Autologous Platelet-Rich Plasma (PRP) Treatment To Optimize Endometrial Thickness

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Abstract- The endometrium plays an important role in the success of a pregnancy. There have been many clinical treatments that have been tried to increase endometrial thickness. These include hormone replacement, growth hormone and aspirin. However, they face numerous difficulties. The platelet-rich plasma method (PRP), was therefore considered. Infertile women suffering from recurrent implantation loss (RIF) or thin endometrium have been treated with intrauterine autologous plasma (PRP). Twelve patients with infertility between the ages of 25 and 40 were chosen for PRP treatment. The data suggests that PRP treatment may improve endometrial thickness as well as receptivity. The study concluded that PRP is effective in increasing endometrium thickness, which can lead to clinical pregnancy.

Index Terms- Platelet-rich plasma (PRP); Thin endometrium; Recurrent implantation failure (RIF)

I. INTRODUCTION

Despite the many advances made in recent years, assisted reproduction techniques (ARTs) still have a low success rate. This shows the need to explore other options for ART cycles. A receptive and functional endometrium are essential for successful implantation. This is also required to ensure synchronized interactions between blastocyst, endometrium and blastocyst. There are many factors that can prevent normal implantation and pregnancy. Women's sperm count and pattern play a significant role in getting pregnant. The minimum endometrial thickness should not exceed 7 mm at the end of the follicular stage. Numerous studies have shown that a sub-optimal level of endometrium can prevent a woman from conceiving [2]. Numerous studies have shown that PRP can be used to increase endometrial growth in patients with thin ends. The use of autologous PRP is now being used in reproductive medicine. Numerous studies on autologous PRP have shown positive results for women suffering from thin endometrium or recurrent implantation failure [3].

There are many options for treating thin endometrium, including exogenous estrogen, low-dose aspirin and vitamin E. The blood levels of growth factors are much higher than normal. The administration of autologous PRP is safe and does not carry any transmissible diseases such as HIV/hepatitis [4].

A high level of platelet growth factors is found in autologous platelet rich plasma (A-PRP). PRP contains a large number of growth factors in biologically defined ratios. This distinguishes it from the recombinant factor. PRP contains platelet and growth factors in levels that range from 80% to 98% [5].

Thin endometrium is still a problem. Therefore, the purpose of this study was to assess the role of autologous plasma platelet-rich Plasma treatment in increasing thickness and receptivity of endometrium in persistently thin cases [6].

II. CASES DESCRIPTION

Twelve patients with poor endometrial development (less than 7 mm) were chosen for the study at Accord Superspeciality hospital. Summary data on patient characteristics and FET outcome is shown Table 1.

All participants received hormone replacement therapy (HRT). Estradiol valerate 6 mg/d started on the third day of the menstrual cycle. It was increased to 12 mg/d days 9-10 due to inadequate endometrial development (7 mm). Due to thin endometrium, PRP was performed on day 11. It was repeated on day 13. If the patient's endometrium was thicker than 7mm by day 11, PRP was performed. It was then repeated on day 13 [18] [7].

PRP preparation process-

PRP was made from autologous peripheral cells by centrifugation in two steps. About 8.5 ml blood was taken from 10 ml of a Syringe. It contained 1.5 ml Acid Citrate Anticoagulant Solution (ACD-A) prefilled in it. Mix the blood in a tube. After 15 minutes, centrifuge at 1200-1500 RPM. RBC was separated, and the sample was again centrifuged at 3000 rpm for ten minutes. To provide growth factors, more concentrated blood was obtained [8]. An IUI cannula was used to inject PRP volume of approximately (0.5-0.8
ml) into the uterus. All aseptic protocols were followed during the slow intrauterine injection. Continued use of estradiol valerate. The same observer performed ultrasound after 48 hours and noted the endometrial thickness. After endometrial thickness was >= 7mm, progesterone was initiated and FET was performed subsequently. Estradiol valerate was continued for two weeks after embryo transfer. Progesterone hormone supplements were continued for 12 weeks if serum b-HCG was within the normal range. To confirm the pregnancy, transvaginal ultrasound was performed. The primary outcome was an endometrial expansion. Secondary outcomes were chemical and medical pregnancies. They were determined by positive serum HCG 2 weeks after FET, and the presence or absence of fetal cardiac activity in the transvaginal ultrasound.

III. INCLUSION CRITERIA

1. Patients who have had their embryo transfers cancelled because of thin endometrium
2. Patients who have undergone frozen embryo transfer cycles.
3. All embryos that were transferred were day five embryos.
4. Culture of Negative Acid-fast Bacillus (AFB), for genital tuberculosis.
5. Normal transvaginal ultrasound in women with no clinically significant abnormalities in the uterus, adnexa or uterus.
6. Patients with a platelet count greater than 1 lac.

