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Original Research Article

## Intrauterine platelet rich plasma versus injection G-CSF for treatment of thin endometrium in infertility

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### ABSTRACT

**Background:** For success in IVF treatment, it is essential that the patient has a responsive endometrium together with many other factors. In spite of numerous treatments available today for growth of endometrium, there is lack of any ideal drug or protocol for increasing endometrial thickness. The study is an attempt to evaluate the role of two drugs for increasing endometrial growth before embryos transfers.

**Methods:** This study is a retrospective cohort study including 50 patients with previously diagnosed as thin endometrium patients who may or may not have failed previous cycles of IVF. Patients were randomly divided into two groups. First group-Group A (n=25) are patients randomly selected to undergo intrauterine PRP instillation for increase in endometrial thickness before embryo transfer. Second group-Group B (n=25) are randomly selected from a retrospective cohort of thin endometrium to take injection GCSF as intrauterine infusion (total dose 300mcg) on day of trigger or day 11 of cycle followed by 60 units subcutaneously after embryo transfer. The difference in endometrial thickness during transfer and the pregnancy outcomes were compared.

**Results:** Injection GCSF was found to be more effective than intrauterine PRP in improving endometrial thickness in patients with thin endometrium with a p-value of <0.0001. It was found that the chemical and clinical pregnancy rates were comparable as the p values were 0.77 and 0.37 respectively and hence statistically not significant. Although patients given injection GCSF had a slightly higher clinical pregnancy rate (44%) as compared to patients given intrauterine PRP which was 28%. All other variables were comparable.

**Conclusions:** In the study it was proven that injection GCSF, is more effective for the treatment of thin endometrium patients as compared to intrauterine PRP infusion. Though the clinical and chemical pregnancy rates were comparable, a higher percentage of women were clinically pregnant in the group given injection GCSF. Intrauterine PRP can also be a good alternative for thin endometrium. More studies and RCTS are needed for comparison to prove the effectiveness of these drugs for treatment of thin endometrium.

**Keywords:** Clinical pregnancy rates, Chemical pregnancy rates, Endometrial receptivity, Injection GCSF, Intrauterine PRP, Thin endometrium

### INTRODUCTION

Implantation is a process dependent on three main factors good quality embryos, receptive endometrium with good

endometrial thickness and the endometrium-embryonal cross dialogue. Hence implantation of a mature embryo into receptive endometrium is key to build a successful pregnancy.<sup>1</sup> Despite many advances in the past decade for

betterment of the thin unresponsive endometrium, implantation failure still continues to befuddle the IVF doctor. Endometrial thickness in turn is an important component of endometrial receptivity.<sup>2</sup> Endometrium below 7mm in thickness is widely considered sub-optimal for transfer and associated with reduced pregnancy rates.<sup>3</sup>

Successful implantation requires a complex molecular process including endometrial integrins, extracellular matrix molecules, adhesion molecules, growth factors and ion channels.<sup>1</sup>

Various strategies have already been developed for tackling thin endometrium including extended use of exogenous estrogen, low dose aspirin, vitamin E (tocopherol), vaginal sildenafil citrate, and electroacupuncture, pentoxifylline and also endometrial scratch before IVF cycles.<sup>4-9</sup> However a number of women with thin endometrium do not conceive despite these remedies.

Intrauterine perfusion of platelet rich plasma was described by Chang et al for patients of thin endometrium.<sup>10</sup> The effectiveness of endometrial improvement has also been described by Zadehmodares et al.<sup>11</sup> The mechanism for increase of thickness of the endometrium by PRP, is that PRP has many cytokines and growth factors including transforming growth factor (TGF- $\beta$ ), platelet derived growth factor (PDGF), interleukin -8 (IL-8) and many factors that promotes cellular migration, proliferation and differentiation processes. Nowadays, PRP has been widely used in different clinical scenarios such as orthopedics, ophthalmology and wound healing.<sup>12</sup>

On the other hand presence of granulocyte colony stimulating factor (GCSF) receptors in placental tissues, trophoblastic cells and endometrial cells indicate the importance of this cytokine in implantation.<sup>13-15</sup> The use of GCSF in assisted reproductive technology (ART) has been reported by many studies to improve the inadequacy of the endometrium.<sup>16,17</sup> It has also been reported that intrauterine or systemic administration of GCSF can improve pregnancy rates in patients of Recurrent Implantation Failure (RIF).

