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Evaluation of the Effect of Platelet-Rich Fibrin (PRF) Protocol and Laser Acupuncture in the Treatment of Infertile Men with Non-Obstructive Azoospermia: A Randomized Clinical Trial

Mohammadreza Razaghi[1], **Reza Nicknama**[2*], **Sona Zare**[3], **Mohammad Seifipoor**[2], **Mohammadmohsen Mazloumfard**[3], **Fatemeh Sheibani**[1], **Parnia Rahnamay Farnood**[1]

[1]Laser Application in Medical Sciences Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Department of Urology, Shohada-e-Tajrish Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Proteomics Research Center, Faculty of paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

***Correspondence to**
Reza Nickanma,
Email: rezanick1995@gmail.com

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Abstract

Introduction: Non-obstructive azoospermia (NOA) is a challenging male infertility disorder with limited treatment options. This study investigated the efficacy of novel reconstructive approaches, specifically platelet-rich fibrin (PRF), with and without laser needling, in improving testicular function and sperm retrieval in patients with NOA.

Methods: In a randomized clinical trial, 40 men with NOA were divided into two groups: PRF + laser and PRF alone. Semen parameters (volume, concentration, motility, morphology, DNA fragmentation), hormone levels (FSH, LH, testosterone), and testicular volume were assessed at baseline, immediately post-intervention, and at one and three months.

Results: Sperm concentration, motility, morphology, and DNA fragmentation rates showed no significant intergroup differences. While semen volume increased within groups post-intervention ($P=0.039$), this change was not significant between groups ($P>0.05$). No serious complications were reported.

Conclusion: In summary, this study found that PRF injection, with or without laser-acupuncture, did not significantly improve sperm parameters in NOA patients in the short term. Further research with larger cohorts, extended follow-up, and precise patient selection is needed.

Keywords: Laser-acupuncture, Male infertility, Non-obstructive azoospermia, Platelet-rich fibrin (PRF), Spermatogenesis

Introduction

Infertility affects approximately one in six couples worldwide, with male-related factors contributing to nearly half of all cases.[1] Azoospermia, defined as the complete absence of spermatozoa in the ejaculate, represents the most severe form of male infertility and is broadly classified into obstructive and non-obstructive types.[2] Non-obstructive azoospermia (NOA), which results from impaired spermatogenesis rather than obstruction of the reproductive tract, accounts for most azoospermia cases and encompasses a heterogeneous spectrum of histopathological patterns, including hypospermatogenesis, maturation arrest, and Sertoli cell-only syndrome, making it one of the most challenging conditions in reproductive medicine.[2,3] Although advances in assisted reproductive technologies have enabled many men with NOA to achieve biological paternity, current treatment remains focused on surgical sperm retrieval rather than restoration of endogenous spermatogenesis, with microdissection testicular sperm extraction (micro-TESE) combined with intracytoplasmic sperm injection representing the current standard of care.[4,5] Nevertheless, sperm retrieval remains unsuccessful in a substantial proportion of patients, no reliable predictor of success has been identified, and medical therapies have shown limited benefit in primary testicular NOA, with established efficacy largely restricted to hypogonadotropic hypogonadism.[6,7]

Among emerging regenerative approaches, autologous platelet concentrates have attracted considerable interest because they provide a concentrated source of growth factors involved in tissue repair and regeneration.[8] Platelet-rich plasma (PRP), the first-generation platelet concentrate, is characterized by rapid release of bioactive molecules and requires anticoagulants during preparation, whereas platelet-rich fibrin (PRF), a second-generation concentrate, forms a three-dimensional fibrin matrix

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without anticoagulants, enabling sustained release of growth factors while providing a biological scaffold that supports angiogenesis, cell migration, proliferation, and tissue remodeling.[9,10] The regenerative potential of platelet concentrates has prompted growing interest in their application to male reproductive disorders. Experimental evidence suggests that platelet-derived biomaterials can attenuate inflammation, reduce oxidative stress and apoptosis, and improve spermatogenesis following testicular injury, supporting their biological potential for testicular regeneration.[11] Clinical application of platelet-derived products in male infertility has yielded encouraging yet heterogeneous findings, with considerable variation in patient populations, intervention protocols, and reported outcomes; most available evidence has focused on PRP rather than PRF.[12]