Table 1. Patients' characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (Year)</th>
<th>Diagnosis</th>
<th>Endometrium(mm) without/with PRP infusion</th>
<th>Embryo transfer</th>
<th>chemical pregnancy</th>
<th>clinical pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>27</td>
<td>Male Factor, Borderline ovarian reserve, tubal factor</td>
<td>5.1/6.3/7.3</td>
<td>2</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>Endometriosis</td>
<td>4.3/6.2/8.4</td>
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<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>38</td>
<td>PCOD</td>
<td>5.3/6.5/7.6</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Condition</td>
<td>Endometrial thickness(mm): Before PRP/48 h after first PRP/48 h after second PRP</td>
<td>Cycle Cancelled</td>
<td>Success</td>
<td>Failure</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>----------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>Poor ovarian reserve, Endometrial factor</td>
<td>4.2/6.8/8.3</td>
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<td>No</td>
</tr>
<tr>
<td>5</td>
<td>26</td>
<td>Endometriosis</td>
<td>5.3/6.7/8.6</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>34</td>
<td>PCOD, Tubal factor</td>
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<tr>
<td>7</td>
<td>32</td>
<td>Tubal factor</td>
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<td>No</td>
</tr>
<tr>
<td>8</td>
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<td>OD Tubal Factor, Mild male facts</td>
<td>5.4/6.7/7.9</td>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>9</td>
<td>40</td>
<td>Advance maternal age, PCOD</td>
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<td>No</td>
<td>No</td>
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<tr>
<td>10</td>
<td>27</td>
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<td>2</td>
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<td>Yes</td>
</tr>
<tr>
<td>11</td>
<td>35</td>
<td>Poor ovarian reserve, Endometrial factor</td>
<td>4.7/5.4/6.1</td>
<td>cycle cancelled</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>37</td>
<td>Poor ovarian reserve, Tubal factor</td>
<td>5.1/5.4/5.7</td>
<td>cycle cancelled</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

*Endometrial thickness(mm): Before PRP/48 h after first PRP/48 h after second PRP

**PCOD: Polycystic ovary syndrome
IV. RESULTS

Figure 1- Pregnancy outcome in 12 patients who underwent frozen embryo transfer after platelet-rich plasma (PRP) instillation

Figure 2- Endometrial thickness in women before and after PRP treatment
In 10 patients, the endometrial thickness rose after PRP infusion and was >7 mm on day 10. After 5 days of progesterone administration, day 5 embryos were successfully transferred. Two blastocyst transfers were performed on 10 patients. Unfortunately, 2 of the cycles had to be cancelled due to persistently thin endometrium. Fourteen patients had clinical pregnancy (40%) out of a total of 10. One patient was diagnosed with biochemical pregnancy (10%). Age factors are very important in the development of endometrial thickening. Women who are 35 years old or older have difficulty getting pregnant.

Statistical analysis

For statistical analysis, IBM (r), SPSS (r), Statistics Version 20.0.0 was used. A one-way ANOVA was followed by LSD's new multiple range test and Duncan's new multivariate tests. Each experiment was performed in three copies and the average values were used for the calculations.

V. DISCUSSION

Despite all the progress made in embryo selection and quality improvements, many patients still experience repeated implantation failure (RIF). Poor endometrial responsiveness has become a major problem in the ART field. The lack of evidence-based treatments is a sign of the problem. Scientists and clinicians are still trying to find a solution. There are many drugs that can be used to improve thin endometrium. These include estrogen, gonadotropins and letrozole. [10].

Recent evidence is proving the positive effect of autologous platelet rich plasma (PRP), in treating thin endometrium. PRP uses autologous plasma from the donor that increases platelet count by about 4-5x more than the circulating blood. The PRP procedure results in regeneration and proliferation of the platelets with a wide range of growth factors and other cytokines. PRP is used in a variety of conditions that are not covered by existing effective treatments. These include osteoarthritis, ligament injuries, skin rejuvenation, hair loss, breast augmentation, wound healing in aesthetic surgery, and bone marrow transplants. In persistently thin cases of endometrial disease, PRP can also be used. [11].

This study was done to improve the success rate of the ART cycle and increase the endometrial thickness. It was successful in 10 patients, but there were 2 failed responses. One patient also experienced biochemical pregnancy. Although the exact cause of this condition is unknown, several factors such as Chromosomal or Genetic abnormalities have been suggested. One of the contributing causes of non-responsive and biochemically pregnant women is inherited or acquired thrombophilias. One reason for failure to respond may be advanced maternal age (>=35 years). The study showed that 4 out 10 patients experienced a clinical pregnancy, which is a good sign. Patients with advanced maternal age can have PRP. Complex errors were seen in women of advanced maternal years. The use of PRP can allow women to have the chance to conceive. It also had a positive effect on women over 38 in our study. It is important to conduct larger trials and follow strict protocols[12].

This study supports the effectiveness of PRP in promoting endometrial development. Two PRP injections were able to produce adequate endometrial development in patients with thin endometrium. Because it was made using autologous blood, PRP is safe and has minimal risk of infection or immunological reactions. Two PRP injections were sufficient to increase the endometrium of patients with thin endometrium. Because it was done from autologous blood, PRP was safe and did not cause any immunological reactions or transmission of infection.
VI. CONCLUSION

The study suggests that PRP treatment can result in positive endometrial development in patients with thin endometrium. The use of PRP to increase endometrial thickness and receptivity for clinical pregnancy is a promising option in reproductive medicine. Because of its potential to promote endometrial renewal, PRP has been widely used in pregnancy. Our data show that PRP effectively increased the endometrium proliferation, implantation rate and clinical pregnancy rate.

REFERENCES

AUTHORS
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