

SYSTEMATIC REVIEW

The Efficacy of Platelet-rich Plasma (PRP) Addition in Human Ejaculated Sperm: A Systematic Review and Meta-analysis

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ABSTRACT

Introduction: To systematically review and meta-analyze existing data from many clinical trials to assess any enhancements in the quality of human ejaculated sperm after PRP treatment. **Materials and methods:** A literature search was conducted in The Cochrane Library, Google Scholar, and PubMed Library up to November 2022 and then followed the guidelines of Prisma Checklist 2020. The eligible studies included in this meta-analysis must be clinical trials comparing human ejaculated sperm with PRP treatment and without any additional PRP. The assessed outcomes were analyzed quantitatively and qualitatively. **Results:** There were ninety-three studies retrieved. After excluding inappropriate publications, four studies were eventually included in the meta-analysis (n=319). There were varied PRP intervention methods across publications, but all of them used PRP 2%. By using random-effects models, we found that there was an improvement of the progressive sperm in groups with PRP treatment (MD=18.79; 95%-CI 13.71, 23.87; $I^2=78%$; $\tau^2=21.67$; $p<0.01$). Sperm concentration and morphology were not included in the meta-analysis, but it was described descriptively that both improved after PRP treatment. All articles included in this analysis have low bias risks. **Conclusion:** After PRP treatment, there is an improvement in sperm progressivity, suggesting the enhanced quality of human ejaculated sperm. Although beneficial in improving sperm motility, strong evidence for further study will be necessary.

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INTRODUCTION

Male infertility management is crucial, as men typically contribute to 20-30% of infertility cases and also play a role in 50% of all cases, that is why all clinicians and researchers are striving to make breakthroughs in its management. Based on epidemiological data, the estimated occurrence of this condition affects approximately 8 to 12% of reproductive-age couples worldwide, with the highest rates in Southeast Asia (1).

Lately, the use of platelet-rich plasma (PRP) for managing male infertility has been growing. PRP therapy is being explored as a potential treatment in men with sperm abnormalities. PRP contains the highest concentration of platelets, 1,5 to 8 times higher than its normal concentration in the whole blood. Additionally,

PRP exhibits a 3- to 5-fold increase in growth factor concentrations. Known for its potent growth factor composition, PRP has demonstrated significant benefits in regenerative therapy by actively stimulating cell proliferation and differentiation processes. As a result, it is believed to potentially enhance sperm quality (2,3). Another essential characteristic, PRP, comes from an autologous product derived from the patient's own blood. Therefore, the utilization of autologous PRP mitigates concerns regarding the risks of allergic reactions, cross-contamination, disease transmission, or immune reaction (4,5). Thus, using autologous PRP appears to be a relatively safe option for sperm treatment. The research initially conducted on experimental animals is now being conducted on humans.

Research on the efficacy of PRP in improving sperm quality varies significantly. Nasser *et al* (6) in 2018, studied the administration of PRP injections in the testes for non-obstructive azoospermia patients and found improvements in spermatogenesis. Similarly, Samova *et al* (7) in 2021, conducted research with

PRP injections in the testes of patients with severe oligoastheno-teratozoospermia, concluding that PRP has beneficial effects on spermatogenesis and enhances sperm concentration and motility. Gudelci *et al* (8,9) in their studies conducted in 2021 and 2022, administered PRP injections in the testes and the seminiferous tubules or interstitial space for patients undergoing IVF-ICSI due to non-obstructive azoospermia and a history of at least one failed microdissection testicular sperm extraction (mTESE), they concluded that sperm cells were found in testicular tissue and fertilization occurred after ICSI. However, the method of administering PRP injections in the testes can also cause side effects such as infection at the injection site, nerve injury, bleeding, and tissue damage, although no side effects of the procedure performed were reported in the above studies.

Researchers also investigated the use of PRP before cryopreservation. Their study mixed PRP with varying concentrations with semen samples, leading to an observed increase in sperm motility progression and membrane integrity. So, it seems that PRP has a protective effect on the cryopreservation of human spermatozoa (10-12).