Low-level laser therapy has also been investigated as a non-invasive regenerative approach because of its ability to modulate cellular metabolism, improve microcirculation, and stimulate tissue repair through photobiomodulation. Laser-acupuncture combines these biological effects with stimulation of traditional acupuncture points while avoiding needle insertion and its associated discomfort. Improvements in semen parameters have been reported following laser-acupuncture in selected infertile men; however, available evidence has largely been limited to men with oligospermia or mixed infertility populations, and its applicability to NOA remains uncertain.[13,14]

Nevertheless, current evidence remains difficult to interpret because available studies predominantly evaluate PRP rather than PRF, include heterogeneous patient populations and treatment protocols, and provide limited evidence specifically in men with NOA.[12] Moreover, whether combining PRF with laser-acupuncture offers additional clinical benefit beyond PRF alone has not been adequately investigated. Therefore, the present randomized clinical trial was designed to evaluate the effects of intratesticular PRF, administered alone or in combination with laser-acupuncture, on semen parameters, hormonal profile, testicular volume, and treatment-related complications in men with non-obstructive azoospermia.

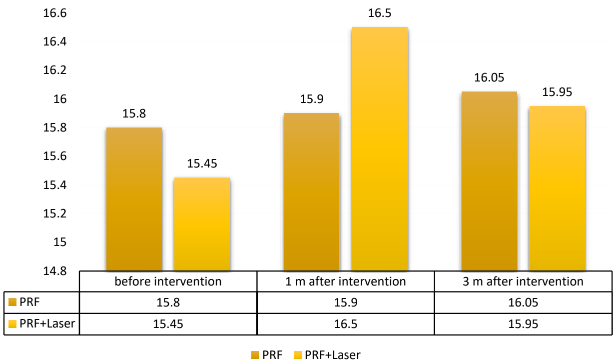
Materials and Methods

Study design

This study was designed as an open-label, randomized clinical trial evaluating the effects of PRF, with or without laser acupuncture, in men with confirmed non-obstructive azoospermia.

Participants

Men younger than 45 years with confirmed non-obstructive azoospermia who were referred to infertility clinics in Tehran were assessed for eligibility. Azoospermic individuals were defined as those with no sperm found in testicular samples, even after microtissue surgery. Patients with recent varicocele or a history of undescended testes were excluded. The CONSORT diagram is provided in Figure 1.



	before intervention	1 m after intervention	3 m after intervention
PRF	15.8	15.9	16.05
PRF+Laser	15.45	16.5	15.95

Figure 1. Testicular volume of patients across the time points

Randomization and blinding

Forty eligible participants were allocated to two study groups using permuted block randomization with a 1:1 allocation ratio. Variable block sizes of 2, 4, and 6 were used to ensure balanced allocation. The randomization sequence was generated using the online Sealed Envelope randomization software. The allocation sequence was placed in sequentially numbered, opaque, sealed envelopes. Every envelope in sequence was opened, and the participant was assigned to either the PRF group or the PRF plus laser-acupuncture group. Due to the nature of the interventions, including intratesticular PRF injection and repeated laser-acupuncture sessions, blinding of participants and treating clinicians was not feasible. Therefore, this study was conducted as an open-label randomized clinical trial. Outcome assessors were also not blinded to group allocation. However, the primary and secondary outcomes were based on objective laboratory and clinical measurements, including semen analysis, hormonal assays, testicular volume assessment, and documented adverse events, which may reduce the potential risk of assessment bias.

Intervention

Patients in the PRF group received a single intratesticular injection of autologous platelet-rich fibrin. For standard preparation of PRF, 20–30 mL of peripheral venous blood was collected from each patient in 9 cc tubes and centrifuged according to the study protocol at 100 g for 4 minutes (PRF Kit, Pars Fundamental Bio Structure Company). After centrifugation, the upper plasma fraction was carefully aspirated under sterile conditions and prepared for injection. Patients in the PRF + laser-acupuncture group received the same PRF injection protocol in addition to laser-acupuncture. Laser acupuncture was performed twice weekly for five weeks, for a total of ten sessions. A low-level laser device with a wavelength of 810 nm and output power of 300 mW was applied to 21 predefined acupuncture points. Each point was irradiated for 5–10 seconds according to the treatment protocol. Semen samples were collected at four time points: before intervention, immediately after intervention, one month after intervention, and three months after intervention. The three-month assessment was prespecified as the final follow-up time point because it approximately corresponds to one complete cycle of human spermatogenesis (accounting for the 70-day spermatogenesis cycle.[15] All complications were documented.

