IMR Press

Review

Administration of autologous platelet rich plasma and the impact on outcomes of assisted reproduction treatment in infertile women

Pelin Kutlu[1,*], Seda Karabulut[2], Oya Korkmaz[2]

[1] *Istanbul Medicana Çamlıca Hospital, IVF Center, 34692 İstanbul, Turkey*

[2] *Department of Histology and Embryology, School of Medicine, Istanbul Medipol University, 34815 İstanbul, Turkey*

*Correspondence: kutlupelin@gmail.com (Pelin Kutlu)

DOI:10.31083/j.ceog4805165

Submitted: 3 March 2021 Revised: 26 March 2021 Accepted: 29 April 2021 Published: 15 October 2021

Objective: There are diverse findings concerning the use of platelet-rich plasma (PRP) in assisted reproduction treatment (ART) cycles of infertile women with low ovarian reserve, ovarian failure or implantation failure due to endometrial problems. A debate continues regarding the benefit of this technique because of the low number of evidence-based studies. *Mechanism*: Different PRP preparation methods have been described in the literature, aiming to obtain the highest number of platelets following centrifugation steps. *Findings in brief*: Research on the use of PRP in female infertility aims to improve the deteriorated hormonal profile, gamete production and implantation of the embryo into the endometrium. *Conclusions*: This paper reviewed literature evaluating the impact of PRP on the outcomes of subsequent ART cycles in infertile women. PRP is a safe and easy-to-apply procedure and can be used as an 'add-on' therapy in patients with reduced ovarian reserve, ovarian failure or implantation failure prior to the in vitro fertilization (IVF) cycle, although it is still regarded as an empirical treatment method. Further studies should be conducted to enlighten the subject.

Keywords

Infertility; IVF; Platelet-rich plasma (PRP); Ovarian failure

1. Introduction

Since the first *in vitro* fertilization (IVF) attempts in the mid-1970s, researchers have been working on developmental approaches to improve infertility outcomes. A woman undergoes a decline with age in the number and quality of her oocytes. These aged oocytes also show genetic abnormalities such as aneuploidies [1]. Supportive treatments are recommended to these patients which may include antioxidants, vitamins or coenzyme Q10 [2]. However, clinical data on these supplementation methods are controversial [3]. Thus, new methods are being investigated to address age factor infertility, as well as insufficient endometrial growth or other indications that result in poor outcomes in assisted reproduction treatments (ART).

Platelet rich plasma (PRP), applied as an intrauterine infusion by Chang *et al.* [4] in 2015, is one of the novel advances for poor endometrial response to standard hormone replacement therapy. Subsequently, many clinical studies on PRP for female infertility have been conducted, most of which are encouraging. It has been performed for premature ovarian failure or insufficiency (POI), poor ovarian response, and poor oocyte and/or embryo quality. These indications represent patients with "poor prognosis" for ART.

PRP is commonly described as the blood plasma which contains high concentrations of platelets [5], approximately 4–5 times greater than in the circulating blood. The physiological processes involved in the platelet-mediated tissue repair comprise both adherence and aggregation around the injured area to form thrombin and fibrin, and the release of substances that promote angiogenesis and inflammation, such as platelet derived growth factor (PDGF), transforming growth factor beta (TGF-β), vascular endothelial growth factor (VEGF), as well as cytokines like platelet factor 4 (PF4) [6]. These growth factors are essential in fibroblast and leukocyte activation, and in proliferation and/or migration of various cell types to the site of injury. In addition, platelet derived factors have been shown to induce endometrial progenitor cell activity [7] and promote stromal cell proliferation [8].

PRP has given hope to patients with endometrial insufficiency, ovarian insufficiency, perimenopausal or menopausal women, and poor responders to ART. Ovarian rejuvenation following PRP application was introduced by Pantos *et al.* [9] at the 2016 ESHRE conference. They reported successful ovarian rejuvenation 1–3 months after PRP therapy. In 2018, Sills *et al.* [6] reported the first data on in vitro fertilization and blastocyst formation after intraovarian injection of autologous platelet rich plasma. This was followed by the case series of Sfakianoudis *et al.* [10], which included 3 patients with increased levels of anti-mullerian hormone (AMH) and reductions in follicle stimulating hormone (FSH), and achieved pregnancy in all three patients. Current research on the use of PRP in female infertility aims to improve deteriorating hormonal profiles, as well as enabling gamete production and implantation of the embryo into the endometrium. However,