There are very few studies that compare the efficacy of inj GCSF and intrauterine PRP in ART cycles. Thus the present study aims to compare these drugs in the distressing condition of thin endometrium causing infertility in various patients.

## METHODS

The present retrospective cohort study was conducted at Nadkarni hospital and test tube baby centre Killa Pardi And 21<sup>st</sup> century hospital and test tube baby centre, Surat, Gujarat, (a private medical training centre), India from August 2018 to May 2019.

Fifty patients diagnosed with thin endometrium due to previous endometrial studies were included in this study.

### Inclusion criteria

- All women attending the OPD for infertility willing to participate in the following study were included
- All married women >24 years and <45 years, anxious to conceive
- Women diagnosed with condition of thin endometrium in previous cycles
- Women with/ without undergone previous IVF cycles
- All women without active debilitating disorders.

### Exclusion criteria

- Women not willing to participate in the study.
- Women suffering from infertility due to factors other than thin endometrium
- Active debilitating disorders like acute PID or other infections.

All the instructions regarding the study were given to the patients regarding regimens of administration of systemic and intrauterine injection GCSF and intrauterine PRP. 25 patients were randomly given Intrauterine GCSF 300mcg on day of trigger or in FET cycles on day 11 or 14 followed by subcutaneous GCSF 60 U daily for 5 days after ET and 25 patients had been given intrauterine PRP on day 11 of menstrual cycle. Based on the retrospective nature of the study, the medical records of each patient were recorded. All the data can be compared between the two groups.

All participants underwent basal hormonal screening, ultrasonography, and hysteroscopy. The pituitary was suppressed using gonadotropin releasing hormone (GnRH) agonist or antagonist. In patients undergoing GnRH agonist, triptorelin 0.05mg subcutaneous daily was administered from the 21<sup>st</sup> day of previous cycle. In GnRH antagonist cycles, 0.25mg was started daily when the leading follicle reached 14mm in diameter. Ovarian stimulation was initiated with recombinant FSH (rFSH) and human menotroin gonadotropin (uHMG), and the daily dose of either rFSH or human menopausal gonadotropin adjusted according to the ovarian response.

Follicle development was monitored using transvaginal ultrasonography and estradiol measurements. Oocyte pick-up was done 36 to 38hours after triggering final oocyte maturation with human chorionic gonadotropin (rhCG). After denudation of oocyte-cumulus complexes, ICSI was performed. In fresh cycles, three to six days following ICSI procedures, up to three good and top quality embryos were transferred. Luteal phase was supported by 400mg intravaginal twice a day and 2.0mg oral estrogen thrice a day. In frozen embryo transfer (FET) cycles, endometrial preparation was started with 6mg/day oral estradiol valerate and tablet aspirin 75mcg

daily. Progesterone intravaginal 400mg was started when a triple-line endometrial pattern and approximately thickness of 7 mm on ultra-sound were seen. Embryos were transferred three to five days later, according to developmental stage of the embryos.

### **Protocol**

#### **Group A**

- Thin endometrium criteria 11<sup>th</sup> day - endometrium less than 7 mm
- Platelet rich plasma (PRP)
- Two days before embryo transfer, peripheral venous blood (15ML) was drawn into 20ml syringe containing 1.5ml anticoagulant solution- Sodium citrate
- Manufacturer's instruction was followed for preparing PRP (Platelet rich plasma) and this tube was centrifuged at 1500rpm for 10 minutes
- The upper plasma layer and the buffy coat were transferred to a fresh tube which in turn was centrifuged at 2500 rpm for 5-8 minutes
- The supernatant was decanted leaving approximately 1 ml of plasma and then resuspension of the pellet in plasma
- Thus approximately 1.5ml-2ml of PRP was prepared.
- This PRP is then instilled intravaginally 2 days prior to scheduled embryo transfer or on day 11 of cycle.

#### **Group B**

- Thin endometrium criteria 11<sup>th</sup> day - Endometrium less than 7mm
- Injection - granulocyte colony stimulating factor intrauterine 300 mcg on day of trigger or day 11 of FET followed by injection GCSF for 5 days subcutaneous after ET
- Both these group of patients were then evaluated for endometrial thickness Before and after embryo transfer followed by any complications following transfer and chemical pregnancy (UPT positive) and subsequently clinical pregnancy which was 1<sup>st</sup> βhcg value more than 100 or positive after 15 days of embryo transfer and 2<sup>nd</sup> βhcg after 20 days of embryo transfer more than double the previous value and confirmed by transvaginal ultrasonography and fetal heart beats.