Outcome measurement

Semen analysis, hormonal assays, testicular volume assessment, and adverse events were evaluated throughout the study. Semen parameters included sperm concentration, motility, morphology, semen volume, and DNA fragmentation. Hormonal assessments included serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone levels. Testicular volume was measured at each assessment, and all treatment-related complications were documented.

Primary and Secondary Endpoints

The primary endpoint was the change in semen parameters from baseline to the scheduled follow-up assessments, including sperm concentration, motility, morphology, semen volume, and DNA fragmentation. Secondary endpoints included changes in the serum hormonal profile (FSH, LH, and testosterone), changes in testicular volume, and the occurrence of treatment-related adverse events during the study period.

Sample size

This study was designed as a pilot randomized clinical trial. Because of the limited availability of eligible men with non-obstructive azoospermia and the lack of sufficient prior clinical data on the expected effect size of intratesticular PRF, with or without laser acupuncture, a formal sample size calculation was not performed. Therefore, the sample size was determined pragmatically based on feasibility, patient availability, and the study's exploratory nature. A total of 40 eligible participants were enrolled and allocated to the PRF group and 20 to the PRF plus laser-acupuncture group.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were presented as frequencies and percentages. Between-group comparisons of continuous variables were performed using the independent-samples t-test. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Within-group changes from baseline to the 3-month follow-up were evaluated using the paired-samples t-test. All statistical tests were two-sided, and a P value < 0.05 was considered statistically significant.

Ethics

The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran (Ethics code: IR.SBMU.MSP.REC.1403.630). The trial was registered in the Iranian Registry of Clinical Trials (IRCT registration number: IRCT20250223064818N1). Written informed consent was obtained from all participants before enrollment, and they were informed that they could withdraw from the study at any time without affecting their medical care.

Results

Baseline characteristics

A total of 40 participants were enrolled and equally allocated to the PRF (n = 20) and PRF+Laser groups. The mean age of the overall cohort was 33.35 ± 5.88 years, with no significant difference between the treatment groups (P > 0.05). Primary infertility was present in 80.0% of participants in both groups. The prevalence of smoking, alcohol consumption, opium use, and underlying medical conditions was comparable between groups (all P > 0.05). The most frequently used medications in the overall cohort were HCG (30.0%) and HMG (27.5%). Similarly, there were no significant between-group differences in the use of concomitant medications (P > 0.05). Baseline characteristics in the treatment groups are presented in Table 1.

Semen parameters

Sperm concentration remained 0 cells/HPF in both treatment groups throughout the study period, with no detectable changes following either intervention. Likewise, total sperm motility and normal sperm morphology remained 0% at all evaluated time points in both groups.

Mean semen volume remained stable throughout follow-up in both treatment groups (Table 2). There were no significant differences between the PRF and PRF+Laser groups at baseline (3.42 ± 0.60 vs. 3.35 ± 0.70 mL, P = 0.721), immediately after intervention (3.40 ± 0.59 vs. 3.44 ± 0.43 mL, P = 0.833), one month after intervention (3.50 ± 0.61 vs. 3.52 ± 0.47 mL, P = 0.909), or three months after intervention (3.44 ± 0.58 vs. 3.47 ± 0.43 mL, P = 0.850). Within-group analyses likewise demonstrated no significant change in semen volume between baseline and the three-month follow-up in either the PRF group (P = 0.620) or the PRF+Laser group (P = 0.314).

Testicular volume

Mean testicular volume showed only minor numerical fluctuations over time in both treatment groups (Figure 1). There were no significant differences between the PRF and PRF+Laser groups before treatment (15.80 vs. 15.45 mL; MD = 0.35, P = 0.370), at one month (15.90 vs. 16.50 mL; MD = −0.15, P = 0.966), or at three months (16.05 vs. 15.95 mL; MD = 0.10, P = 0.806). Similarly, within-group comparisons between baseline and three months demonstrated no statistically significant changes in either the PRF group (MD = 0.25, P = 0.234) or the PRF+Laser group (MD = 0.50, P = 0.056).

