JSTMU Journal of Shifa Tameer-e-Millat University

https://j.stmu.edu.pk

Open Access

CASE REPORT

Treatment of unexplained thin endometrium with autologous platelet-rich plasma in a frozen embryo transfer cycle

Sara Mahmood Qureshi[1], Salma Kafeel[2], Riffat Bibi[3], Naveed Iqbal[4]

[1] Clinical Embryologist, Salma Kafeel Medical Services, Blue Area, Islamabad, Pakistan
[2] Consultant Gynecologist, Salma Kafeel Medical Services, Blue Area, Islamabad, Pakistan
[3] Clinical Scientist, Salma Kafeel Medical Services, Blue Area, Islamabad, Pakistan
[4] Consultant Gynecologist, Salma Kafeel Medical Services, Blue Area, Islamabad, Pakistan

Author`s Contribution

[1] Manuscript writing, referencing and proof reading
[2] synthesis, planning and picture editing
[3] Planning and management of research

Article Info.

Conflict of interest: Nil
Funding Sources: Nil

Correspondence

Naveed Iqbal
naveediqbaldr@gmail.com

Cite this report as: *Qureshi SM, Kafeel S, Bibi R, Iqbal N. Treatment of unexplained thin endometrium with autologous platelet-rich plasma in a frozen embryo transfer cycle. JSTMU. 2019; 2(2):80-82.*

A B S T R A C T

Inadequate endometrial proliferation is a known cause of implantation failure in assisted reproductive technology cycles. It is generally agreed that >9 mm endometrial thickness is associated with higher implantation. Several strategies have been explored to enhance endometrial proliferation. However, the results are either poor, inconsistent or subject to safety concerns. A 34-year old woman presented with unexplained thin endometrium in successive frozen embryo transfer (FET) cycles. Autologous platelet-rich plasma (PRP) was infused in the uterine cavity on day 10 of second FET cycle enhancing endometrial thickness, which post-PRP infusion measured 10.9 mm. Blastocyst-stage embryos were transferred resulting in a successful pregnancy. Autologous intrauterine infusion of PRP positively impacts endometrial proliferation and implantation which is safe, low resource and minimally invasive.

Keywords: *Frozen Embryo Transfer, Thin Endometrium, platelet-rich plasma, endometrial thickness*

Introduction

Endometrium plays a critical role in the establishment and maintenance of a normal pregnancy. In humans, the endometrium becomes receptive to implantation six days following ovulation, when the embryo reaches the blastocyst stage.1 Implantation is a highly coordinated, complex event, between the intrauterine factors and the embryo, regulated by ovarian steroids, progesterone, and estrogen.2 Moreover, mediated by various molecular modulators such as growth factors and cytokines, functioning in a spatio-temporal manner thus, facilitating endometrial decidualization, blastocyst attachment, and invasion.1 Despite significant advances in Assisted Reproductive Technologies (ART), implantation failure due to inadequate endometrial receptivity is a major cause of failure in ART cycles.[1]

In clinical practice, ultrasound evaluation of the endometrial thickness is an important marker for endometrial receptivity. There is a general consensus that endometrial thickness of at least 7 mm (and preferably >9mm) favors higher implantation.[2] Over the years, several strategies have been implored to enhance endometrial thickness and quality such as extended high estrogen therapy, low dose aspirin, tocopherol, pentoxifylline, arginine, vaginal administration of sildenafil citrate, electroacupuncture, intrauterine perfusion of Granulocyte colony-stimulation factor (G-CSF)[3] and stem cell therapy.[2,4,5] However, the results have either been poor, unknown, inconsistent or subject to safety concerns.

Autologous platelet-rich plasma (PRP) is considered a safe alternative approach. Moreover, demonstrated to

stimulate mitogenesis and proliferation of the endometrial cells, in turn, activating endocrine-paracrine pathways facilitating endometrial remodeling, embryo maternal crosstalk therein promoting implantation and pregnancy.[1]

Here we present for the first time in Pakistan the utility of intrauterine infusion of autologous PRP in a case of unexplained thin endometrium during a frozen embryo transfer (FET) cycle, resulting in a successful pregnancy.