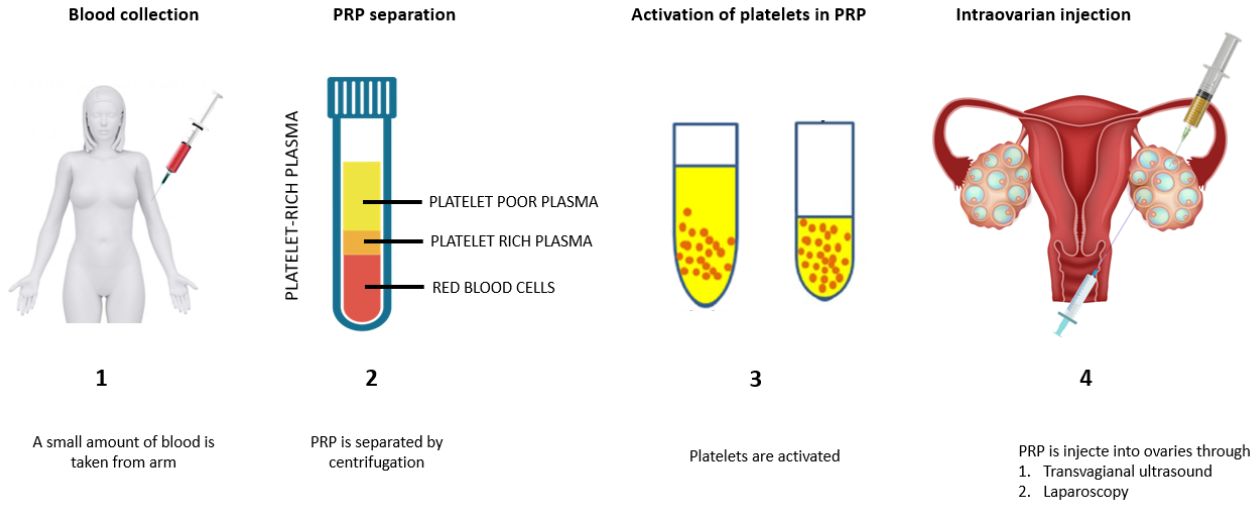

Fig. 1. Schematic representation of PRP preparation and application.

this treatment is an "add-on" therapy performed prior to the standard methods of IVF treatment.

The present study focuses on the outcomes of PRP administration into the ovaries or endometrium of women undergoing IVF. The aim of this paper is to review the literature and evaluate the effect of PRP on the outcomes of subsequent ART cycles in infertile women with poor ovarian reserve, ovarian insufficiency or repeated implantation failures due to endometrial problems.

2. Methods for PRP preparation

Different methods of PRP preparation have been described in the literature, all of which aim to obtain the highest number and purity of platelets as a layer, following centrifugation steps.

15–50 mL of blood were collected from the antebrachial vein into tubes which were then centrifuged at rotation speeds ranging from 270 g to 1500 g for periods ranging from 5 to 10 minutes. The layers formed were separated according to the method of each laboratory or according to the instructions of the manufacturer whenever ready-to-use kits were used. In various methods, centrifugation was repeated following the separation procedure. In some techniques, calcium including additives were used to activate the mixture. The prepared solution was then infused into the uterine cavity or injected into the cortex of each ovary using aspiration needles or infused into the uterine cavity [4, 6, 10–14], according to the need of each patient (Fig. 1).

3. PRP physiology

Platelets are the elements of blood which play important role in hemostasis at situations of vascular injury. The process starts with adherence and aggregation of the platelets forming a procoagulant surface at the injury site, and subsequent thrombin and fibrin generation. However, another important role of the platelets is to release substances that promote tissue repair and mediate angiogenesis and inflammation. They secrete cytokines such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), vascular endothelial growth factor (VEGF), platelet factor 4 (PF4) and CD40L. These growth factors play an important role in fibroblast and leukocyte activation and proliferation and/or migration of various cell types to the injury site. Furthermore, platelet-derived factors induce endometrial progenitor cell activity [7] and promote stromal cell proliferation [8].