Hormonal outcomes

Follicle-stimulating hormone

Serum FSH concentrations remained comparable between treatment groups throughout follow-up (Figure 2). No significant between-group differences were observed

Table 1. Baseline characteristics of patients in each treatment group

Characteristics	Groups			*P*-value[1]
	Overall (N = 40)	PRF (N = 20)	PRF + laser (N = 20)	
Demographics				
Age, years	33.35 ± 5.88	33.45 ± 6.07	33.25 ± 5.84	> 0.05
Infertility status, n (%)				> 0.05
Primary	32 (80.0)	16 (80)	16 (80)	
Secondary	8 (20.0)	4 (20)	4 (20)	
Habitual and Past Medical History				
Alcohol Consumption, n (%)	6 (15.0)	3 (15.0)	3 (15.0)	> 0.05
Current Smoking, n (%)	12 (30.0)	5 (25.0)	7 (35.0)	0.49
Opium, n (%)	11 (27.5)	6 (30.0)	5 (25.0)	0.723
Hypertension, n (%)	5 (12.5)	3 (15.0)	2 (10.0)	> 0.05
Diabetes Mellitus, n (%)	2 (5.0)	0 (0)	2 (10.0)	0.487
Major Depressive Disorder, n (%)	3 (7.5)	1 (5.0)	2 (10.0)	> 0.05
Obsessive Compulsive Disorder, n (%)	2 (5.0)	1 (5.0)	1 (5.0)	> 0.05
Hodgkin Lymphoma, n (%)	1 (2.5)	0 (0)	1 (5.0)	> 0.05
Non-alcoholic Fatty Liver Disease, n (%)	1 (2.5)	0 (0)	1 (5.0)	> 0.05
Medications				
HMG, n (%)	11 (27.5)	6 (30.0)	5 (25.0)	0.723
HCG, n (%)	12 (30.0)	6 (30.0)	6 (30.0)	> 0.05
L-carnitine, n (%)	2 (5.0)	1 (5.0)	1 (5.0)	> 0.05
Valsartan/ Amlodipine, n (%)	3 (7.5)	3 (15.0)	0 (0)	0.231
Clomiphene, n (%)	6 (15.0)	2 (10.0)	4 (20.0)	0.661
Sertraline, n (%)	4 (10.0)	2 (10.0)	2 (10.0)	> 0.05
Amino Acid Supplementation (Sperm Aid), n (%)	3 (7.5)	1 (5.0)	2 (10.0)	> 0.05
Losartan, n (%)	2 (5.0)	0 (0)	2 (10.0)	0.487
Metformin, n (%)	2 (5.0)	0 (0)	2 (10.0)	0.487

[1]: Independent Sample T-test, Pearson's Chi-Square Test, Fisher's Exact Test
Continuous data are presented as mean ± standard deviation
Categorical data are presented as frequencies and percentages
Abbreviations: HMG, Human Menopausal Gonadotropin; HCG, Human Chorionic Gonadotropin; PRF, Platelet-rich Fibrin

before intervention (MD = –0.01, *P* = 0.849), one month after intervention (MD = –0.05, *P* = 0.935), or at three months (MD = 0.29, *P* = 0.212). Likewise, neither the PRF group (MD = –0.13, *P* = 0.411) nor the PRF+Laser group (MD = –0.44, *P* = 0.084) demonstrated a significant change in FSH concentration between baseline and the three-month follow-up.

Luteinizing hormone

Serum LH concentrations also remained stable during follow-up (Figure 3). Between-group comparisons

Table 2. Semen volume in the two groups across the time points

Groups	Time				*P*-value[1]
	Pre-intervention	Post-intervention	1st Month Follow-up	3rd Month Follow-up	
PRF	3.42 ± 0.6	3.4 ± 0.59	3.5 ± 0.61	3.44 ± 0.58	0.620
PRF + laser	3.35 ± 0.7	3.44 ± 0.43	3.52 ± 0.47	3.47 ± 0.43	0.314
P-value[2]	0.721	0.833	0.909	0.850	

[1]: Paired Sample Test comparison between pre-intervention and 3rd month follow-up findings
[2]: Comparison of findings at each time point using independent Sample T-test
Continuous data are presented as mean ± standard deviation
Abbreviation: PRF, Platelet-rich fibrin

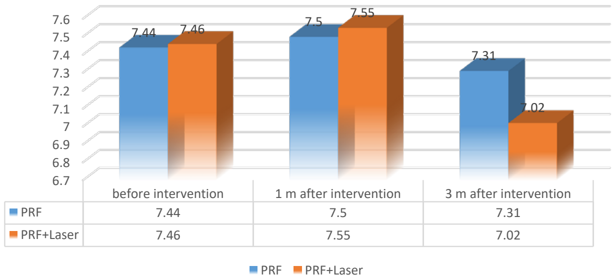


Figure 2. Serum follicle-stimulating hormone (FSH) concentration in each treatment group across the time points

showed no significant differences at baseline (MD = –0.17, *P* = 0.489), one month (MD = 0.01, *P* = 0.968), or three months (MD = –0.07, *P* = 0.785). Similarly, no significant within-group changes were observed from baseline to three months in either the PRF group (MD = 0.16, *P* = 0.331) or the PRF+Laser group (MD = 0.06, *P* = 0.400).