### **Outcome variables**

#### **Primary variables**

- Endometrium thickness before embryo transfer
- Endometrium thickness after embryo transfer
- Number of embryos transferred
- Number of blastocyst transferred
- Complications
- Chemical pregnancy rate

- Clinical pregnancy rate.

#### **Secondary variables**

- Age
- BMI(kg/m<sup>2</sup>)
- Day 2 LH levels (mIU/ml)
- Day2 FSH levels (mIU/ml)
- Serum AMH (ng/ml)
- Type of stimulation- agonist
- Antagonist
- Fresh/frozen cycles
- Factor for thin endometrium.

#### **Statistical analysis**

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram and, pie-diagram.

All Quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-wilk test was also conducted to assess normal distribution and p-value of >0.05 was considered as normal distribution.

For normally distributed quantitative parameters the mean values were compared between study groups using Independent sample t-test (2 groups). For non normally distributed quantitative parameters, medians and interquartile range (IQR) were compared between study groups using Mann Whitney u test (2 groups).

Categorical outcomes were compared between study groups using Chi square test/Fisher's Exact test (If the overall sample size was <20 or if the expected number in any one of the cells is <5, Fisher's exact test was used).

p value <0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.(1)

IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

### **RESULTS**

Sample sizes of 50 subjects were included in the final analysis.

Both the groups had 25 women each hence the distribution was 50% in each group. This study shows a distribution of 50% of patients treated with injection GCSF and 50% of the patients treated with intrauterine Platelet Rich Plasma for previously diagnosed thin endometrium. Thin endometrium may be the primary cause of infertility in these patients.

**Table 1: Comparison of mean of secondary variables between the study groups (N=50).**

Parameter	Study group		p value
	Platelet rich plasma (PRP) (N=25) (Mean±SD)	Granulocyte colony stimulating factor (GCSF) (N=25) (Mean±SD)	
Age	32.04±5.66 years	32.88±4.94	0.579
BMI	23.78±4.03 kg/m <sup>2</sup>	24.14±4.35	0.768
D2 LH (Miu/ml)	3.8 (2.2, 4.7)	3.08 (2.09, 3.98)	0.256
D2 FSH (Miu/ml)	5.8 (2.45, 6.95)	4.9 (3.9, 6.045)	0.705
SR AMH (ng/ml)	2.16 (1.46, 3.205)	1.89 (1.06, 2.27)	0.107
Fresh cycles	14 (64.35%)	17 (68%)	0.477
FET cycles	11 (35.65%)	8 (32%)	0.037

Table 1 shows that the mean age in both the groups A and group B IS 32.04±5.66 years and 32.88±4.94 years respectively and the p-value is 0.579 which is not statistically important hence it can be said that both the groups have age as a parameter that is comparable. Hence age does not act as a compounding factor in the comparison in both the groups. The mean BMI in both the groups A and group B IS 23.78±4.03 and 24.14±4.35 respectively and the p-value is 0.768 which is not statistically significant hence it can be safely said that both the groups a comparable BMI. Hence BMI does not act as a compounding factor in the comparison in both the groups.

Day 2 luteinising hormone is measured in Miu/ml and is a good indicator of down regulated cycles. The mean values for both groups A and B is 3.8 and 3.08 respectively. The p-value is 0.256 and hence is statistically not significant. Hence groups were comparable. Day 2 serum follicle stimulating hormone is measured in Miu/ml and is a good indicator of the status of hypo thalamo-pituitary axis. The mean values for both groups A and B is 5.8 and 4.9 respectively. The p - value is 0.705 and hence is statistically not significant. Hence groups were comparable. Serum Anti-Mullerian hormone is measured in ng/ml and is a good indicator of ovarian reserve. The mean values for both groups A and B is 2.16 and 1.89 respectively. The p - value is 0.107 and hence is statistically not significant. Hence the variable in both groups were comparable. The groups A and B were also distributed and evaluated according to fresh and frozen cycles.