Several studies have also been conducted on the addition of PRP in human ejaculated sperm, and the results have varied. Apart from the efficacy and safety of PRP, professionals may benefit from this method's ease and simplicity. This procedure typically requires minimal patient intervention, does not necessitate anesthesia, and can be performed in an outpatient clinic setting. However, evidence from studies trialing PRP on human ejaculated sperm has been inconsistent. Given the lack of definitive clinical evidence confirming its effectiveness and the limited available data, the role of PRP therapy in treating male infertility remains unclear. Small-scale studies with differing methodologies and variable results highlight the need for secondary analysis to provide a comprehensive summary. Therefore, this review aims to assess the efficacy of PRP treatment on human ejaculated sperm by conducting a systematic review and meta-analysis of existing data from clinical trials.

MATERIALS AND METHODS

Protocols

We performed a comprehensive systematic search using relevant search terms from electronic databases such as The Cochrane Library, Google Scholar, and PubMed. We included all of the studies that specify infertile men's suggestions for experimental study, and sperm quality (sperm concentration, motility, and morphology) was measured with and without PRP addition into human ejaculated sperm.

We used the recommendations of the Cochrane

Handbook for Systematic Reviews of Interventions. To improve the results, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist guidelines (13-15). This study was registered in the PROSPERO International Prospective Register of Systematic Reviews with the registered number CRD42023467231.

Eligibility criteria

The inclusion and exclusion criteria for the studies were predetermined before the literature search. Studies included in this systematic review and meta-analysis cover the following criteria: i) the study had to be a clinical trial in human ejaculated sperm; ii) the intervention was PRP treatment, iii) the outcomes are sperm quality parameters such as sperm concentration, motility, and morphology.

The exclusion criteria were as follows: i) non-experimental studies (case-control studies, case series, cross-sectional studies, and cohort studies); ii) studies on frozen sperm or post-thawed sperm; iii) non-English language studies; iv) studies conducted on beings other than humans.

Research papers also were not included in our review if we could not access their full texts or if they lacked adequate details about their methods or results. Studies were disregarded if they did not have accessible, retrievable, and documented follow-up information or if the authors did not reply to our inquiries. We reached out to the corresponding author for further clarification; however, in the event of non-response, the data sets were excluded.

Sources and search strategies

The Population, Intervention, Comparison, and Outcome (PICO) elements served as the inclusion criteria for this systematic review were: i) Population: men with infertility; ii) Intervention: PRP addition; iii) Comparison: without PRP addition; iv) Outcome: sperm quality (sperm concentration, motility and morphology).

The initial search to locate appropriate studies was conducted in the electronic databases of Google Scholar, PubMed, and Cochrane, with no restrictions on the year of publication, using the subsequent search terms: ("sperm" OR "spermatozoa" OR "spermatocyte") AND ("platelets rich plasma" OR "platelets rich fibrin" OR "platelets rich fibrinogen" OR "PRP" OR "PRF" OR "thrombocyte rich plasm" OR "thrombocyte rich fibrin").

In addition to the electronic search, we also manually investigated the literature. For both types of literature searches, the year of publication was limited to November 2022. After that, we manually extracted relevant articles from the reference lists.

Study selection process

Four authors participated in this review. Three authors designed the study and guided the methodology. Two authors independently selected the resources or evidence to be included in this systematic review. The other two authors independently examined the titles and abstracts of the electronic searches based on the eligibility criteria. Duplicate published literature was identified and excluded after the initial screening. If the studies were deemed potentially relevant by the reviewer, full articles were retrieved for more detailed assessment and analysis. If there was any uncertainty about the inclusion, the study was reviewed and discussed among all reviewers.

Data synthesis and charting process

Two reviewers independently reviewed all eligible studies. The subsequent data has been extracted and documented; those are: i) author's name, ii) year of publication, iii) the country where the research took place, iv) study design, v) characteristics of the participants of study or populations; vi) treatment characteristics (interventions and comparisons); vii) outcomes (sperm quality such as sperm concentration, motility, and morphology).

If the reviewers found the study relevant, the full articles were procured for further scrutiny. The findings were culled from each qualifying paper and confirmed by a pair of reviewers. In case of any uncertainty regarding the inclusion of the study, it was assessed and discussed with the other two reviewers. The data that were extracted were promptly abstracted onto a pre-established standard electronic abstraction form.