4. Therapeutic applications of PRP

Following the first publication by Kingsley *et al.* in 1954 [15] and the first therapeutic application by Levin *et al.* in 1964 [16], PRP has been used in different fields of medicine such as dermatology, neurology, dentistry, plastic surgery and musculoskeletal system disorders. Animal studies were conducted in order to better understand the *in vivo* outcomes, which have shown significant improvements in leukocyte infiltration, inflammatory response, cell proliferation, and tissue regeneration [17, 18]. As the role of growth factors in tissue regeneration is better understood [19], PRP has gained more interest.

The systematic review of Kaur *et al.* [20] briefly explained the role of PRP administration in different conditions within the field of gynecology, reproductive endocrinology and infertility. According to the studies involved in that review, PRP was demonstrated to be used in gynecological disorders such as cervical ectopy, vulvar dystrophy, wound healing after caesarian section, in urogenital disorders such as genital fistulas, urinary incontinence, and in reproductive medicine such as premature ovarian failure (POF), ovarian torsion, refractory endometrium and repeated implantation failure (RIP), and was shown to be related to faster wound healing,

decreased post-operative pain and reduced fever rate.

The ovaries and endometrium are the two main targets of PRP exposure in the treatment of female infertility, as two important steps in successful conception are the formation of the oocytes and the implantation of the embryo into the uterus.

5. PRP in assisted reproduction

In assisted reproduction, various methods are used to prepare the endometrium for implantation in both fresh and frozen-thawed embryo transfer cycles. Some embryo transfer procedures may be cancelled or delayed due to poor endometrial thickness, which has generally been defined as less than 7 mm [21, 22]. Extended estrogen treatment and adjuvant therapy such as low dose aspirin or vaginal Sildenafil have been used [23], however, a consensus is not yet agreed.

Studies regarding the effect of PRP application on assisted reproduction are summarized in Table 1 (Ref. [4, 11, 12, 14, 24–26]). The first application of PRP as an intrauterine infusion in order to improve endometrial thickness was by Chang *et al.* [4], on women who had insufficient endometrial thickness and showed no response to conventional therapy. PRP induced endometrial growth in all 5 patients involved, and 4 achieved pregnancy.

The study of Zadehmodarres revealed similar outcomes. This study was performed on 10 patients with a history of cancelled cycles due to inadequate endometrial growth (less than 7 mm). Endometrial thickness was shown to increase 48 h after the first PRP and to reach more than 7 mm thickness after the second PRP in all patients. Five patients out of ten were observed to be pregnant, and in four, the pregnancy progressed normally [11].

Likewise, in the randomized clinical study of Eftekhar *et al.* [12] which included 83 patients with poor endometrial response to standard hormone replacement therapy (endometrial thickness <7 mm), endometrial thickness of the study group was found to be significantly higher compared to the control group following PRP infusion. Implantation and clinical pregnancy rates were significantly higher in the study group as well.

In 2019, Kim *et al.* [24] enrolled 24 women with 2 or more filed IVF cycles and refractory thin endometrium with a <7 mm thickness. In their prospective interventional study, both endometrial thickness, and pregnancy and implantation rates were found to be significantly increased following intrauterine infusion of autologous PRP. Coksuer *et al.* [25] performed intrauterine PRP in 34 patients who had suboptimal endometrial lining and unexplained infertility and demonstrated a significant improvement in both endometrial thickness 48 hours after PRP application, and in the clinical pregnancy rate.

A total of 123 patients with a history of more than 2 failed IVF cycles were included in the retrospective cohort study of Mehratza *et al.* [26], 67 of whom were included in the PRP group, and the remaining 56 were included in the Granulocyte Colony Stimulating Factor (GCSF) group. The clinical pregnancy rate was observed to be significantly higher in the PRP group ($p < 0.05$).

Sills *et al.* [6] reported the first data on in vitro fertilization and blastocyst formation after intraovarian injection of autologous platelet rich plasma, which was followed by the case series of Sfakianoudis *et al.* [10] which included 3 patients with increased levels of anti-mullerian hormone (AMH) and reduced follicle stimulating hormone (FSH), and achieved positive pregnancies in all three patients.

