

# Intrauterine infusion of autologous platelet-rich plasma in women undergoing assisted reproduction: A systematic review and meta-analysis

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## Abstract

Prior studies have provided conflicting results regarding the use of platelet-rich plasma (PRP) in women undergoing in-vitro fertilization (IVF) or intracytoplasmic injection (ICSI). The objective of this study was to evaluate the effect of the intrauterine infusion of PRP on the outcome of embryo transfer (ET) in women undergoing IVF/ICSI. We searched databases, including PubMed, Embase, Scopus, Web of Science, and the Cochrane Database of Clinical Trials (CENTRAL). Meta-analysis using a random-effects model was performed to calculate the pooled estimates. Seven studies involving 625 patients (311 cases and 314 controls) were included. The probability of chemical pregnancy ( $n = 3$ , risk ratio (RR): 1.79, 95 % confidence intervals (CI): 1.29, 2.50;  $P < 0.001$ ,  $I^2 = 0$  %), clinical pregnancy ( $n = 7$ , RR: 1.79, 95 % CI: 1.37, 2.32;  $P < 0.001$ ,  $I^2 = 16$  %), and implantation rate ( $n = 3$ , RR: 1.97, 95 % CI: 1.40, 2.79;  $P < 0.001$ ,  $I^2 = 0$  %) was significantly higher in women who received PRP compared with control. There was no difference between women who received PRP compared with control group regarding miscarriage (RR: 0.72, 95 % CI: 0.27, 1.93;  $P = 0.51$ ,  $I^2 = 0$  %). Following the intervention, endometrial thickness increased in women who received PRP compared to control group (SMD: 1.79, 95 % CI: 1.13, 2.44;  $P < 0.001$ ,  $I^2 = 64$  %). The findings of this systematic review suggest that PRP is an alternative treatment strategy in patients with thin endometrium and recurrent implantation failure (RIF). Further prospective, large, and high quality

randomized controlled trials (RCTs) are needed to identify the subpopulation that would most benefit from PRP.

## **Introduction**

Implantation failure can occur during any of the three stages of implantation, i.e., apposition, adhesion, and invasion (Hoozemans et al., 2004). There are several reasons for implantation failure, but it can be classified into four main categories: altered endometrial receptivity, embryonic defects, abnormal embryo-endometrial cross-talk and impairment in the regulation of immunologic mediators (Diedrich et al., 2007).

Various interventions have been employed to increase the implantation rate and subsequently the chance of live birth in couples with RIF like hysteroscopic correction of cavity pathology (Margalioth et al., 2006), treatment of thin endometrium (Lebovitz and Orvieto, 2014), endometrial stimulation (Paulson, 2011), blastocyst transfer (Glujovsky et al., 2016), cytoplasmic transfer (Barritt et al., 2001), intrauterine administration of autologous peripheral blood mononuclear cells (Maleki-Hagiagha et al., 2019), endometrial scratching (Gibreel et al., 2015), and use of immunomodulators (D'hooghe, 2003). However, even with these new treatment approaches, many patients still are suffering from RIF. Therefore, there is a need for an alternative treatment with more success in patients with a history of treatment failure.

Recently, some progress in treating RIF and thin endometrium has been made with the use of the PRP. PRP, also known as autologous conditioned plasma, is a concentrate of PRP protein derived from fresh whole blood, centrifuged to remove red blood cells and has anti-inflammatory and pro-regenerative functions (Bos-Mikich et al., 2018). The main idea of using the PRP in patients with previous ET failures is based on the regulation of expression of growth factors and cytokines in the endometrium which was first presented by Chang et al., 2015 (Chang et al., 2015).

Previous studies have provided conflicting results regarding the use of PRP in patients with RIF or thin endometrium (Eftekhar et al., 2018; Chang et al., 2019; Kim et al., 2019; Mehrafza et al., 2019; Nazari et al., 2019). Based on our knowledge, there are a lack of conclusive results and a comprehensive review regarding the effect of PRP on the outcome of IVF/ICSI cycles. Therefore, in this systematic review and meta-analysis, we aimed at investigating the studies that evaluated the effect of intrauterine infusion of PRP in women undergoing IVF/ICSI cycles.

## **Section snippets**

### **Methods**

This systematic review and meta-analysis addressed the efficacy of intrauterine infusion of PRP compared with control (no intervention or other treatments) in sub-fertile women for improving clinical outcomes after assisted reproduction. We followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

### **Summary of the literature search**

The initial electronic literature search yielded 2,672 publications (775 from PubMed, 239 from Embase, 1,196 from Scopus, 376 from Web of Science, 82 from Cochrane Library and 4 through other sources). All citations were saved in reference manager software (Endnote) to identify the 1,565 duplicates. The titles and abstracts of these citations were scrutinized to exclude irrelevant papers, resulting in 17 potentially eligible studies. After reading the full texts, ten articles were excluded

### **Discussion**

In this study, we included seven studies that evaluated the effect of intrauterine infusion of PRP for 625 women (311 cases and 314 controls) with a thin endometrium (two studies) or recurrent implantation failure (five studies) undergoing frozen-thawed ET cycle. Compared with control group, those in the PRP group exhibited better beneficial effects including clinical pregnancy, chemical pregnancy, implantation rate, and endometrial thickness, and the advantages remained after subgroup analysis

### **Conclusion**

Our systematic review and meta-analysis showed that intrauterine administration of PRP, irrespective of study design and study population, increases the clinical pregnancy rate in women experienced frozen-thawed ET cycle. Further prospective, large, and high quality randomized controlled trials (RCTs) are needed to identify the subpopulation that would most benefit from PRP.

### **Authors' roles**

M.S. and A.M.H. were responsible for defining the research question. M.S. and S.R. designed the strategy for the literature search. S.M., M.R. and M.R.

participated in study selection. A.M.H. and M.S. performed the quality assessment of included studies. Data extraction was carried out by S.R. and M.R. Data analysis was performed by A.M.H, M.S. and S.M. were the major contributors in manuscript writing. M.S. and A.M.H drafted the manuscript and revised content based on feedback.

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# **A Case Series on Platelet-Rich Plasma Revolutionary Management of Poor Responder Patients**

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Abstract

Poor responders are described as those In Vitro Fertilization (IVF) patients who are failing to respond to controlled ovarian stimulation protocols. Extensive research has focused on crafting the optimal treatment.

However, it appears that each approach fails to be established as effective or guaranteed towards successful management. Platelet-Rich Plasma (PRP) is a novel, highly promising approach that has been successfully applied for an array of medical issues. In this case series, we present 3 poor responder patients with the common denominator of: failed IVF attempts, poor oocyte yield, and poor embryo quality. The option of oocyte donation was rejected. All patients were treated with autologous PRP ovarian infusion following written consent. Within a 3-month interval, follicle-stimulating hormone decreased by 67.33%, while Anti-Müllerian hormone increased by 75.18%. These impressive results on the biochemical infertility markers alone are classified as a complete biological paradox, coupled by improved embryo quality. Results report a natural conception at 24 weeks, an uncomplicated healthy pregnancy at 17 weeks and a successful live birth. To our knowledge, this is the first time such an approach and results are reported, where PRP treatment on poor responders lead to overcoming their challenging reproductive barrier.

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