Testosterone

Serum testosterone concentrations remained unchanged in both treatment groups throughout the study period (Figure 4). No significant between-group differences were detected before intervention (MD = –0.12, *P* = 0.407), at one month (MD = –0.14, *P* = 0.499), or at three months (MD = –0.12, *P* = 0.544). Furthermore, within-group comparisons between baseline and three months revealed no statistically significant changes in testosterone concentrations in either the PRF group (MD = 0.15, *P* = 0.226) or the PRF+Laser group (MD = 0.07, *P* = 0.425).

Safety outcomes

Both interventions were well tolerated, and no significant differences in treatment-related adverse events were observed between the two groups. The incidence of erythema was identical in both groups (15.0%, *P* > 0.999), while the frequencies of pruritus (15.0% vs. 0%, *P* = 0.231), pain (20.0% vs. 20.0%, *P* > 0.999), and burning sensation (15.0% vs. 5.0%, *P* = 0.605) were likewise comparable between the PRF and PRF+Laser groups, respectively.

Discussion

This study aimed to assess the efficacy of autologous platelet-rich fibrin (PRF) and laser-acupuncture in improving reproductive function in men with non-obstructive azoospermia (NOA). This randomized clinical

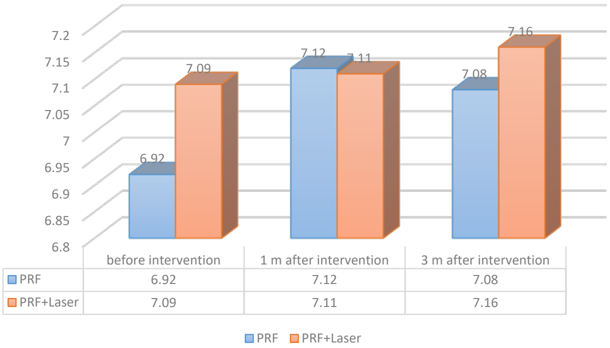


Figure 3. Serum luteinizing hormone (LH) concentration in each treatment group across the time points

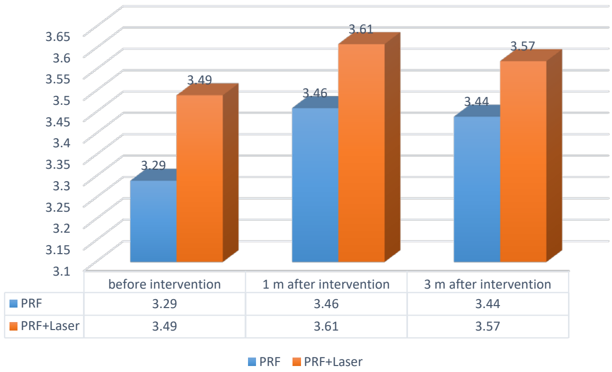


Figure 4. Serum testosterone concentration in each treatment group across the time points

trial evaluated the impact of PRF injections and laser acupuncture on sperm parameters (volume, concentration, motility, morphology) and DNA.[14]

The findings revealed no significant differences between the groups in sperm concentration, motility patterns, morphology, or DNA fragmentation index. PRF, laser, and their combined interventions did not significantly improve key sperm parameters. While semen volume showed a significant intragroup increase over time ($p = 0.039$), there were no significant intergroup differences. Progressive motility remained negligible. No serious clinical complications were reported.[16]

In conclusion, a single PRF injection and short-term laser-acupuncture did not significantly enhance spermatogenesis parameters (concentration, morphology, motility, or DNA integrity) in NOA men during the study period, indicating a lack of demonstrable therapeutic effect.[17]