Four pilot studies were conducted in the Genesis Athens Clinic in order to assess the clinical efficacy of PRP [27]. They were designed as prospective observational cohort studies. Patients were classified into four categories according to their diagnosis: premature ovarian response (POR), premature ovarian insufficiency (POI), perimenopause and menopause.

Anti-mullerian hormone (AMH), antral follicle count (AFC) and oocyte yield were addressed as the primary outcome measures in the POR study, restoration of menstrual cycles and follicle stimulating hormone (FSH) levels were main outcomes for the POI perimenopausal and menopausal studies. Among the patients with POR, significant improvement was observed in both the ovarian reserve status, demonstrated by FSH levels which dropped by 33% ($p < 0.001$), and the ICSI outcomes ($p = 0.03$). Among the patients with POI, menstruation recovery was observed in 18 out of 30, and a statistically significant improvement was observed in the levels of AMH, FSH and AFC, which confirmed the authors' previous findings. Thirteen out of 30 patients were reported to respond positively to PRP treatment. Menstruation regularity, improved hormonal levels and AFC were reported for 24 out of 30 perimenopausal women. The authors concluded that PRP infusion yielded promising results for treating ovarian insufficiency. The increase in serum AMH levels were statistically highly significant, with p values of less than <0.0001 in all groups. Melo *et al.* [14] have also found a significant increase in serum AMH with PRP infusion (p value < 0.001).

The studies of Cakiroglu *et al.* and Sills *et al.* [6, 13] revealed significantly increased levels of AMH following intraovarian PRP infusion ($p < 0.01$ and $p = 0.0016$, respectively).

Melo *et al.* and Sills *et al.* [6, 14] have shown significant reductions in serum FSH levels ($p = 0.001$ and $p < 0.0001$, respectively), while the FSH reduction in the study of Sfakianoudis *et al.* [27] was observed in all groups except women with poor ovarian reserve. However, the reduction observed in the study of Cakiroglu *et al.* [13] was not statistically significant ($p = 0.87$).

The studies of Sfakianoudis *et al.*, Melo *et al.* and Cakiroglu *et al.* [13, 14, 27] revealed statistically significant increases in antral follicle count ($p < 0.01$ in all three studies).

These four major studies, which included 663 subfertile women, were systematically reviewed by Panda *et al.* [28]. Regarding the post-PRP Intracytoplasmic sperm injection (ICSI) outcomes, the total number of retrieved oocytes,

Table 1. Studies investigating the application of PRP: platelet-rich plasma.

Author	Application type	Characteristics	PRP group	Compared group	Results
Chang Y. (2015) [4] (1)	intrauterine infusion of PRP		(N: 5)	—	Successful endometrial expansion and pregnancy were observed in all the patients after PRP infusion. Intrauterine PRP infusion represents a new method for addressing thin endometrium with a poor response.
		Age	34.8		
		Endometrial thickness (mm)	Before PRP: 6.22 After PRP: 7.52		
		Pregnancy (%)	5 (100)		
		Outcome (%)	4 (80)		
Zadehmodarres S. (2017) [11] (2)	intrauterine infusion of PRP		(N: 10)	—	According to this study, it seems that PRP was effective for endometrial growth in patients with thin endometrium.
		Age	34.3		
		Endometrial thickness (mm)	Before PRP: 4.8 48 h after 1st PRP 5.82 48 h after 2nd PRP 7.25		
		Chemical pregnancy (%)	5 (50)		
		Clinical pregnancy (%)	4 (40)		
Eftekhar M. (2018) [12] (3)	intrauterine infusion of PRP		(N: 40)	Control (N: 43)	PRP may be effective in improving endometrial growth, and possibly pregnancy outcomes in women with a thin endometrium.
		Age	31.98 ± 2.26	32.40 ± 2.63	
		Endometrial thickness (mm)	Before PRP: 6.09 ± 0.47 After PRP: 8.67 ± 0.64	Before PRP: 6.15 ± 0.37 After PRP: 8.04 ± 0.27	
		Implantation	21%	9.37%	
		Chemical pregnancy (%)	14 (35.0)	8 (18.0)	
		Clinical pregnancy (%)	3 (32.5)	6 (14.0)	
		Ongoing pregnancy (%)	11 (27.0)	6 (14.0)	
Kim H. (2019) [24] (4)	intrauterine infusion of PRP		(N: 20)	—	The use of autologous PRP improved the implantation, pregnancy, and live birth rates of patients with refractory thin endometrium. We assume that the ability of autologous PRP to restore the endometrial receptivity of damaged endometrium has some effects other than simply increasing the endometrial thickness.
		Age	38.4 ± 4.3		
		Endometrial thickness (mm)	Before PRP: 5.4 ± 0.8 After PRP: 6.0 ± 1.6		
		Implantation	12.7 (7/55)		
		Clinical pregnancy (%)	30 (6/20)		
		Ongoing pregnancy (%)	20 (4/20)		
		Live birth (%)	20 (4/20)		
Coksuer H. (2019) [25] (5)	intrauterine infusion of PRP		(N: 34)	Control (N: 36)	We showed that intrauterine autologous PRP infusion is a safe, inexpensive adjuvant treatment for optimizing endometrium especially in patients with RIF history and intrauterine PRP infusion improved not only endometrial lining but also in vitro fertilization success and pregnancy outcome.
		Age	29.41 ± 4.54	29.41 ± 4.54	
		Endometrial thickness (mm)	On FET day: 10 (8–14)	ON FET day: 10 (8–13.5)	
		FSH (IU/L)	7.3 (4.6–9.5)	6.9 (3.5–9.7)	
		LH (IU/L)	7.2 (5.2–8.9)	6.5 (4.3–8.5)	
		Biochemical pregnancy (%)	4 (11.7)	15 (41.6)	
		Clinical pregnancy (%)	12 (35.2)	8 (22.2)	
		Live birth (%)	14 (41.2)	6 (16.7)	