The numbers of fresh cycles were 14 out of 25 in group given intrauterine platelet rich plasma and 17 out of 25 cycles were fresh cycles in group given injection GCSF. The p-value is 0.477 hence not statistically significant and thus comparable in both groups. The groups A and B were also distributed and evaluated according to fresh and frozen cycles. The numbers of frozen cycles were 11 out of 25 in group given intrauterine platelet rich plasma and 8 out of 25 cycles were fresh cycles in group given injection GCSF. The p- value is 0.037 hence not

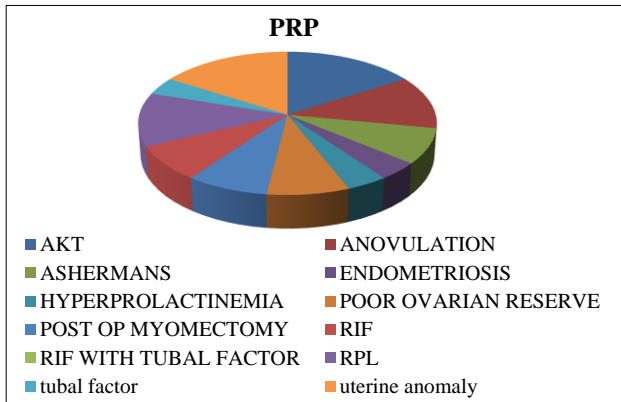
statistically significant and thus comparable in both groups.

**Table 2: Comparison of factor for thin endometrium between the study group (N=50).**

Factor for thin endo	Study group	
	Platelet rich plasma (PRP) (N=25)	Granulocyte colony stimulating factor (GCSF) (N=25)
AKT	4 (16%)	3 (12%)
Anovulation	3 (12%)	1 (4%)
Ashermanns syndrome	2 (8%)	2 (8%)
Endometriosis	1 (4%)	0 (0%)
Hyperprolactinemia	1 (4%)	0 (0%)
Poor ovarian reserve	2 (8%)	5 (20%)
Post op myomectomy	2 (8%)	3 (12%)
RIF	2 (8%)	3 (12%)
RIF with tubal factor	0 (0%)	1 (4%)
RPL	3 (12%)	2 (8%)
Tubal factor	1 (4%)	1 (4%)
uterine anomaly	4 (16%)	4 (16%)

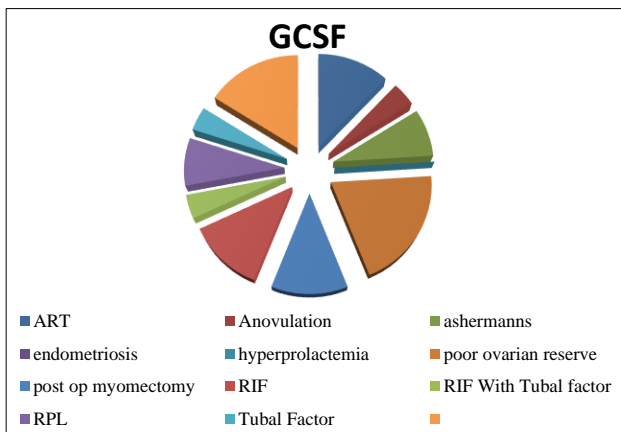
Table 2 shows the distribution of factors of infertility and possibly thin endometrium in both the group of patients.the most frequent factor for thin endometrium is AKT-or patients on anti-kochs treatment followed by uterine anomalies. Similarly in group given inj GCSF, the factor that frequently recurs is uterine anomalies and poor ovarian reserve. The distribution of various other factors have been discussed here like tubal factor, RIF And RPL And endometriosis and ashermanns syndrome which are commonly associated with thin endometrium. Both the groups have similar distribution of factors. The distributions of factors associated with thin endometrium in these patients with infertility are demonstrated in the pie chart. The factors involved are patients who were treated for tuberculosis (ART), anovulatory cycles, Ashermanns syndrome, endometriosis, tubal factor, recurrent pregnancy loss etc.

Both the groups suffered from the similar distribution of these variables (Figure 1, Figure 2).



\* No statistical test was applied-due to 0 subjects in the cell

**Figure 1: Distribution of factors of infertility in group given intrauterine PRP for thin endometrium.**



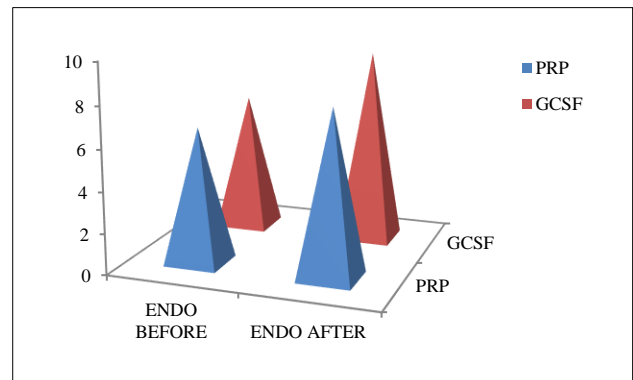
**Figure 2: Distribution of factors of infertility in group given Injection GCSF for thin endometrium.**