A retrospective study by Al-Nasser et al. (2018) on 71 men with non-obstructive azoospermia (NOA) found that intratesticular PRP injection showed limited spermatogenesis recovery and reduced persistent azoospermia only in patients with spermatocytes on initial FNA. Hormonal changes, such as increased FSH, were not statistically significant, and the study lacked standard semen parameters and controls for spontaneous recovery.[18] In contrast, the present randomized clinical trial using PRF alone or with laser showed no significant effect on sperm concentration, motility, morphology, or DNA fragmentation. These divergent results may be due to differences in study design (retrospective vs. RCT), biological intervention (liquid PRP vs. sustained-release PRF), evaluation parameters (FNA vs. complete semen analysis), and patient histology, especially the better response in Al-Nasser et al.'s (2018) study among patients with active germ cells at baseline.[19] Thus, the therapeutic efficacy of PRP/PRF in NOA is not definitive and likely depends on baseline spermatogenesis, platelet product type, and follow-up duration.

In a recent study by Gudelci et al. (2024), which was a prospective case-series study of 135 men with non-obstructive azoospermia and at least one failed mTESE, intratesticular PRP injection significantly improved sperm retrieval rates [19], sperm retrieval rates were 27.5% in patients with one failed mTESE and 16.4% in those with two or more failed mTESE, and IVF results after PRP also showed high fertilization rates (86–100%) and favorable pregnancy rates (22–36%). These findings suggest that PRP may partially activate spermatogenic pathways in a subgroup of patients with testicular tissue with relative reparability. In comparison, the present study, with a randomized clinical trial design and using PRF, did not observe any significant improvement in semen parameters, including concentration, motility, morphology, and DNA integrity, in NOA patients without a history of spermatogenesis stimulation and in a setting where they often lacked active germ cells. The difference between the two studies can be attributed to several important factors: first, the target population in the study by Gudelci et al. [20] included patients who had failed mTESE, indicating minimal spermatogenesis, whereas the patients in the present study largely lacked detectable activity in the spermatogenic pathway. Second, PRP is a liquid with rapid release of growth factors, while PRF has a fibrin network and a more sustained release, which may have less efficacy in the short term. Third, the primary outcomes in the study by Gudelci et al. [19] were sperm retrieval rate and IVF outcomes, which are much more sensitive performance indicators than semen parameters, whereas our study relied on stringent semen parameters. In addition, the length of follow-up, histological heterogeneity (Sertoli-cell-only and maturation arrest), and differences in the severity of testicular injury may also determine the course of response to intervention. Thus, while studies such as Gudelci's study suggest a possible role for PRP in patients with residual biological capacity, the findings of this study suggest that in NOA patients with no detectable spermatogenic activity and in the short term, PRF and its combination with laser acupuncture are unable to produce clinically meaningful improvements in sperm parameters.

A recent study by Gudelci et al. (2024) found that intratesticular PRP injections significantly improved sperm retrieval rates (27.5% for one failed mTESE, 16.4% for two or more) and IVF outcomes (86-100% fertilization, 22-36% pregnancy) in men with non-obstructive azoospermia (NOA) and a history of failed mTESE, suggesting PRP may activate spermatogenesis in some patients.

In contrast, our randomized clinical trial using PRF did not show similar improvements in semen parameters (concentration, motility, morphology, DNA integrity) in

NOA patients without prior spermatogenesis stimulation and often lacking active germ cells. This discrepancy likely stems from several factors: Gudelci et al.'s study targeted patients with minimal spermatogenesis, while ours included those with no detectable spermatogenic activity. Additionally, PRP offers rapid growth factor release, whereas PRF provides a slower, sustained release, potentially impacting short-term efficacy. Finally, Gudelci et al. measured sensitive outcomes like sperm retrieval and IVF success, while our study focused on stringent semen parameters. Other contributing factors could include follow-up duration, histological variations, and the severity of testicular injury. Therefore, while Gudelci's study indicates a potential role for PRP in patients with residual biological capacity, our findings suggest that PRF and its combination with laser acupuncture may not yield significant short-term improvements in sperm parameters for NOA patients without detectable spermatogenic activity.