The methodological quality of the study was assessed according to the recommendation by "The Cochrane Handbook with risk of bias 2 (RoB 2)", including assessments of the randomization process, deviations from the intended intervention, missing outcome data, measurement of the outcome, selection of the reported result, and finally, the conclusion for each study (16).

Statistical analysis

We extracted and included studies on sperm motility, especially progressivity. The pooled analysis compared the difference between the sperm given PRP versus controls (no PRP addition). The effect size was measured using the calculation of Mean Difference (MD) with a corresponding 95% Confidence Interval using the random-effects model. The heterogeneity of the studies was assessed with forest plots by τ^2 and I^2 values. The effect size and heterogeneity were considered significant at a p -value <0.05 . Statistical analyses were conducted

using the meta package of RStudio version 2023.06.1.

RESULTS

Selection sources of evidence

A total of 93 studies were retrieved while conducting the preliminary electronic literature search (18 from the Cochrane Library, 20 from Google Scholar, and 55 from PubMed Library databases—and 2 were found to be duplicates by using the reference manager Endnote). Upon screening the title and abstract, 78 studies were excluded. One article was excluded due to the absence of full text, and eight studies were also ruled out as their intervention and outcomes were not suitable. After excluding inappropriate publications, four studies were eventually included in the meta-analysis ($n=319$). The literature search and studies selection flow diagram are outlined in Figure 1.

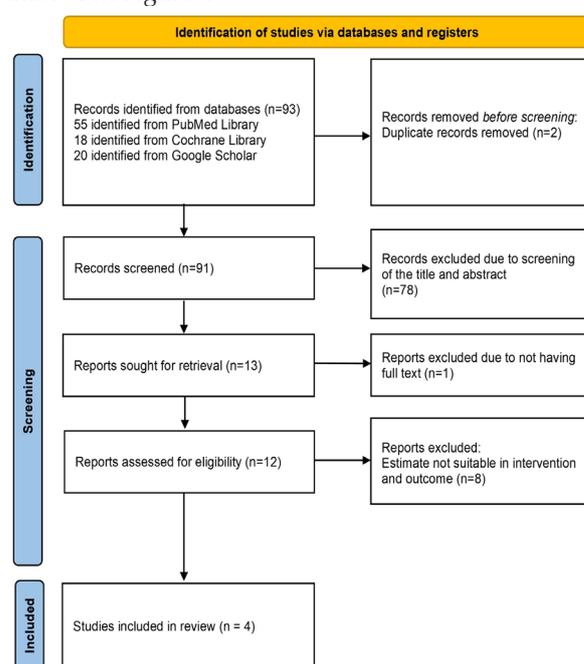


Figure 1: PRISMA Flow diagram of the literature search and studies selection

Study characteristics and data extraction of included studies

In this systematic review, we included four studies. The main characteristics of all included studies are shown in Table 1. All the studies were conducted between 2019-2021. Three studies were conducted in Iran (17-19) and one in Indonesia (2), and were all clinical trials designed. No randomized controlled trials (RCT) were identified. The populations of these studies were men who visited infertility clinics. All of the samples are fresh human ejaculated sperm. The sample size ranges from 40 to 119 participants.