Both the groups either underwent antagonist protocol or long agonist protocol. It turned out that the women given antagonist and long agonist protocols were same in number in both groups hence this variable was comparable. These groups had no relevant complications during the stimulation. Only 1 patient had an episode of ovarian hyperstimulation syndrome in group B undergoing the antagonist cycle. The cause of OHSS was polycystic ovarian disease.

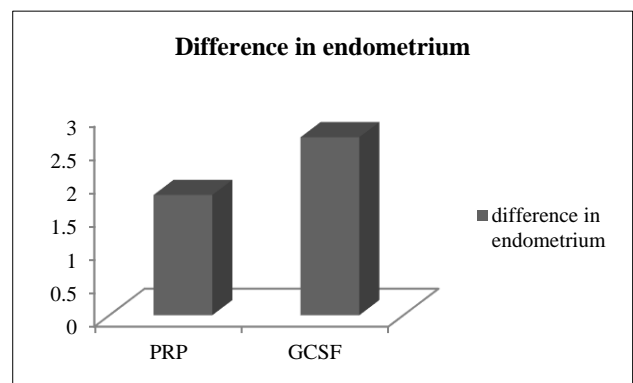
The number of grade A embryos transferred In Group A and Group B are compared in this study. The distribution shows that 1 embryo was transferred on day 3 in 2 women in group A and 4 women in group B, while 2 day 3 embryos were transferred in 16 women in group A and 17 women in group B. 7 Women in group A were transferred with 3 grade 1 embryos while 4 women in group B. The p-value was 0.469 hence statistically not significant hence the parameter was comparable in both the groups.

The number of GRADE 1AA day 6 blastocyst transferred in Group A and Group B were also compared in this study. The distribution shows that 1 blastocyst was transferred on day 5-6 in 17 women in group A and 13 women in group B, while day 6 blastocysts were transferred in 2 women in group A and 3 women in group B. The p-value was 0.301 hence statistically not significant hence the parameter was comparable in both the groups.

In a comparative study of endometrium before embryo transfer and after administration of drugs, in Group A endometrium before administration of intrauterine PRP is  $6.57 \pm$  in group B  $0.63$  which is comparable to group B and after 48 hours of administration of injection GCSF is  $8.04 \pm 1.13$ . The endometrium before administration of injection GCSF is  $6.73 \pm 0.41$  which is comparable to group A and after 48 hours of administration the mean endometrial thickness became  $9.4 \pm 0.71$ , which in comparison to Group A is statistically significant with p value is  $< 0.0001$ .



**Figure 3: Comparison for endometrium before and after intrauterine PRP and Inj G-CSF.**



**Figure 4: Graph representing difference in endometrium in both the drugs.**

The mean of the endometrial thickness before and after are compared in both the groups with injection GCSF showing higher increase in endometrial thickness than intrauterine PRP after 48 hours of administration. This could be demonstrable through the p value of the

differences in endometrium over 48 hours which was 0.0001 and was statistically significant (Table 3).

The graph demonstrates a higher increase in endometrium in group B though it is statically significant and it demonstrates the difference in the thickness of endometrium of both the groups of 48 hours of administration of the respective drugs. The p value is 0.0001 which is statically significant (Figure 3).

Figure 4 shows the difference in the endometrium after 48 hours of giving intrauterine PRP in one group and injection GCSF in the other group.

The difference of endometrium after 48 hours of administration of intrauterine Platelet rich plasma was  $1.804 \pm 0.839$  and that of Group B that is administration of injection GCSF is  $2.67 \pm 0.546$  which on comparison was statistically significant (Figure 4).

