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Original Research Article

Comparative analysis of sperm count, hormonal profile and testicular volume before and after intra-testicular PRP therapy in non-obstructive azoospermia

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ABSTRACT

Background: Non-obstructive azoospermia (NOA) is a major cause of male infertility, with limited treatment options. Platelet-rich plasma (PRP), which is rich in growth factors, has been proposed as a regenerative therapy. This study conducted a comparative analysis of sperm count, hormonal profiles and testicular volume before and after intratesticular autologous PRP therapy in men with NOA.
Methods: This self-controlled clinical trial was conducted at the Department of Reproductive Endocrinology and Infertility, BSMMU, Dhaka, from January 2022 to July 2023. Thirty men with NOA underwent intratesticular injection of autologous PRP (2–3 ml per testis). Baseline and follow-up assessments at 1 and 3 months included semen analysis, clinical and ultrasound measurements of serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone and testicular volume. Data were analyzed using SPSS v26.
Results: No spermatozoa were detected in semen samples at baseline, 1 month or 3 months post-treatment. Hormonal profiles showed mild fluctuations without significance (FSH: 33.1 to 24.3 mIU/ml, p=0.061, LH: 9.5 to 9.6 mIU/ml, p=0.562, testosterone: 392.0 to 435.1 ng/dl, p=0.062). Mean testicular volume increased from 9.5±2.3 ml to 11.2±2.4 ml (p=0.004) using the Prader orchidometer and from 10.0±2.4 ml to 11.3±2.4 ml (p=0.002) using ultrasound. Side effects included transient pain (20.0%) and hematoma (20.0%), with no infections reported.
Conclusions: Intratesticular PRP increased testicular volume but did not restore spermatogenesis or alter hormones significantly in NOA patients. Although safe and biologically plausible, its clinical utility requires validation through larger, long-term trials.

Keywords: Male infertility, Nonobstructive azoospermia, Platelet-rich plasma

INTRODUCTION

Infertility affects approximately 15% of couples worldwide, with male factors contributing to nearly half of all cases.[1] Among these, azoospermia defined as the absence of spermatozoa in the ejaculate is one of the most severe conditions and is reported in 15% of infertile men. Azoospermia is broadly classified into obstructive azoospermia (OA) and NOA, accounting for 40% and 60% of cases, respectively.[2] While OA results from physical blockages within the male genital tract, NOA is caused by intrinsic testicular failure leading to impaired

spermatogenesis.[3] Patients with NOA typically present with small, soft testes and elevated gonadotropins, reflecting impaired germ cell activity. The etiology of NOA is multifactorial. Primary testicular failure, congenital hypogonadotropic hypogonadism and incomplete or ambiguous testicular dysfunction are well-documented causes.[4]

Genetic factors also play a significant role, with chromosomal anomalies such as Klinefelter syndrome, Y-chromosome microdeletions and structural rearrangements being implicated. Environmental and iatrogenic factors including chemotherapy, radiotherapy, cryptorchidism and varicocele further contribute to impaired spermatogenesis.[5] Despite extensive evaluation, up to 60% of NOA cases remain idiopathic.[3]

Management of NOA poses considerable challenges. Traditional approaches include surgical sperm retrieval techniques such as testicular sperm extraction (TESE) and testicular sperm aspiration (TESA), which are often combined with intracytoplasmic sperm injection (ICSI).[6] However, the success of these procedures is limited and many patients require donor sperm or adoption as alternative options.[7] Hormonal therapies have shown variable results and overall, effective medical treatments remain elusive. Recent advances in regenerative medicine have introduced novel modalities, among which autologous PRP therapy has gained increasing attention.[8]

PRP is an autologous concentration of platelets suspended in plasma, prepared by centrifugation of venous blood. Platelets release multiple growth factors upon activation, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and transforming growth factor beta (TGF-β).[9] These factors regulate angiogenesis, cellular proliferation and tissue repair, underpinning PRP's application in regenerative medicine.[10] Clinically, PRP has demonstrated therapeutic benefits across diverse specialties, including Orthopedics, sports medicine, dermatology and maxillofacial surgery. In reproductive medicine, its potential has been explored in enhancing endometrial receptivity, improving ovarian reserve and reducing implantation failure.[11]