Table 1. Continued.

Author	Application type	Characteristics	PRP group	Compared group	Results
Mehrafza M. (2019) [26] (6)	intrauterine infusion of PRP		(N: 67)	GCSF (N: 56)	It seems that intrauterine infusion of PRP can positively affect pregnancy outcome in RIF patients in comparison with systemic administration of GCSF and more studies need to be designed to conclude the effectiveness of this method.
		Age	31.85 ± 5.22	33.46 ± 5.17	
		FSH (mIU/L)	4.59 ± 1.71	5.29 ± 2.18	
		LH (mIU/L)	3 (0.1–15)	2.95 (0.3–8)	
		Fertilization (%)	500/858 (58.3)	376/605 (62.1)	
		Implantation (%)	33/204 (17.2)	15/143 (10.5)	
		Chemical pregnancy (%)	29/67 (43.3)	15/56 (26.8)	
		Clinical pregnancy (%)	27/67 (40.3)	12/56 (21.4)	
Melo P. (2020) [14] (7)	intracortical ovarian PRP injection		(N: 46)	Control (N: 37)	PRP injections are effective and safe to improve markers of low ovarian reserve prior to ART.
		Age	41(39–44)	41 (39–44)	
		AMH (ng/mL)	Pre-treatment: 0.62 (0.47 to 0.76) Post-treatment: 1.01 (0.9 to 1.3)	Baseline: 0.68 (0.41 to 0.78) Follow-up 3 months: 0.58 (0.39 to 0.76)	
		FSH (mIU/L)	Pre-treatment: 13.6 (12.9 to 17.5) Post-treatment: 9.07 (8.3 to 10.5)	Baseline: 14.9 (13.1 to 17.8) Follow-up 3 months: 15.0 (13.4 to 17.9)	
		Biochemical pregnancy (%)	12 (26.1)	2 (5.4)	
		Clinical pregnancy (%)	11 (23.9)	1 (5.4)	
		Live birth (%)	4 (8.7)	1 (2.7)	

FET, fresh embryo transfer; GCSF, Granulocyte Colony Stimulating Factor; RIF, Repeated implantation failure.

mature oocytes, number of fertilized oocytes, number of cleavage stage embryos and cancellation rate were significantly better in the study of Sfakianoudis *et al.* [27], when compared to the previous ICSI cycle as control. The number of good-quality embryos was also higher, though not significantly so.

In the study of Melo *et al.* [14], the total number of retrieved oocytes, the fertilization rate and the number of good-quality embryos were significantly higher after PRP, compared to the control group.