Case report

A 34-year old woman, married for 5 years presented at our clinic with unexplained infertility. The baseline hormonal profile revealed all parameters within normal limits.

Table 1: Baseline hormonal profile of the female partner

Hormonal Test	Result
Anti-Mullerian Hormone (AMH)	3.52 ng/mL
Day 3 Follicle Stimulating Hormone (FSH)	6.67 mIU/mL
Prolactin	25.7 ng/mL
Triiodothyronine (T3)	1.7 nmol/L
Thyroxine (T4)	8.1 µg/dL
Thyroid Stimulating Hormone (TSH)	1.68 µmIU/mL

Gynecologic findings revealed bilateral patent tubes, both ovaries normal in size and echotexture with right ovary measuring 3.4 by 2.5 cm and left ovary measuring 3.8 by 3.0 cm, respectively. Additionally, no ovarian mass or cyst was observed. The male partner was 35 years old with normozoospermia, reported no history of medical or surgical interventions. Screening tests of HEP B, C, HIV, and VDRL were normal for both partners. Intrauterine Insemination (IUI) cycle was proposed as the first line of treatment. Two attempts of IUI were undertaken both proving to be uneventful. In both IUI cycles, the measured endometrial thickness was >9 mm on day 11 of the menstrual cycle.

The couple was now recommended an in vitro fertilization (IVF) cycle. Standard long agonist protocol was followed.6 15 oocytes were collected, 8 fertilized normally following Intracytoplasmic sperm injection (ICSI). Day 3 embryo transfer was scheduled with three embryos of top quality, 7 10 cell grade 1 transferred successfully. The remaining 5 embryos of top quality were vitrified. The endometrial thickness prior to embryo transfer was 14.3 mm in the fresh IVF cycle. Two weeks following embryo transfer βHCG test revealed an unsuccessful pregnancy. Frozen embryo transfer (FET) cycle was advised to the couple. Preparation of endometrium as described previously by hormonal replacement therapy (HRT) protocol was initiated.6 In the first FET cycle due to insufficient endometrial response (<7mm), the cycle was abandoned. In the proceeding menstrual cycle, the patient was scheduled for the second FET cycle, using the same regime.

Table 2: Ultrasound and hormonal assays of the patient on day 10-11 of the menstrual cycle, during respective frozen embryo transfer cycles.

Parameter	First FET Cycle	Second FET Cycle
Endometrium Thickness	5.8 mm	3.5 mm
Estradiol level	113.2 pg/mL	103.2 pg/mL
Progesterone	<0.05 ng/mL	0.18 ng/mL
Luteinizing Hormone (LH)	9.80 mIU/mL	13.4 mIU/mL

On day 10 of the second FET cycle, due to inadequate endometrial response. Intrauterine autologous PRP was administered. PRP was prepared by drawing 10mL venous blood in an Ethylenediaminetetraacetic acid-coated tube and subjected to a single-step centrifugation process at 1200 rpm for 12 minutes. Following centrifugation, the overlaid plasma was isolated in a sterile tube for infusion. Approximately 5 ml of PRP was infused into the uterine cavity with an IUI catheter. Four days post-PRP administration the endometrium thickness measured 10.9 mm.

Three embryos of quality 7 cell Grade 1, 6 cell Grade 1 and 9 cell Grade 1 were thawed 72 hours after beginning vaginal progesterone (cycle day 12) and cultured till day 5. On day 5 embryos progressed to Blastocyst 3Ab, 3Bc and Morula stage, according to Gardner and Schoolcraft grading system 7 and were

transferred. Two weeks following embryo transfer serum βHCG was 1068 mIU/mL, a single intrauterine gestational sac was observed.

