regenerative Medicine of the University Hospital CHEIKH KHALIFA of Casablanca, we assume that PRP injection would be beneficial to treat erectile dysfunction and we verify the efficacy and tolerance of this therapy on our patients [9,10].

2. PATIENTS AND METHODS

This is a retrospective study spread over 12 months (March 2021 to March 2022) involving a sample of 40 patients with erectile dysfunction with an age ranging from 34 to 71 years and an average of 52.5 years. Initial assessment and follow-up of patients was based on the International Index of Erectile Function (IIEF5) with a score of (5-10) indicating severe erectile dysfunction, (11-15) moderate, (16-20) mild, (21-25) no erectile dysfunction.

IIEF5 was assessed be for each PRP injection and periodically at 3 and 6 months. We opted for a standard 3-injection regimen (one injection every 15 days). No patient in the study was receiving any other treatment for erectile dysfunction.

2.1 Preparation of Matrix PRP

To prepare PRP, the patient's blood was collected in a sterile vacuum tube containing 0.5 ml sodium citrate (anticoagulant) and 2 ml non-cross-linked hyaluronic acid (HA) (under the inert separating gel). The tubes were then centrifuged at 3000 rpm for 5 minutes. The plasma and HA layers were then homogenized (the inert gel separating them from the red blood cells and leukocyte ring).

The aim was to recover a maximum number of platelets deposited on the surface of the separating gel, there by obtaining a platelet-enriched combination of Plasma + HA (with a final concentration slightly higher than its physiological value, and a viability of 70%). 3 cc of Matrix PRP were injected into each corpus cavernosum with a 25G needle.

No anesthesia was applied at the injection site.

During the intracavernosal injection, a tourniquet was applied for 20 minutes to ensure maximum retention of the PRP at the injection site and to optimize its action in contact with the corporacavernosa, while limiting any wastage and avoiding compression of the dorsal penile artery, as well as the superficial and deep dorsal vein.

Intracavernosal autologous PRP was applied to patients 3 times at 15-day intervals. Injection sites varied from 1 cm in the median region of the penis. Due to the limited number of studies on PRP and erectile dysfunction, there is no clear consensus. In this study, we used this dose and time interval in line with similar studies with PRP.

3. RESULTS

Patient demographics are shown in Table 1, 3 patients were excluded (out of follow-up) age ranged from 34 to 71 years with an average of 52, 5 years.

36 patients (90%) were married, 2 divorced and 2 single. Body mass index averaged 32.2.

18 patients (45%) were known diabetics, 10 patients (25%) were hypertensive, 12 patients (30%) were known dyslipedimics, 6 patients (15%) were glucose intolerant, 4 patients had undergone cystectomy, 2 patients had undergone prostatectomy.

No patient experienced significant pain during the injection, very minimal bleeding was observed in 2 patients, 1 patient presented a local inflammatory reaction 3cm in diameter which resolved spontaneously after 2 hours, no patient presented urethral discharge of the injection fluid.

Table 1. List of variables and their values

Variable	Value
Average Age	52, 5
Familystatus	
Married	36 patients (90%)
Divorced	2 patients (5%)
Single	2patients (5%)
BMI (average)	32,2
Duration of erectile dysfunction	6 ans
HTA	12 patients (30%)
Diabetes	18 patients (45%)
Dyslipidemia	12 patients (30%)
Impaired glucose tolerance	6 patients (15%)
Cystectomy	4 patients (10%)
Prostatectomy	2 patients (5%)

All in all, a significant improvement in IEF5 was demonstrated in all patients, with the mean IEF5 of all patients rising uniformly after each dose, plateauing at months 3 and 6.

The IEF5 of 55% of patients improved after the 1st dose, with 70% of patients showing improvement after the 2nd dose, then stagnating at 80% after the3rd dose.