6. Conclusions

Autologous PRP has become a non-surgical option to improve a wide range of medical situations. Current research on the use of PRP in female infertility aims to improve the deteriorating hormonal profile, as well as enable gamete production and implantation of the embryo into the endometrium. According to the reported outcomes of the above-mentioned studies, this method can enhance the pregnancy potential of a patient especially in the subfertile and infertile groups. Moreover, the risks of immunological reaction or transmission of infectious diseases are minimal since PRP is prepared from autologous blood samples. The risks of PRP therapy potentially include infection, bleeding, and nerve damage but appear to be minimal.

As a result, it may be concluded that PRP can be used as an "add-on" therapy in patients with diminished ovarian reserve prior to the IVF cycle. This is a safe and easy-to-apply method although it is still considered an empirical treatment method. Further studies with a randomized design and larger sample size should be conducted in order to better understand the effect on outcomes in female infertility.

Author contributions

PK and SK developed the original idea and wrote the manuscript. OK conducted the literature search and prepared the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of interest

The authors declare no conflict of interest. Seda Karabulut is the Guest Editor of this journal, given her role as Guest Editor, had no involvement in the peer-review of this article and has no access to information regarding its peer-review.

References

[1] Battaglia DE, Goodwin P, Klein NA, Soules MR. Influence of maternal age on meiotic spindle assembly in oocytes from naturally cycling women. Human Reproduction. 1996; 11: 2217–2222.

[2] Collins GG, Rossi BV. The impact of lifestyle modifications, diet, and vitamin supplementation on natural fertility. Fertility Research and Practice. 2015; 1: 11.

[3] Showell MG, Mackenzie-Proctor R, Jordan V, Hart RJ. Antioxidants for female subfertility. Cochrane Database of Systematic Reviews. 2017; 7: CD007807.

[4] Chang Y, Li J, Chen Y, Wei L, Yang X, Shi Y, *et al.* Autologous platelet-rich plasma promotes endometrial growth and improves pregnancy outcome during *in vitro* fertilization. International Journal of Clinical Experimental Medicine. 2015; 8: 1286–1290.

[5] Bos-Mikich A, de Oliveira R, Frantz N. Platelet-rich plasma therapy and reproductive medicine. Journal of Assisted Reproduction and Genetics. 2018; 35: 753–756.

[6] Sills ES, Rickers NS, Li X, Palermo GD. First data onin vitrofertilization and blastocyst formation after intraovarian injection of calcium gluconate-activated autologous platelet rich plasma. Gynecological Endocrinology. 2018; 34: 756–760.

[7] Gargett CE, Chan RWS, Schwab KE. Hormone and growth factor signaling in endometrial renewal: role of stem/progenitor cells. Molecular and Cellular Endocrinology. 2008; 288: 22–29.

[8] Aghajanova L, Houshdaran S, Balayan S, Manvelyan E, Irwin JC, Huddleston HG, *et al. In vitro* evidence that platelet-rich plasma stimulates cellular processes involved in endometrial regeneration. Journal of Assisted Reproduction and Genetics. 2018; 35: 757–770.

[9] Pantos K, Nitsos N, Kokkali G, Vaxevanoglou T, Markomichali C, Pantou A, *et al.* Ovarian rejuvenation and folliculogenesis reactivation in peri-menopausal women after autologous platelet-rich plasma treatment. ESHRE 32nd Annual Meeting. 2016; 3–6.

[10] Sfakianoudis K, Simopoulou M, Nitsos N, Rapani A, Pantou A, Vaxevanoglou T, *et al.* A case series on platelet-rich plasma revolutionary management of poor responder patients. Gynecologic and Obstetric Investigation. 2019; 84: 99–106.

[11] Zadehmodarres S, Salehpour S, Saharkhiz N, Nazari L. Treatment of thin endometrium with autologous platelet-rich plasma: a pilot study. JBRA Assisted Reproduction. 2017; 21: 54–56.

[12] Eftekhar M, Neghab N, Naghshineh E, Khani P. Can autologous platelet rich plasma expand endometrial thickness and improve pregnancy rate during frozen-thawed embryo transfer cycle? A randomized clinical trial. Taiwanese Journal of Obstetrics and Gynecology. 2018; 57: 810–813.

