شبكة المعلومات الجامعية

# بسم الله الرحمن الرحيم


HOSSAM MAGHRABY

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# التوثيق الالكتروني والميكروفيلم

HOSSAM MAGHRABY

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# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

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HOSSAM MAGHRABY

# Effect of intrauterine infusion of autologous platelet rich plasma in patients with refractory thin endometrium undergoing in vitro fertilization

Thesis

Submitted for partial fulfillment of Master degree
in Obstetrics and Gynecology


By

**Aya Mohsen Zaki**

M.B.B.Ch., 2014
Resident in Al-Agouza Police Hospital

Under Supervision of

**Prof. Hatem Hussein El-Gamal**

Professor of Obstetrics and Gynecology,
Faculty of Medicine, Ain Shams University

**Prof. Amany Ahmed Osman**

Professor of Clinical Pathology
Faculty of Medicine, Ain Shams University

**Prof. Mostafa Fouad Gomaa**

Professor of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

**Dr. Mohamed Mahmoud Salman**

Lecturer of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University



**Faculty of Medicine**
**Ain Shams University**
**2021**

# Acknowledgments

*First and foremost, I feel always indebted to* **Allah,** *the* ***Most Beneficent*** *and* ***Merciful*** *who gave me the strength to accomplish this work.*

*My deepest gratitude to* **Prof. Hatem Hussein El-Gamal,** *Professor of Obstetrics and Gynecology,, Faculty of Medicine, Ain Shams University, for his valuable guidance and expert supervision, in addition to his great deal of support and encouragement. I really have the honor to complete this work under his supervision.*

*I would like to express my great and deep appreciation and thanks to* **Prof. Amany Ahmed Osman,** *Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, and her patience in reviewing and correcting this work.*

*I must express my deepest thanks to* **Prof. Mostafa Fouad Gomaa,** *Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for guiding me throughout this work and for granting me much of his time. I greatly appreciate his efforts.*

*I can't forget to thank with all appreciation* **Dr. Mohamed Mahmoud Salman,** *Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, whom tirelessly and freely gave comments on various drafts of this piece of work regarding the ozone work.*

*Last but not least, I would like to thanks all* ***members of ART unit*** *and* ***Clinical Pathology Department****, for their positive cooperation and help in the Practical part of this work.*

*Special thanks to my* **Parents,** *my* **Husband** *and all my* **Family** *members for their continuous encouragement, enduring me and standing by me.*

*Aya Mohsen Zaki*

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# List of Abbreviations

| Abbr. | Full-term |
|---|---|
| **ACD-A** | **:** Acid citrate dextrose solution A |
| **AMH** | **:** Anti-Müllerian hormone |
| **APCs** | **:** Antigen-presenting cells |
| **ART** | **:** Assisted reproductive technology |
| **avb3** | **:** Alpha v/beta 3 integrin |
| **BMI** | **:** Body mass index |
| **cAMP** | **:** Cyclic adenosine monophosphate |
| **CAMs** | **:** Cellular Adhesion Molecules |
| **CD** | **:** Cluster of differentiation |
| **cGMP** | **:** Cyclic guanosine monophosphate |
| **CI** | **:** Confidence interval |
| **CL** | **:** Corpus luteum |
| **COX-2** | **:** Cyclooxygenase-2 |
| **CSF-1** | **:** Colony stimulating factor-1 |
| **CTGF** | **:** Connective tissue growth factor |
| **DCs** | **:** Dendritic cells |
| **DSCs** | **:** Decidual stromal fibroblast cells |
| **E2** | **:** Estradiol E2 |
| **ECM** | **:** Extracellular matrix |
| **EGF** | **:** Epidermal growth factor |
| **EMSCs** | **:** Endometrial mesenchymal stem cells |

**EMT** : Endometrial thickness
**ERA** : Endometrial receptivity array
**ESCs** : Endometrial stromal fibroblast cells
**ESR1** : Estrogen receptor alpha
**ET** : Embryo transfer
**EVCTs** : Extravillous cytotrophoblast cells
**FBC** : Full blood count
**FET** : Frozen embryo transfer
**FSH** : Follicle-stimulating hormone
**GAS1** : Growth Arrest Specific 1
**GFs** : Growth factors
**GM-CSF** : Granulocyte monocyte colony stimulating factor
**GnRH** : Gonadotropin releasing hormone
**GS** : Gestational sac
**hCG** : Human chorionic gonadotropin
**HGF** : Hepatocyte growth factor
**HLA** : Human leukocyte antigen
**HRT** : Hormone replacement therapy
**HSD17βII** : 17β-hydroxysteroid dehydrogenase-type 2
**ICM** : Inner cell mass
**ICSI** : Intracytoplasmic sperm injection
**IGFBP-1** : Insulin like growth factor binding protein
**IL** : Interleukin
**IM** : Intramuscular
**IQR** : Interquartile range