Experimental and early clinical studies suggest PRP may also play a role in testicular regeneration. Animal models have demonstrated structural and functional recovery of testes exposed to gonadotoxic insults when treated with PRP, with improvements in spermatogenesis and steroidogenesis.[12]

Preliminary clinical studies indicate possible benefits of PRP therapy in improving testicular microenvironment, though restoration of spermatogenesis remains uncertain.[13] These findings raise the possibility of PRP as a therapeutic adjunct in male infertility, specifically in patients with NOA, where conventional options are limited.

Given the paucity of controlled data, this study was designed as a comparative analysis to evaluate changes in sperm count, hormonal profile and testicular volume before and after PRP therapy in men with non-obstructive azoospermia.

METHODS

This was a self-controlled clinical trial conducted at the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. The study period was from January 2022 to July 2023. A total of 30 patients diagnosed with non-obstructive azoospermia (NOA) were included in this study.

Inclusion criteria

Male patients aged 20–50 years. Azoospermia confirmed by ≥2 semen analyses performed at least 4 weeks apart. Diagnosis of NOA with serum FSH>10 mIU/ml. Reduced testicular volume (<15 ml).

Exclusion criteria

Serum FSH>50 mIU/ml. Gross genital tract abnormalities (e.g., varicocele, hydrocele, inguinal hernia). Systemic medical conditions (e.g., chronic liver disease). Bleeding disorders. Recent testicular or accessory gland infection. Chromosomal disorders (e.g., Klinefelter syndrome). Positive tumor markers (free hCG, AFP, LDH). Testicular USG showing micro-calcifications or focal lesions. Dilated seminal vesicles on transrectal USG. Recent use of cytotoxic drugs impairs spermatogenesis.

Study procedure

Eligible patients were recruited following diagnostic confirmation and informed consent. Baseline semen analyses, hormonal assays (FSH, LH, testosterone) and scrotal ultrasonography were performed. PRP was prepared in the Department of Transfusion Medicine using 50 ml of venous blood collected in anticoagulant tubes. Samples underwent centrifugation at 1,200 rpm for 12 minutes, followed by a second centrifugation at 3,300 rpm for 7 minutes to yield 8–10 ml of PRP. Approximately 2–3 ml of PRP was injected into each testis under total intravenous anaesthesia using a 16G needle, with care to avoid major anatomical structures. Prophylactic antibiotics were administered perioperatively. Patients were observed for 4 hours post-procedure, monitored for immediate complications and discharged with analgesics. Follow-up assessments at 1 and 3 months included semen analysis, hormonal assays and scrotal ultrasound with Doppler to evaluate testicular volume and detect any new pathology.

Ethical considerations

The study received approval from the Institutional Review Board (IRB) of BSMMU. Written informed consent was

obtained from all participants, ensuring autonomy and voluntary participation. Patient confidentiality was maintained through anonymization of data. All procedures adhered to the principles of the Helsinki Declaration (1964). Confidentiality of patients was strictly maintained during the study.

Data analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean±SD or median with range, while categorical variables were presented as frequencies and percentages. Repeated measures ANOVA and Friedman test were applied for within-group comparisons across time points. Statistical significance was defined as $p<0.05$.

RESULTS

The majority of patients (53.3%) were in the age group of 31–40 years, with a mean age of 35.8±5.7 years. Private employment was the predominant occupation (60.0%). Eighteen participants (60.0%) resided in urban areas and most belonged to the middle-income group (60.0%). Overweight BMI (25.0–29.9 kg/m²) was observed in 18 patients (60.0%), with a mean BMI of 25.2±1.6. All participants presented with primary infertility. Table 2 showed that the sperm count on the semen sample of all patients was zero at the 1st and 3rd month post procedure. All patients remained azoospermic.