Table 1: The characteristics of the included studies

AUTHORS, YEARS, LOCATION AND STUDY DESIGN	POPULATION	INTERVENTION	COMPARISON	OUTCOME
Abduljabar, 2021, Iran, Clinical trial	60 infertile men, divided into 2 groups: 15 normozoospermia infertile men, and 45 asthenozoospermia infertile men	Each semen sample was divided into 3 tubes. 1 st tube: before activation (0,5 ml), 2 nd tube: after the glass wool filtration (GWF) activation technique (1ml), 3 rd tube: activated by adding PRP 2% to the medium used for glass wool filtration activation (1 ml) Incubation with PRP 2% in 1 hour	1 st tube: semen before activation, 2 nd tube: semen after glass wool infiltration	Both GWF and GW-F+PRP showed increased and improved sperm motility, but the PRP was superior to the GWF alone in increasing progressively motile sperm and decreasing immotile sperm. PRP can upgrade the morphology of the sperm.
Ma'alla, 2021, Iran, Clinical trial	Semen samples from 119 men either had normozoospermia or had mild to moderate sperm abnormalities (excluded patients with azoospermia, or patients with severe oligoasthenoteratozoospermia)	The semen sample was divided into 3 groups: 1 st using Ferticult flushing medium (250 µm); 2 nd group using phosphate buffer saline (250) µm contains 10% human serum albumin (HSA); 3 rd group using phosphate buffer saline (250) µm contains 10% HSA with added 2% PRP. Incubation with PRP 2% in 45 minutes Samples are then prepared by the swim-up procedure	1 st tube: Ferticult flushing medium. 2 nd tube: PBS contain 10% HAS	Swim-up-flushing media resulted in the highest sperm concentration, total count, total motility, progressive motility, lowest immotile sperm, the highest concentration of active motile sperm, and highest normal morphology sperm, followed by swim-up- PBS+PRP (HAS) and then by swim-up-PBS (HAS).
Angellee, 2021, Indonesia, Clinical trial	40 males who underwent infertility treatment (no categorized sperm quality)	1 st tube: Fresh samples 2 nd tube: samples incubated with PRP for 1 hour.	No addition of PRP	The semen samples incubated with PRP produced significantly better quality in terms of concentration, motility, progressive motility, morphology, and the percentage of sperm with good fertilisation.
Hamdan, 2021, Iraq, Clinical trial	100 sperm samples from infertile men (no categorized sperm quality)	1 st tube: without adding PRP 2 nd tube: adding directly PRP 2% Incubation with PRP 2% in 15 minutes	No addition of PRP	There was a highly significant rise in total motility and progressive motility.

The study that was conducted by Abduljabar *et al* (17) used in this review compared sperm activated with glass wool filtration (GWF) alone versus adding PRP 2% after the filtration by the glass wool method. Specifically in this study, the specimen was followed by one hour of PRP incubation at a temperature of 37°C. This study involved 15 samples of normozoospermia and 45 samples of asthenozoospermia. There was no data on the duration of abstinence, age, body mass index (BMI), and other risk factors. The outcome of this study was the addition of PRP to glass wool filtration in semen preparation improves progressive sperm motility and reduces the number of immotile sperm PRP can also enhance sperm morphology.

The study by Ma'alla *et al* (18) compared the sperm influenced by phosphate buffer saline 250µm containing 10% human serum albumin (HSA) to the sperm influenced by phosphate buffer saline 250µm containing 10% HSA with added 2% PRP. The samples are subsequently processed using the swim-up method to evaluate the primary parameters of the sperm. The samples were incubated in PRP for about 45 minutes. This study involved 119 infertile men

with either normozoospermia or mild to moderate sperm abnormalities, and they excluded patients with azoospermia and severe oligoasthenoteratozoospermia. The duration of abstinence was 2-7 days, with participants aged between 18-54 years old, and no BMI data or other risk factors. The outcomes were the addition of PRP to phosphate buffer saline improves sperm concentration, motility, and morphology.

In other studies, Hamdan *et al* (19) and Angelee *et al* (2) compared the addition of PRP 2% versus no intervention. The study by Hamdan *et al* (19), compared incubated semen samples with PRP intervention to semen samples without PRP intervention from the control group (different patients). They involved 100 infertile men, but no information regarding categorized sperm quality. There was no data on the duration of abstinence, age, BMI, and other risk factors. The sperm samples were incubated for 15 minutes with PRP. The outcomes were a significant increase in total motility and progressive sperm motility.

The study by Angellee *et al* (2), compared the semen samples from the same patients before and after being

incubated with PRP. This study involved 40 infertile men but no information about the characteristics of the sperm. The average age of the participants was 39 years old, with a BMI of 27,55 kg/m², 33% of participants being overweight and obese, 42,5% having a history of smoking, and 7,5% having a history of alcohol consumption. The average duration of abstinence was 3 days. The semen samples were incubated for one hour with PRP at room temperature. The outcomes were significant improvement in sperm quality (concentration, motility, and morphology) and the percentage of sperm fertilization ability.

All the sperm samples in all of the studies were collected by masturbation. Although the intervention methods in those studies varied, all of them used 2% PRP.