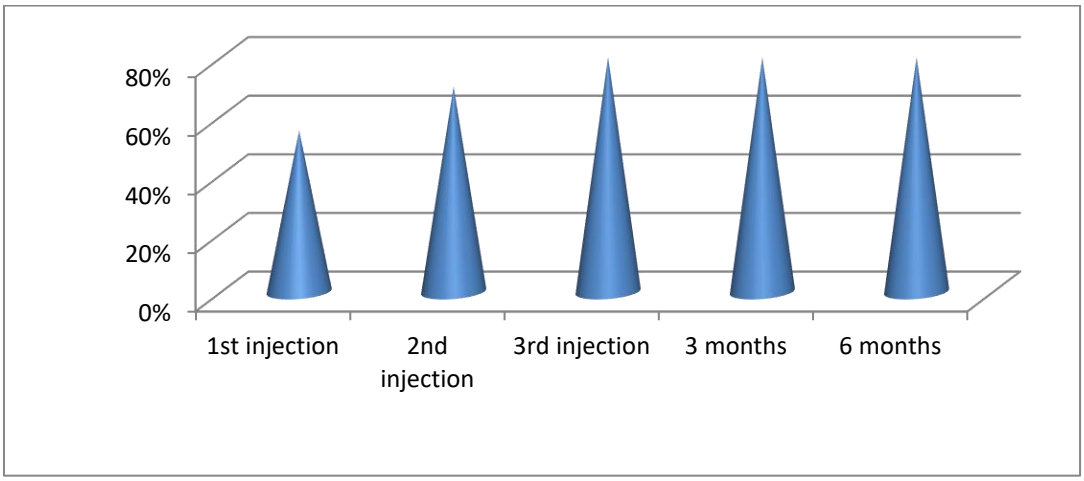

Fig. 1. Bar graph showing improvement in IEF5

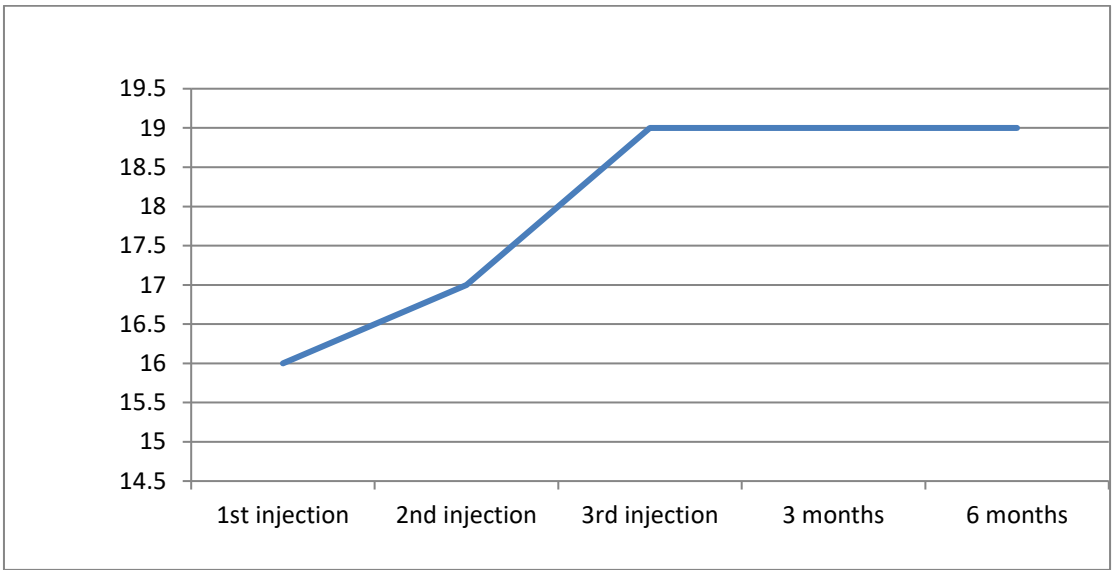

Fig. 2. Evolution of IEF5

4. DISCUSSION

Erectile dysfunction (ED) is the most widely studied sexual dysfunction. It is defined as the persistent or recurrent inability to obtain or maintain an erection permitting satisfactory sexual intercourse [11,12].

The prevalence of ED is less than 10% in men under 50, and more than 20% in men over 60. Aging, cardiovascular disease as a whole, diabetes, hypercholesterolemia, smoking, depression and psychiatric illnesses, psychological disorders and unfavorable socioeconomic conditions are all risk factors for ED. Drug-induced ED must be systematically investigated. ED can be psychogenic, organic or mixed: psychogenic and organic [15,16,17,18].

The pathophysiological mechanisms are diverse, involving alterations in central or peripheral nerve control, penile arterial vascularization, endothelial function, smooth muscle tone and the structure of the corpora cavernosa, and even hormonal involvement. Indeed, ED may be a symptom of an under lying vascular disorder.The probability of developing vasogenic ED is increased by 3.04 times in hypertension, 2.57 times in diabetes and 1.83 times in dyslipidemia. Prospective and cross-sectional studies have found that obesity and metabolic syndrome are associated with increased ED [19].

The management of erectile dysfunction is as complex as its etiopathogenesis, and highly effective treatment remains a challenge for the clinician given the multitude of pathophysiological parameters involved. IPDE5s are the most widely used therapeutic class, with daily regimens or on-demand injections before intercourse. Intracavernosal injections of prostaglandins are an alternative to IPDES5s, stimulating cyclic AMP and thus promoting muscle fiber relaxation and vasodilation, which are essential for erection.

However, all these treatments face 3 main challenges:

-symptomatic therapies, none of which can cure ED

average patient satisfaction, especially after long-term use

-High cost

Recently, new therapeutic strategies have been tested for erectile dysfunction and Peyronie's disease, aimed at repairing the penile cellular lesions at the root of the disorder. These new therapies involve injecting autologous biological products into the corpora cavernosa, with the aim of improving erectile function and/or reducing albuginea fibrosis [13,14].