Table 3 showed that serum FSH, LH and testosterone levels were not statistically significant when compared between pre-treatment vs the 3rd month of post-treatment, respectively. Table 4 showed that mean testicular volume was statistically significant when compared between pre-treatment (9.5±2.3 ml) and 3rd month of post-treatment (11.2±2.4 ml) on both sides. Table 5 showed that mean right testicular volume was significantly higher at 3rd month of post treatment (10.0±2.4 vs 11.3±2.4 ml) from pre-treatment.

Mean left testicular volume was also statistically significant when compared between pre-treatment (9.6±2.3 ml) and 3rd month of post treatment (10.7±2.1 ml). Six patients (20.0%) experienced postoperative pain and six (20.0%) developed intra-testicular hematoma. No infections occurred.

Table 1: Demographic characteristics of study population (n=30).

Demographic characteristics		Number of patients	(%)
Age (in years)	21–30	8	26.7
	31–40	16	53.3
	41–50	6	20
	Mean±SD	35.8±5.7	
	Range	28.0–44.0	
Occupational status	Private job	18	60
	Businessman	3	10
	Government job	3	10
	Garment worker	3	10
	Teacher	3	10
Residence	Urban	18	60
	Rural	12	40
Monthly income	Lower middle	12	40
	Middle	18	60
BMI (kg/m²)	18.5–24.9	12	40
	25.0–29.9	18	60
	Mean±SD	25.2±1.6	
	Range	22.8–26.9	
Infertility type	Primary	30	100
	Secondary	0	0

Table 2: Pre and post-treatment semen parameters (n=30).

Timepoint	Sperm count
Pre-treatment	0
Post-treatment, 1 month	0
Post-treatment, 3 months	0

Table 3: Pre and post-treatment hormonal parameters (n=30).

Variable	Pre-treatment	1 month	3 months	P value (pre vs 3 months)
Serum FSH (mIU/ml)	33.1 (18.2–42.0)	27.0 (24.2–35.5)	24.3 (19.1–31.2)	0.061
Serum LH (mIU/ml)	9.5 (5.7–15.8)	11.6 (9.1–16.5)	9.6 (7.8–14.0)	0.562
Serum testosterone (ng/dl)	392.0 (291.0–520.0)	420.2 (280.0–454.0)	435.1 (334.0–456.0)	0.062

Table 4: Pre and post-treatment testicular volume (Prader orchidometer) (n=30).

Testis	Pre-treatment (ml)	1 month (ml)	3 months (ml)	P value (pre vs 3 months)
Right	9.5±2.3	11.5±2.4	11.2±2.4	0.004
Left	9.5±2.3	11.2±2.4	11.2±2.4	0.004

Table 5: Pre and post-treatment testicular volume (scrotal ultrasound) (n=30).

Testis	Pre-treatment (ml)	1 month (ml)	3 months (ml)	P value (pre vs 3 months)
Right	10.0±2.4	11.2±2.4	11.3±2.4	0.002
Left	9.6±2.3	10.6±2.3	10.7±2.1	0.003

Table 6: Side effects (n=30).

Side effect	Number of patients	(%)
Pain	6	20
Intra-testicular hematoma	6	20
Infection	0	0

DISCUSSION

NOA represents one of the most severe forms of male infertility, characterized by the complete absence of sperm in the ejaculate due to impaired spermatogenesis. Despite advances in assisted reproductive techniques, therapeutic strategies that directly restore sperm production remain elusive. In this study of 30 men with NOA, intra-testicular injection of autologous PRP was associated with significant increases in testicular volume but did not result in sperm detection in semen samples at three months. Hormonal parameters showed minor fluctuations without statistical significance and side effects were limited to transient pain and hematoma.

The age distribution of patients, with a mean of 35.8 years and most clustered in the 31–40 range, is consistent with previous PRP studies in male infertility. Al-Nasser et al reported a similar mean age of 37.6 years, while Angellee et al, described an average of 39.9 years in their cohort.[13,14] These findings indicate that men with NOA typically present during peak reproductive years, reflecting the urgent clinical need for effective interventions. The predominance of overweight individuals in this study mirrors earlier findings that high BMI negatively influences semen parameters and fertility potential, although the relationship with sperm retrieval outcomes in NOA remains debated. Belloc et al showed a detrimental association between BMI and semen quality, while Iwatsuki et al found no effect on sperm retrieval success, though they noted correlations between BMI and gonadotropin levels.[5,15]