**Table 3: Descriptive analysis of endometrium before PRP (mm), endo after 48 hrs of PRP (mm) and injection GCSF before and after 48 hrs in study population (N=25).**

Parameter	Mean±SD	Median	Minimum	Maximum	95% C. I	
					Lower	Upper
Endometrium before PRP (mm)	6.57±0.63	6.80	5.20	7.2	6.24	7.37
Endometrium before Inj GCSF	6.73±0.41	6.90	5.40	7.00	6.56	6.90
P value- 0.1741						
Endometrium after 48 hours of PRP (mm)	8.04±1.13	7.80	7.00	12.70	7.53	8.35
Endometrium after inj GCSF 48 hours	9.4±0.71	8.80	7.00	11.60	8.31	9.9
P value <0.0001						
Endometrium diff PRP after ET	1.804±0.839	2	0.5	3.8	1.37	2.23
Endometrium diff GCSF after ET	2.67±0.546	2.5	0.7	3	1.55	2.1
P value- <0.0001						

**Table 4: Comparison of chemical pregnancy between the study group (N=50).**

Chemical pregnancy	Study group		Chi square	p-value
	Platelet rich plasma (PRP)	Granulocyte colony stimulating factor (GCSF)		
0	14 (56%)	12 (48%)	0.080	0.777
1	11 (44%)	13 (52%)		
<b>Clinical pregnancy</b>				
0	18 (72%)	14 (56%)	0.781	0.3768
1	7 (28%)	11 (44%)		

The chemical pregnancy rates were compared here in Table 4. Chemical pregnancy means that only the  $\beta$  HCG levels are raised and there is no evidence of clinical pregnancy as yet and it may or may not result in clinical pregnancy. In group A patients administered with intrauterine PRP showed  $\beta$ HCG positive in 11 patients out of 25. In group B where patients were administered injection GCSF 13 out of 25 showed  $\beta$ HCG positive. (ectopic as well as missed abortions are included in chemical pregnancy but not clinical pregnancy) . The above table shows that in the group stimulated with intrauterine PRP 7 OUT of 25 showed clinical pregnancy which meant the transvaginal ultrasonography showed evidence of gestational sac, a fetal pole and cardiac activity. While in group B Where patients were stimulated with injection GCSF showed a clinical pregnancy rate of 11 out of 25 that is 44% which is evidently higher than in group given intrauterine PRP hence proving its effectiveness over intrauterine PRP for improving outcomes in thin endometrium patients. It was

found that the chemical and clinical pregnancy rates the p values were 0.77 and 0.37 respectively and hence statistically not significant (Table 4).

**DISCUSSION**

Many researchers have found that the chances of pregnancy reduces if the endometrium was 7mm or less.<sup>3</sup> Another treatments such as low dose aspirin and vaginal sildenafil increase blood supply of the uterus rather than increase the endometrial thickness.<sup>18,19</sup> In study injection GCSF intravaginally followed by subcutaneous route has proven to be more efficacious compared to intrauterine PRP for improvement of endometrial thickness in patients diagnosed with thin endometrium. However the chemical and clinical pregnancy rates do not differ much. GCSF has been administered by subcutaneous and the intrauterine route. However which delivery method is superior is still debatable and remains to be determined.

In another study it was reported that patients with a good response to ovarian stimulation cycles had shown high levels of G-CSF in blood and follicular fluid compared to patients who had low ovulation stimulation response. Also her pregnancy rate in the first group was 33.5% whereas there was no pregnancy in the other group. Also GCSF plays a part in the implantation window due to its presence in the endometrium during implantation.<sup>20</sup> Due to the action of macrophages one may debate that GM-CSF may have better prognosis for endometrial thickness.<sup>21</sup> Local GCSF significantly decreases CD16 And CD56 and it also increases LIF (Leukemia inhibiting factor), as a result of which pregnancy rates may improve.

Finally it is also important to point out the limitation of the study. This study is non- randomized and with a small study group. Our main observation was the effectiveness of injection GCSF over intrauterine PRP. But this conclusion however needs to be confirmed by larger prospective RCTS. Hence further trials and researches are needed to prove the foresaid efficacy.

## CONCLUSION

Through the analysis done in this study it becomes evidently clear that injection GCSF is superior in its action as compared to intrauterine Platelet Rich Plasma in increasing the endometrial thickness in patients diagnosed as thin endometrium for infertility. Although the other variables were comparable, the chemical and clinical pregnancy rates when compared showed a slightly higher effect of injection GCSF over intrauterine PRP as the clinical and chemical pregnancy rates, though not statistically significant, were slightly higher than that of group given intrauterine PRP.