**IR** : Implantation rate
**IS** : Implantation sites
**IVF** : In vitro fertilization
**LH** : Luteinizing hormone
**LIF-R** : LIF receptor
**L-PRP** : Leukocyte PRP
**MBSCs** : Bone marrow stem cells
**MMP-3** : Metalloproteinase-3
**MRI** : Magnetic resonance imaging
**MS** : Mid-secretory
**MUC-1** : Mucin-1
**NAD** : Nicotinamide adenine dinucleotide
**NMES** : Neuromuscular electrical stimulation
**NO** : Nitric oxide
**OCP** : Oral contraceptive pill
**OPU** : Ovum pick up
**P4** : Progesterone
**PDGF** : Platelet-derived growth factor
**pET** : Personalized embryo transfer
**PGE2** : Prostaglandin E2
**PGT** : Pre- implantation genetic testing
**PPP** : Platelet poor plasma
**P-PRP** : Leukocyte-poor or pure PRP
**PR** : Progesterone receptor
**PRP** : Platelet rich plasma

**REA** : Repressor of E2 activity
**RIF** : Recurrent implantation failure
**RPM** : Revolution per minute
**RR** : Risk ratio
**S.C** : Sub cutaneous
**SD** : Standard deviation
**sFLT1** : FMS-like tyrosine kinase 1
**SMA** : Smooth muscle actin
**SVF** : Stromal vascular fraction
**TE** : Trophectoderm
**TGF-β** : Transforming growth factor-beta
**TNF-α** : Tumor necrosis factor-alfa
**Treg T** : Regulatory T
**TSH** : Thyroid stimulating hormone
**TV U/S** : Transvaginal ultrasound
**uNK** : Uterine natural killers
**VEGF** : Vascular endothelial growth factor
**WOI** : Window of implantation
**ZP** : Zona pellucida

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## ABSTRACT

**Background:** Since the first introduction of (IVF-ET), the technology has evolved rapidly, and the pregnancy rate with it has significantly increased. However, treatment of refractory thin endometrium during IVF is a relatively challenging problem, considering that optimal endometrium thickness is one of critical factors for successful implantation and pregnancy. Autologous intrauterine PRP infusion is an adjuvant therapeutic alternative for enhancing the EMT and Echo pattern. It was settled that PRP could expand EMT and improve pregnancy outcomes with its high content of growth factors and cytokines in addition to its role in regulation of immunological interaction between embryo and endometrium.

**Aim of the work:** The aim of the study is to evaluate the effect of autologous PRP in improving the ongoing pregnancy rate in patients with refractory thin endometrium undergoing IVF.

**Patients and Methods:** After explanation of the nature of the study, ethical committee approval and written consents would be obtained from patients, this prospective single arm clinical trial was performed on a total number of 85 infertile women with a refractory thin endometrium, characterized by atrophy with endometrial interface measurements below 7 mm by ultrasound on the day of hCG injection in fresh ET cycle, which does not respond to standard medical therapies after more than 2 cycles of previous medical therapy,6 cases were excluded (2 cases declined to participate and 4 cases withdrawn from the study ) and 13 cases were cancelled (6 cases had poor ovarian response, 3 cases had poor quality embryos,1case had degenerated egg, and 3 cases were COVID 19 positive ), who were candidates for IVF cycle at the ART Unit of Ain Shams University Maternity Hospital in a period from January 2021 and August 2021 with the same inclusion and exclusion criteria using long luteal phase GnRHa protocol.

**Results:** There was statistically significant increase in EMT "mm" and enhancement of endometrial pattern after intrauterine PRP infusion with p- value < 0.001 for both of them. Regarding EMT ((6.19±0.34) mean EMT on D1 ( day of hCG injection in fresh IVF cycles & PRP infusion vs, (7.75±0.48) mean EMT on D2 ( the day of OR ), and (8.97±0.65) on D3 ( day of ET)) and according to endometrial patterns on D1 (15.2%, 47% and 37.9%) of patients had patterns A, B and C, respectively vs, D2 (47%,45.5% and 7.6%) of patients had patterns A, B and C, respectively, and D3 (51.5% and 48.5% ) of patients had patterns A, B and C, respectively. Regarding risk factors affecting chemical pregnancy ; multivariate analysis of current study revealed that EMT (mm) and endometrial pattern at D2 and D3 were the best independent predictors of chemical pregnancy, with statistically significant difference between chemical pregnancy (positive and negative) according to EMT and pattern as [OR (C.I.95%), p-value] were [2.452 (0.674- 8.924) 0.037] and [2.869 (0.789-10.441), p-value 0.043] respectively. Regarding outcomes of embryo transferred cycles; statistical analysis of current results showed that there were high positive pregnancy results (implantation, chemical, clinical and ongoing pregnancy and miscarriage rates) as a result of intrauterine PRP infusion.

**Conclusion:** As evident from the current study, Intrauterine PRP infusion as an adjuvant on day of hCG injection, significantly improved EMT and endometrial pattern distribution at the days of OR and ET of infertile women with refractory thin endometrium. EMT (mm) and endometrial pattern at the day of OR and at the day of ET were the most significant independent predictors of chemical pregnancy. Autologous intrauterine PRP infusion had some aspects to restore the damaged endometrium, not only increasing the EMT but also enhancing the endometrial vascularity & receptivity. Implantation rate, chemical, clinical and ongoing pregnancy rates were significantly improved and miscarriage rate was significantly decreased as a result of intrauterine PRP infusion.



**Keywords:** Platelet rich plasma (PRP), Embryo transfer (ET), Endometrial thickness (EMT), In vitro fertilization (IVF), Human chorionic gonadotropin (hCG), Assisted Reproductive Technique (ART), Gonadotropins releasing hormone agonist (GnRHa).