Risk of Bias Assessment

The summary of the risk of bias in this study is shown in Figure 2. All studies were assessed need some concern for the randomization process. One study was assessed with some concern about deviation from the intended intervention, while the other three studies were assessed to be at low bias risk. All studies were at low bias risk for missing outcome data, measurement of the outcome, and the selection of the reported result. One study needs some concern for overall studies, and three studies have a low bias risk.



Figure 2: The summary of the Risk of Bias (RoB) assessment

Synthesis of results

There was a similarity in the assessed outcomes among the four studies, which is the progressive motility of sperm. Four studies that compared the progressive sperm motility rates between the PRP group and the control group (no PRP addition), using semen samples from 319 participants, showed a significant probability of increasing the progressivity of the sperm motility in the PRP group (MD=18.79; 95%-CI 13.71, 23.87, I²=78%; τ₂=21.67; p<0.01). The summary findings are shown in Figure 3.

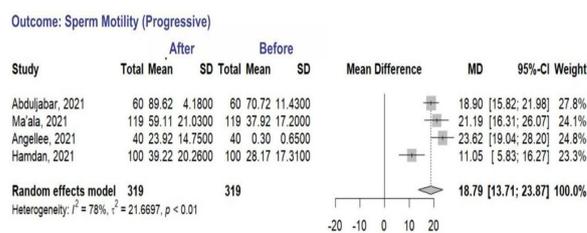


Figure 3: Forest plot detailed mean difference (MD) and 95%-confidence interval (CI) for sperm motility (progressive)

Sperm concentration and morphology were not included in the meta-analysis. However, the studies suggest an increase in these parameters, as Table I shows, based on the study conducted by Abduljabar *et al*, Ma'alla *et al* and Angellee *et al* (17,18,2).

DISCUSSION

Male factor infertility is one of the determining factors for the success of Assisted Reproductive Technologies (ARTs). Global companies are concerned about the culture media, combinations, and techniques utilized for the activation of semen samples from infertile men. Various approaches to treating infertility have been suggested in recent years. Although numerous studies on the efficiency of various semen preparation techniques have been published, there is not enough data to endorse any particular sperm preparation method. Generally speaking, comparative studies on sperm preparation techniques have looked at recovery rates and typical semen characteristics. New laboratory techniques have been used in the past ten years to assess how sperm preparation practices affect sperm quality. (17,18).

Recently, in the past few years, PRP has been one option for improving sperm quality. PRP and its contents are believed to be able to make changes to sperm quality. Platelets are known to contain many active proteins that have therapeutic effects on angiogenesis, mitotic, adhesive, chemotaxis, anti-angiogenesis, and neurotropic processes (20). Activated PRP contains growth factors, such as transforming growth factor- β (TGF- β), fibroblast growth factor (FGF), platelet-derived growth factors (PDGF), epidermal growth factor (EGF), insulin-like growth factor 1 (IGF-1), vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), peptide hormones, and others, contribute to the

therapeutic effects (10, 21). Various studies and literature show that germ cells secrete VEGF, BMP-4, IGF-1, EGF, PDGF, and FGF. The synergy of these growth factors positively influences spermatogenesis and enhances fertility (22). It is believed that PRP which is rich in growth factors has a positive effect on spermatogenesis and fertility. The pregnancy rate is greatly increased by adding these growth elements to the intrauterine insemination (IUI) trend and sperm washing preparation within sperm activation (17,18).

Platelets contain three major granules: dense granules, α -granules, and lysosomes. Dense granules and α -granules have been extensively researched and are crucially significant (23). Platelets dense granules consist of adenosine-triphosphate (ATP), calcium and zinc ions, histamine, serotonin, and superoxide dismutase (SOD), which are essential factors for preserving tissue and cell homeostasis (10). Platelets α -granules contain growth factors, cytokines, adhesion molecules, cell-activating agents, angiogenesis factors, and coagulation proteins. Each of the components individually showed positive impacts on human sperm quality and function (24).

In our study, it can be seen that PRP significantly increases total sperm motility and sperm progressive motility. Abduljabar *et al* (17) have shown that progressive sperm motility (A+B) increases by 26% in PRP+GWF compared to GWF alone. Ma'alla *et al* (18) have shown that progressive sperm motility (A+B) increases by 55% in swim-up PBS+PRP compared to swim-up PBS. Hamdan *et al* (19) showed that total sperm motility increased by around 25% and progressive sperm motility (A+B) by 39% when PRP was added to the incubation process compared to fresh samples and Angellee *et al* (2) using the same sperm sample, compared before and after the addition of PRP, there was an increase in total sperm motility by 2,5 times and sperm progressive motility improved up to 80 times.