Previous research on non-obstructive azoospermia (NOA) has explored intratesticular PRP injections, showing limited improvements in spermatogenesis, sperm recovery, or IVF outcomes in some patients (Al-Nasser et al, 2018; Gudelci et al, 2024). This study, however, differentiates itself by utilizing PRF, a second-generation platelet product. PRF possesses a 3D fibrin matrix without anticoagulants, offering a slower, more stable, and prolonged release of growth factors compared to PRP.[20,21] While this characteristic benefits tissue regeneration and wound healing, its impact on testicular tissue, which requires rapid and short-term cellular stimulation, might differ.[11,22]

Furthermore, successful PRP studies often focused on patients with existing spermatogenic activity, such as those with residual germ cells despite mTESE failure. This study, conversely, primarily investigated NOA patients with minimal or absent spermatogenic activity, a factor that could influence treatment response. Thus, the present study, centered on PRF, offers an innovative and complementary perspective to PRP research. The differing outcomes likely stem from two main factors: 1) the fundamental biological distinctions between PRF and PRP in terms of growth factor release, fibrin structure, and interaction with testicular tissue, and 2) variations in patient baseline characteristics and residual germ cell counts. These points not only account for the observed discrepancies but also highlight the need for further PRF research to optimize dosage, injection frequency, PRF type, and compatibility with testicular physiology.

While Wang et al. (2021) demonstrated PRF's efficacy in treating female infertility post-uterine adhesion removal by improving pregnancy rates, endometrial thickness, and reducing adhesion severity [23], these findings are not directly transferable to male infertility. Endometrial tissue exhibits high regenerative capacity and readily responds to PRF-released growth factors. In contrast, NOA patients' testicular tissue often lacks the germ cells necessary for spermatogenesis, and its regenerative response is significantly more limited. Moreover, PRF's gradual growth factor release may be insufficient to stimulate the intricate, multi-step process of spermatogenesis. Therefore, PRF's success in uterine disorders does not guarantee its effectiveness in NOA, as tissue type, cellular baseline, and repair capacity play crucial roles in determining outcomes between these two areas.

Pang et al. (2025) conducted the first systematic review on PRP's role in male infertility, revealing that while some early studies suggested benefits like improved semen parameters and sperm retrieval, their limited quality (case reports, retrospective, small cohorts) prevented definitive conclusions. The review highlighted the absence of standardized trials, diverse PRP methods, and patient heterogeneity as barriers to firm scientific conclusions.[12] Our current study, using PRF (a more stable PRP version) in an RCT design, found no significant effect on sperm parameters in NOA patients. This suggests that promising PRP results may be specific to particular populations, residual spermatogenic activity, or specific PRP protocols and thus are not generalizable. Both Pang's review and our study underscore the need for more rigorous, homogeneous research, particularly high-quality RCTs, to establish the effectiveness of platelet products in treating male infertility.

The relatively short follow-up period should be considered an important limitation of this study. Although the three-month follow-up was selected because it approximately corresponds to one complete cycle of human spermatogenesis and represented the prespecified follow-up period in the study protocol, regenerative or spermatogenic responses may require observation over more than one spermatogenic cycle. Therefore, the absence of significant improvement in semen parameters in the present study should be interpreted as evidence of no demonstrable short-term effect rather than definitive evidence of long-term inefficacy. The open-label design represents another limitation of this study, as participants, treating clinicians, and outcome assessors were aware of group allocation. Although the outcomes were primarily objective laboratory and clinical measures, the possibility of performance or assessment bias cannot be entirely ruled out.

Conclusion

In the short term, intratesticular PRF injection, with or without laser acupuncture, does not significantly improve sperm parameters in men with non-obstructive azoospermia. This aligns with recent findings on the limited efficacy of platelet products, suggesting that further research with larger studies, longer follow-ups, and careful patient selection is needed for PRF.

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Authors' Contribution
Conceptualization: Mohammadreza Razaghi, Mohammadmohsen Mazloumfard
Data Curation: Reza Nicknama, Fatemeh Sheibani
Formal Analysis: Mohammad Seifipoor
Investigation: Reza Nicknama, Fatemeh Sheibani
Methodology: Sona Zare
Project Administration: Mohammadreza Razaghi, Sona Zare
Resources: Sona Zare
Software: Mohammad Seifipoor
Supervision: Mohammadreza Razaghi
Validation: Sona Zare, Fatemeh Sheibani
Visualization: Sona Zare
Writing–Original Draft: Sona Zare, Reza Nicknama
Writing–Review & Editing: Sona Zare, Reza Nicknama, Parnia Rahnamay Farnood

Competing Interests
The authors declare that they have no competing interests

Ethical Approval
The study protocol was registered with the Iranian Registry of Clinical Trial (ID: I IRCT20250223064818N1) and approved by Shahid Beheshti Medical Science University Authority Research Ethics Board (IR.SBMU.MSP.REC.1403.630).

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