The persistence of azoospermia following PRP injection is a central finding. This outcome is consistent with the clinical observations of Al-Nasser et al who noted improved testicular histology after PRP but no reliable restoration of sperm in semen analyses.[13] Similarly, Kutluhan et al demonstrated in an experimental torsion model that PRP enhanced Leydig cell proliferation and spermatogenesis histologically, yet functional sperm recovery remained inconsistent.[16] The absence of spermatozoa in the current study may reflect either the severity of germ cell depletion in NOA or the short follow-up period of three months, as spermatogenesis requires multiple cycles to manifest visible recovery. Valeriy et al, showed in murine models that PRP promoted morpho-functional restoration of damaged testes, though these improvements required time to translate into functional spermatogenesis.[12]

Hormonal findings in this study were in line with previous literature. The modest decline in follicle-stimulating hormone (FSH) and slight rise in testosterone were nonsignificant but suggestive of subtle improvements in testicular microenvironment. Al-Nasser et al, also reported nonsignificant changes in FSH and testosterone following PRP, while Dehghani et al, demonstrated enhanced steroidogenesis in animal models treated with PRP.[13,17] Although FSH is considered a marker of spermatogenic

activity, reductions alone are insufficient to indicate fertility restoration without corroborating histological or semen evidence. The hormonal stability observed supports the local rather than systemic action of PRP.

A particularly noteworthy finding was the significant increase in testicular volume, confirmed by both clinical and sonographic assessments. Increases of approximately 1.6–1.7 ml per testis at three months were observed, suggesting improved tissue regeneration. These results corroborate the experimental evidence of Kutluhan et al, who described increased Leydig cell proliferation and steroidogenic activity following PRP therapy.[16] Similar outcomes were reported by Valeriy et al, where murine testes treated with PRP after gonadotoxic insult showed marked recovery of structure and function.[12] The regenerative potential is biologically plausible given the abundance of growth factors in PRP, including platelet-derived growth factor, vascular endothelial growth factor and transforming growth factor-β, which stimulate angiogenesis, cellular proliferation and tissue repair.

The safety profile of PRP was further confirmed in this cohort. Postoperative pain and intra-testicular hematoma occurred in 20% of patients each, but both were self-limiting and required no additional intervention. No infections or systemic side effects were recorded. These findings are consistent with previous reports, where adverse events were minimal in both human and animal studies. Al-Nasser et al, reported no major complications in their trial, while similar safety outcomes have been described in urological applications of PRP.[13]

Overall, the results of this study suggest that intra-testicular PRP may improve testicular morphology but does not reliably restore spermatogenesis in NOA within a short observation period. Improvements in testicular volume confirm the biological activity of PRP, but its translation into functional fertility remains uncertain. Somova et al, reported improvements in semen parameters among men with oligoasthenoteratozoospermia treated with PRP, suggesting that patients with less severe testicular impairment may respond more favourably.[18] By contrast, in cases of complete germ cell depletion, as in most NOA patients, the regenerative stimulus provided by PRP may be insufficient. This underscores the importance of patient selection and the potential role of PRP as an adjunct rather than a standalone therapy.

In summary, intra-testicular PRP therapy in NOA appears safe and biologically plausible, offering measurable improvements in testicular volume but not achieving restoration of spermatogenesis. These findings align with existing experimental and clinical literature, suggesting that PRP may enhance testicular tissue health but requires further validation before adoption into routine clinical practice.

This study had some limitations. Which are single-center study with a limited sample size. Short follow-up (3 months), insufficient to capture long-term effects. Lack of histological evaluation due to patient refusal. Outcomes restricted to semen analysis, hormones and testicular volume, without sperm retrieval attempts.

CONCLUSION

Intra-testicular autologous PRP therapy with Nonobstructive azoospermia (NOA) resulted in significant increases in testicular volume but did not restore spermatogenesis or significantly alter hormonal parameters. The treatment was safe, with only mild, transient side effects reported. While promising in improving testicular morphology, its role in fertility restoration remains unproven.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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