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## REFERENCES

- Davidson LM, Coward K. Molecular mechanisms of membrane interaction at implantation. *Birth Defects Res C Embryo Today.* 2016;108:19-32.
- Cakmak H, Taylor HS. Implantation failure: molecular mechanisms and clinical treatment. *Hum Reprod Update.* 2011;17:242-53.
- Check JH, Nowroozi K, Choe J, Dietterich C. Influence of endometrial thickness and echo patterns on pregnancy rates during in vitro fertilization. *Fertil Steril.* 1991;56:1173-5.
- Chen MJ, Yang JH, Peng FH, Chen SU, Ho HN, Yang YS. Extended estrogen administration for women with thin endometrium in frozen-thawed in-vitro fertilization programs. *J Assist Reprod Genet.* 2006;23:337-42.
- Khairy M, Banerjee K, El-Toukhy T, Coomarasamy A, Khalaf Y. Aspirin in women undergoing in vitro fertilization treatment: a systematic review and meta-analysis. *Fertil Steril.* 2007;88:822-31.
- Takasaki A, Tamura H, Miwa I, Taketani T, Shimamura K, Sugino N. Endometrial growth and uterine blood flow: a pilot study for improving endometrial thickness in the patients with a thin endometrium. *Fertil Steril.* 2010;93:1851-8.
- Sher G, Fisch JD. Effect of vaginal sildenafil on the outcome of in vitro fertilization (IVF) after multiple IVF failures attributed to poor endometrial development. *Fertil Steril.* 2002;78:1073-6.
- Ho M, Huang LC, Chang YY, Chen HY, Chang WC, Yang TC, Tsai HD. Electroacupuncture reduces uterine artery blood flow impedance in infertile women. *Taiwan J Obstet Gynecol.* 2009;48:148-51.
- Potdar N, Gelbaya T, Nardo LG. Endometrial injury to overcome recurrent embryo implantation failure: a systematic review and meta-analysis. *Reprod Biomed Online.* 2012;25(6):561-71.
- 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.
- Zadehmodarres S, Salehpour S, Saharkhiz N, Nazari L. Treatment of thin endometrium with autologous platelet-rich plasma: a pilot study. *JBRA Assist Reprod.* 2017;21(1):54-6.
- Dhillon RS, Schwarz EM, Maloney MD. Platelet-rich plasma therapy - future or trend? *Arthritis Res Ther.* 2012;14:219.
- Rahmati M, Petitbarat M, Dubanchet S, Bensussan A, Chaouat G, Ledee N. Granulocyte-colony stimulating factor related pathways tested on an endometrial ex-vivo model. *PLoS One.* 2014;9(9):e102286.
- Uzumaki H, Okabe T, Sasaki N, Hagiwara K, Takaku F, Tobita M, et al. Identification and characterization of receptors for granulocyte colony-stimulating factor on human placenta and trophoblastic cells. *Proc Natl Acad Sci USA.* 1989;86(23):9323-6.
- Saito S, Fukunaga R, Ichijo M, Nagata S. Expression of granulocyte colony-stimulating factor and its receptor at the fetomaternal interface in murine and human pregnancy. *Growth Factors.* 1994;10 (2):135-43.
- Barad DH, Yu Y, Kushnir VA, Shohat-Tal A, Lazzaroni E, Lee HJ, et al. A randomized clinical trial of endometrial perfusion with granulocyte colony-stimulating factor in vitro fertilization

- cycles: impact on endometrial thickness and clinical pregnancy rates. *Fertil Steril.* 2014;101(3):710-5.
17. Li Y, Pan P, Chen X, Li L, Li Y, Yang D. Granulocyte colony-stimulating factor administration for infertile women with thin endometrium in frozen embryo transfer program. *Reprod Sci.* 2014;21(3):381-5.
  18. Weckstein LN, Jacobson A, Galen D, Hampton K, Hammel J. Low-dose aspirin for oocyte donation recipients with a thin endometrium: prospective, randomized study. *Fertil Steril.* 1997;68:927-30.
  19. Sher G, Fisch JD. Effect of vaginal sildenafil on the outcome of in vitro fertilization (IVF) after multiple IVF failures attributed to poor endometrial development. *Fertil Steril.* 2002;78:1073-6.
  20. Salmassi A, Schmutzler AG, Schaefer S, Koch K, Hedderich J, Jonat W, et al. Is granulocyte colony-stimulating factor level predictive for human IVF outcome? *Hum Reprod.* 2005;20:2434-40.
  21. Gleicher N, Kim A, Michaeli T, Lee H, 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. *Hum Reprod.* 2013;28:172-7.

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