Platelet-rich plasma (PRP) is blood plasma enriched with platelets by centrifugation, thus eliminating the majority of leukocytes and erythrocytes. It is a concentrated source of autologous platelets which, once injected, release platelet factors responsible for tissue

healing by degranulation. The main platelet factors released are VEGF (Vascular Endothelial Growth Factor), FGF (Fibroblast Growth Factor), IGF (Insulin like Growth Factor), TGF (Transforming Growth Factor), PDGF-AB (Platelet Derived Growth Factor). These factors influence cell growth and collagen synthesis, and activate angiogenesis. They therefore represent a set of signals capable of stimulating cell growth and remodeling of damaged tissue, justifying their interest as inducers of healing in poorly vascularized tissue.

PRP was first used for a variety of aesthetic indications, before being extended to pathologies involving muscle, cartilage, tendon or nerve regeneration. Although several clinical studies have shown unquestionable regenerative effects on a wide range of tissues, the lack of standardization of the manufacturing process has led to considerable heterogeneity in product composition, making it impossible to compare results.

“Despite accumulating evidence from molecular and animal studies, limited data suggest the use of PRP in daily clinical practice” [24].

In a double-arm randomized clinical trial, Evangeleos Poulios et al. compared a group of 30 mild ED patients receiving a monthly intracavernosal injection of PRP with a similar group receiving placebo and assessed at months one, three and six. The trial showed a significant gain of 3.9 points in IEF5 score and satisfaction in patients treatedwith PRP. The authors concluded that PRP is a promising therapeutic alternative for the treatment of ED [23].

“In a multicenter randomized Russian study, patients with erectile dysfunction were divided into 3 groups: (Group 1, 30 patients):three sessions of intracavernosal injections of activated PRP with 10% CaCl2 once a week; (Group 2, 30 patients) the same PRP protocol combined with PDE5i; (Group 3, 15 patients): PRP inactivated once a week for three weeks. All groups showed a significant improvement in erectile function compared with baseline, and none of the adverse events were reported.33 Furthermore, the authors concluded that PRP contains the necessary concentration of growth factors for a therapeutic effect. Nevertheless, in these studies, there was no placebo arm and no long-term evaluation was carried out” [24].

Matz et al. retrospectively examined “the safety and feasibility of platelet-rich fibrin matrix (PRFM) in four patients with erectile dysfunction, eleven with lapeyronie's disease and one patient with both conditions. Among seven patients evaluated with IIEF-5, the latter increased on average by 4.14 points, while no major adverse events were reported in any patient”.

Ruffo et al. evaluated “the effect of PRP combined with low-intensity shockwave therapy in two published trials. In the first study, 100 patients received shockwave therapy alone twice a week for 6 weeks (Group 1, 58 patients) or in combination with PRP injections once a week for 6 weeks (Group 2, 55 patients). In the other study, 112 patients received shockwave therapy once a week for 6 weeks only (Group 1, 53 patients) or in combination with PRP injections once every 2 weeks for 6 weeks (Group 2, 59 patients). In both trials, at 12”and 24 weeks, the combined treatment significantly improved erectile function compared with baseline or shockwave monotherapy [20,21].

Ding et al studied the effect of PRP on the regeneration and restoration of cavernous nerve function after injury. The PRP effect was studied 3 months later. PCI was measured to assess erectile function. EF in the PRP group was improved; PCI was significantly higher than that in the untreated group, but lower than that in the placebo group ($P < 0.05$). Cavernous nerve myelination in the PRP-treated group was significantly higher than in the untreated group, but also lower than in the placebo group ($P < 0.05$). Study limitations included a small sample size and the administration of PRP at the site of cavernous nerve injury. In addition, the scientists used a non-standard method of electric field stimulation and a non-quantitative estimate of nerve regeneration was made [22].

Preclinical studies were also carried out in Taiwan by C Wu et al in 2012 and Y Wu et al in 2013. In the 2012 study,60 rats in the experimental group received PRP therapy immediately after cavernous nerve injury. 4 weeks later, ICP was 1/3 higher in rats treated with PRP compared with animals that did not receive PRP therapy ($P < 0.05$). After treatment, the number of myelinated axons in the cavernous and dorsal nerves of the animals was significantly higher than in the untreated group. PRP administration significantly reduced the level of apoptotic markers (TGF-b1, TUNEL, PI) and, consequently, apoptotic cells, including the cavernous body fibrosis marker TGF-b1 ($P < 0.05$).

A reduction in fibrosis was also confirmed by histological study of penile tissue. Absence of type III collagen and prevalence of type I collagen was observed in specimens from the treated group. The authors believe that platelet granule growth factors acted as gaspedals of the nerve repair process due to their neuro-regenerative and neuroprotective properties, and inhibitors of the fibrosis process in the corpora cavernosa.

5. CONCLUSION

With the advent of IPDE5s, regenerative medicine therapy looks set to take on greater therapeutic importance. We consider our results to be promising and fruitful. Nevertheless, randomized studies with large patient samples are needed, as well as a focus on different treatment regimens. Precise coding of treatment doses and indications remains the cornerstone for standardization of this therapy.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study was validated by the ethical committee of the Mohammed 6 University of Health Sciences, and was conducted at the regenerative medicine center of the CHEIKH KHALIFA University Hospital in Casablanca.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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