The ability of sperm to move forward effectively is crucial in assessing semen quality and serves as one of the reliable indicators of successful fertilization. Good sperm motility enhances fertilization. Sperm motility can be influenced by both endogenous and exogenous factors. Sperm motility is controlled by both internal and external pH levels, as well as the concentrations of calcium ions (Ca^{2+}) and bicarbonate ions (HCO_3^-). Calcium ions and bicarbonate ions activated soluble adenylate cyclase. They are responsible for producing cAMP in sperm cells and play a role in increasing the beat frequency of spermatozoa. Calcium ions as secondary messengers and regulate cAMP levels within the cell. If intracellular Ca^{2+} levels are low, the flagellum beats asymmetrically, so that spermatozoa do not move forward. Several studies have reported that extracellular Ca^{2+} increases sperm motility, but this is still debatable (25-27, 19). Platelet dense granules consist of calcium ions, thus potentially also supporting the availability

of extracellular calcium that affects progressive sperm motility. However, further research is needed to prove this relationship and determine the optimal level of calcium to support good sperm motility.

According to Saucedo *et al* (28), findings from a different investigation show that FGF also may greatly improve both the total and progressive motility of sperm besides the function of regulating cellular proliferation, differentiation, and apoptosis. In ejaculated sperm, fibroblast growth factor receptors (FGFRs) were found in the acrosomal region of sperm and the flagellum. When sperm were exposed to FGF2, there was an increase in the phosphorylation of FGFR in the flagellum and the activation of extracellular signal-regulated kinase (ERK) and protein kinase B (PKB or Akt) signaling pathways (29). The incubation of sperm with FGF2 resulted in a notable rise in the percentage of total and progressive sperm motility, along with an improvement in sperm kinematics and enhanced intracellular Ca^{2+} levels and acrosomal loss compared to the control (28).

Besides that, the combined effects of TGF- β and VEGF, a component found in α -granules, improve sperm motility (30, 10). Sharkey *et al* (31) found a positive correlation among the three isoforms of TGF- β , activin, and follistatin, indicating a potential co-regulation of their production. It can be said that PRP further enhances the working effect of existing TGF- β in seminal fluid. The length of abstinence appears to affect the overall levels of TGF- β 1, TGF- β 2, activin A, and follistatin. Levels of TGFB1, TGFB2, activin A, and follistatin all rose with longer periods of abstinence, it was corresponding to an increase in ejaculate volume. Based on this research, the length of abstinence showed a positive correlation with sperm concentration and volume but a negative correlation with sperm motility. There was also an inverse relationship between TGF- β 1 and age. Unfortunately, in this reviewed study, not all the duration of abstinence and age were mentioned. VEGF besides having a crucial role in cell proliferation, cell cycle maintenance, and cell apoptosis prevention also enhanced sperm motility but the impact on sperm motility was dependent on the specific concentration. All motion parameters were influenced in a concentration-dependent manner (30, 32). Therefore, it can be concluded that an appropriate concentration of VEGF in PRP can enhance sperm motility.

Human spermatozoa contain platelet-activating factor (PAF), and its endogenous levels of PAF are positively correlated with sperm motility and pregnancy rates (33). PAF is a bioactive phospholipid that mainly produced by platelets, neutrophils, mast cell, macrophages and endothelial cell (34). In human spermatozoa, PAF receptors are predominantly found in the neck and midpiece regions of spermatozoa. The midpiece, where the mitochondria are found, plays a key role in sperm motility. Exogenous PAF markedly enhances the

forward movement of spermatozoa (35). Although still controversial because Wu *et al* (36) research concluded that PAF is involved in human spermatozoa acrosome reaction via activation of ERK, it does not specifically increase sperm motility.

The components of platelet-dense granules also contribute to increased sperm motility. Zinc superoxide dismutase (SOD) was reported to play an important role in protecting sperm motility by increasing the integrity of the sperm membrane (37). Serotonin (5-hydroxytryptamine/5-HT) can cause a significant increase in sperm motility and tyrosine phosphorylation activity in human sperm (38).