Discussion

On a cellular level, endometrial PRP in humans has been demonstrated to promote the migration of primary endometrial epithelial cells, endometrial stromal fibroblasts and mesenchymal stem cells (MSC). Additionally, the enhanced migration of bone marrow-derived MSC has also been identified, following the infusion of intrauterine PRP.8 Moreover, the high amounts of growth factors such as platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF) also anti-inflammatory cytokines such as IL-10, stimulates endometrial proliferation and tissue regeneration.[9]

Endometrial PRP infusion has been reported to improve fertility treatment outcomes in patients with a thin endometrium,[1,9] also with a history of recurrent implantation failure.[10] However, its utility concerning unexplained thin endometrium has not been previously reported. Here we report for the first time the use of intrauterine PRP infusion in a patient with an unexplained cause of thin endometrium and its beneficial effect on endometrial growth, resulting in a successful pregnancy. Autologous PRP is a relatively safe technique with minimal risk of disease transmission, immunological reaction, and cancers.[4] With respect to endometrial PRP, it is a low resource and minimally invasive procedure. Our case report highlights that intrauterine PRP infusion is a beneficial strategy to cope with cycle cancellation due to poor endometrial response in FET cycles and to enhance the treatment outcomes.

Conclusion

In our opinion, this is the first report of successful pregnancy utilizing endometrial PRP in a woman with unexplained thin endometrium despite acquiring adequate endometrial response in prior cycles. Our case report highlights, the beneficial impact of autologous endometrial PRP in order to enhance implantation.

References

1. Bos-Mikich A, Ferreira MO, de Oliveira R, Frantz N. Platelet-rich plasma or blood-derived products to improve endometrial receptivity? *J Assist Reprod Genet.* 2019; 36(4):613-20. DOI: https://doi.org/10.1007/s10815-018-1386-z
2. Lebovitz O, Orvieto R. Treating patients with "thin" endometrium–an ongoing challenge. *Gynecol Endocrinol*. 2014; 30(6):409-414. DOI: https://doi.org/10.3109/09513590.2014.906571
3. Gleicher N, Kim A, Michaeli T, Lee HJ, Shohat-Tal A, Lazzaroni E, et al. A pilot cohort study of granulocyte colony-stimulating factor in the treatment of unresponsive thin endometrium resistant to standard therapies. *Human Reproduction*. 2012; 28(1):172-177. DOI: https://doi.org/10.1093/humrep/des370
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. *Int J Clin Exp Med*. 2015; 8(1):1286-90.
5. Kunicki M, Lukaszuk K, Liss J, Skowrońska P, Szczyptańska J. Granulocyte colony stimulating factor treatment of resistant thin endometrium in women with frozen-thawed blastocyst transfer. *Syst Biol Reprod Med*. 2017; 63(1):49-57. DOI: https://doi.org/10.1080/19396368.2016.1251505
6. Wright KP, Guibert J, Weitzen S, Davy C, Fauque P, Olivennes F. Artificial versus stimulated cycles for endometrial preparation prior to frozen–thawed embryo transfer. *Reprod.* Biomed. Online. 2006; 13(3):321-325. DOI: https://doi.org/10.1016/S1472-6483(10)61434-4
7. The Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting. *Human Reproduction*. 2011; 26(6):1270-1283. DOI: https://doi.org/10.1093/humrep/der037
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. *J Assist Reprod Genet*. 2018; 35(5):757-770. DOI: https://doi.org/10.1007/s10815-018-1130-8
9. Chang Y, Li J, Wei L, Pang J, Chen J, Liang X. Autologous platelet-rich plasma infusion improves clinical pregnancy rate in frozen embryo transfer cycles for women with thin endometrium. *Medicine.* 2019; 98(3). DOI: 10.1097/MD.0000000000014062
10. Farimani M, Poorolajal J, Rabiee S, Bahmanzadeh M. Successful pregnancy and live birth after intrauterine administration of autologous platelet-rich plasma in a woman with recurrent implantation failure: A case report. *Int J Reprod Biomed*. 2017; 15(12):803-6.