[13] Cakiroglu Y, Saltik A, Yuceturk A, Karaosmanoglu O, Kopuk SY, Scott RT, *et al.* Effects of intraovarian injection of autologous platelet rich plasma on ovarian reserve and IVF outcome parameters in women with primary ovarian insufficiency. Aging. 2020; 12: 10211–10222.

[14] Melo P, Navarro C, Jones C, Coward K, Coleman L. The use of autologous platelet-rich plasma (PRP) versus no intervention in women with low ovarian reserve undergoing fertility treatment: a non-randomized interventional study. Journal of Assisted Reproduction and Genetics. 2020; 37: 855–863.

[15] Kingsley CS. Blood coagulation: evidence of an antagonist to factor VI in platelet-rich human plasma. Nature. 1954; 173: 723–724.

[16] Levin RH, Freireich EJ, Chappell W. Effect of storage up to 48 hours on response to transfusions of platelet rich plasma. Transfusion. 1964; 4: 251–256.

[17] Notodihardjo PV, Morimoto N, Kakudo N, Matsui M, Sakamoto M, Liem PH, *et al.* Gelatin hydrogel impregnated with platelet-rich plasma releasate promotes angiogenesis and wound healing in murine model. Journal of Artificial Organs. 2015; 18: 64–71.

[18] Borrione P, Fagnani F, Di Gianfrancesco A, Mancini A, Pigozzi F, Pitsiladis Y. The role of platelet-rich plasma in muscle healing. Current Sports Medicine Reports. 2017; 16: 459–463.

[19] Scully D, Naseem KM, Matsakas A. Platelet biology in regenerative medicine of skeletal muscle. Acta Physiologica. 2018; 223: e13071.
[20] Kaur KK, Allahbadia G, Singh M. Autologous Platelet rich plasma (PRP): a possibility of becoming a revolutionary therapy in the field of gynaecology and reproductive endocrinology and infertility-a systematic review. Progress in Women's Health Care. 2019; 1: 1–13.
[21] Richter K, Bugge K, Bromer J, Levy M. Relationship between endometrial thickness and embryo implantation, based on 1,294 cycles of in vitro fertilization with transfer of two blastocyst-stage embryos. Fertility and Sterility. 2007; 87: 53–59.
[22] El-Toukhy T, Coomarasamy A, Khairy M, Sunkara K, Seed P, Khalaf Y, *et al.* The relationship between endometrial thickness and outcome of medicated frozen embryo replacement cycles. Fertility and Sterility. 2008; 89: 832–839.
[23] Groenewoud ER, Cantineau AEP, Kollen BJ, Macklon NS, Cohlen BJ. What is the optimal means of preparing the endometrium in frozen–thawed embryo transfer cycles? A systematic review and meta-analysis. Human Reproduction Update. 2013; 19: 458–470.
[24] Kim H, Shin JE, Koo HS, Kwon H, Choi DH, Kim JH. Effect of autologous platelet-rich plasma treatment on refractory thin endometrium during the frozen embryo transfer cycle: a pilot study. Frontiers in Endocrinology. 2019; 10: 61.
[25] Coksuer H, Akdemir Y, Ulas Barut M. Improved in vitro fertilization success and pregnancy outcome with autologous platelet-rich plasma treatment in unexplained infertility patients that had repeated implantation failure history. Gynecological Endocrinology. 2019; 35: 815–818.
[26] Mehrafza M, Kabodmehri R, Nikpouri Z, Pourseify G, Raoufi A, Eftekhari A, *et al.* Comparing the impact of autologous platelet-rich plasma and granulocyte colony stimulating factor on pregnancy outcome in patients with repeated implantation failure. Journal of Reproduction & Infertility. 2019; 20: 35–41.
[27] Sfakianoudis K, Simopoulou M, Grigoriadis S, Pantou A, Tsioulou P, Maziotis E, *et al.* Reactivating ovarian function through autologous platelet-rich plasma intraovarian infusion: pilot data on premature ovarian insufficiency, perimenopausal, menopausal, and poor responder women. Journal of Clinical Medicine. 2020; 9: 1809.
[28] Panda SR, Sachan S, Hota S. A systematic review evaluating the efficacy of intra-ovarian infusion of autologous platelet-rich plasma in patients with poor ovarian reserve or ovarian insufficiency. Cureus. 2020; 12: e12037.