The above matters can be considered as reasons for the increase in progressive sperm motility with the addition of PRP.

In this study, 319 samples were collected by masturbation. The PRP group showed a significant beneficial effect compared with the control group in increasing the progressivity of sperm motility. In all of the studies using PRP 2%. Based on multiple trials and pilot studies with various PRP concentrations (2%, 5%, and 10%), the results revealed that 2% is the ideal concentration for PRP preparation, yielding significant effects (19). The study by Bader *et al* (39), suggests that PRP 2% was regarded as the best concentration to achieve a significant increase in progressive and total motility compared to concentrations 5% and 10%. However, some other studies have used varying concentrations in their research especially in the study group on PRP administration before cryopreservation, Yan *et al* (10) showed that PRP 5% more superior to 2%, and 10% in improved sperm progressive motility, viability, and membrane integrity after cryopreservation, while Mirzaei *et al* (11) and Nabavinia *et al* (12) used PRP 1%. The study by Nabavinia *et al* (12), proves that the use of PRP 1% incubation treatment in sperm is more effective in increasing the percentage of sperm progressive motility compared to PRP 0,5% and 0,25%. While Mirzaei *et al* (11), showed that progressive and total sperm motility and viability were significantly higher in PRP 1% compared to 5%, and 10%. So, for the optimal dosage of PRP, more research in large-scale participants is still needed. However, in our study, incubation with the concentration of PRP 2% has already shown significant results in improving sperm progressivity

The duration of the incubation varied from 15 minutes to 1 hour, with satisfactory results concerning the increment in human ejaculated sperm quality, specifically progressive sperm motility. Therefore, the long duration of incubation may not affect the magnitude of changes in the quality of the sperm produced. However, further research is needed on this matter.

We also cannot conclude the effect of PRP on severe sperm abnormalities because Abduljabar's study (17) only involved patients with normozoospermia and asthenozoospermia. In Ma'alla's study (18), patients with severe oligoasthenoteratozoospermia were excluded, while in the other two studies, there were no specific categories in patient's sperm quality. So, further research is still needed regarding the effects of PRP on each category of sperm abnormalities based on WHO sperm categories.

PRP effects on concentration increment and sperm morphology could not be assessed in the meta-analysis because the available journals we searched were limited, but from the three studies above that assessed this, we can conclude descriptively that incubation of sperm with 2% PRP can improve sperm concentration and morphology.

Of the four journals included in this study, only Angellee's research (2) mentions age, BMI, and risk factors, such as smoking habits, alcohol consumption, and exposure to drugs. These factors should be taken into account as they can affect sperm quality (40).

To ensure reliable and precise results and maximize potential benefits in the future, it is crucial to identify the optimal dosage through more research and an appropriate incubation period of PRP addition in human ejaculated sperm. It is also important to know the fertilization ability of sperm after incubation with PRP, to assess the success of this infertility management. Moreover, the encouraging results of our study have laid the groundwork for the execution of future systematic, randomized controlled trials. Consequently, a more comprehensive systematic review and meta-analysis of this correlation is needed. The use of PRP should be deemed experimental until definitive, major RCTs are available.

Strength and limitation

The strength of this meta-analysis lies in the systematic evaluation of the effectiveness of adding PRP to human ejaculated sperm. This research can also provide new insight into the use of PRP, which is now starting to be carried out in infertility clinic settings, especially on human ejaculated sperm.

This review had a limitation: only four journal clinical trials were suitable for our inclusion criteria. The author did multiple searches and found that clinical trials in human ejaculated sperm are too limited. In this analysis, we included four clinical trial studies. Three of these studies were deemed to have a low risk of bias, while the other one raised some concerns. Also, the heterogeneity in the meta-analysis (variation in study outcomes) between studies was high. There was a difference in the method and the incubation period with PRP that

might have affected the accuracy of the outcome that we found. The analysis did not include any randomized controlled trials (RCTs).

CONCLUSION

After PRP treatment, there is an improvement in sperm progressivity, suggesting the enhanced quality of human ejaculated sperm. Although beneficial in improving sperm motility, strong evidence for further study will be necessary.

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