

# Ovarian rejuvenation therapy with PRP (plasma rich in platelets)-an innovative solution for women's infertility

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Many women in the Western countries try to become pregnant at older ages, but they have never considered the status of their quality of embryos. This means that the lower the quality of eggs they have, the bigger is the dilemma to use or not to use their own eggs in IVF technologies that they usually go in order to obtain successful pregnancies. New scientific attempts have gone through nowadays in order to regenerate their ovarian tissue and so they can have more possibilities for a successful pregnancy.

The scientific research for the management of ovarian insufficiency started since the early 1950s including infertility due to aging or insults, and it was restricted by the belief that ovaries are not amendable to renewal [1]. Later, in 2004, studies with mice challenged the idea of a fixed ovarian reserve being endowed during the perinatal period [2]. Later many studies showed that ovarian again may be reversible [3,4].

PRP (plasma rich in Platelets) is a natural product where a high level of platelets is concentrated, but with growth factors concentration 3 to 5 times greater than plasma. Growth factors are stored in granules, and include platelet derivate growth factor (PDGFs), Transforming growth factor-beta (TGF- $\beta$ ), vessel endothelial growth factor (VEGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), e insulin growth factor (IGF), and some others [5,6]. These cytokines play an important role in cellular proliferation, chemotaxis and differentiation of mesenchymal and other cells and promote angiogenesis [6]. The protocol for ovarian rejuvenation includes two steps. The first is the preparation of the PRP. This begins from drawing blood for the woman and then isolate with specific techniques including centrifugation and aspiration of the PRP. Then second part is the injection of the PRP to the two ovaries by laparoscopy [7]. Then AMH (anti-Mullerian hormone), FSH, LH and Estradiol levels are measured at monthly intervals in women who do not menstruate, and during the menstrual flow in menstruating women for a period of six months. If the AMH levels rise, while the FSH, LH, and estradiol levels become lower, there is objective evidence of ovarian rejuvenation is demonstrated [7].

Promising results have been reported so far in websites, but not much data in journals exist about ovarian rejuvenation by PRP until today. In one of the studies, Harvard researchers have shown that stem cells are present in the human ovary, so it is quite possible that they can be transformed into eggs by Growth Factors contained in the individuals' own white blood cells and platelets which have been injected into the ovary [8]. Also, Callejo et al. reported an interesting case in a woman without ovaries. They injected PRP in the ovarian tissue and observed after four and a half months the ovarian function to be restored and the first spontaneous menstruation ensued. Then, after successful drug

stimulation, they managed to get good quality eggs and through an IVF trial, the woman got pregnant [9]. The last study published this year by Sills ES. et al., included extended PRP application to ovarian tissue with a view to document impact on ovarian reserve among women attending for infertility treatment. PRP was freshly isolated from patients (n=4) with diminished ovarian reserve as determined by at least one prior IVF cycle canceled for poor follicular recruitment response or estimated by serum AMH and/or FSH, no menses for  $\geq 1$  year. Immediately following substrate isolation and activation with calcium gluconate, approximately 5 mL of autologous PRP was injected into each ovary under direct transvaginal sonogram guidance. For each study subject, AMH, FSH, and serum estradiol data were recorded at two-week intervals post-PRP and compared to baseline (pre-PRP) values. IVF occurred  $78 \pm 22$  (range = 59-110) days after activated PRP injection, and results appeared independent of patient age, infertility duration, baseline platelet concentration or pretreatment antral follicle count. Each patient had at least one blastocyst suitable for cryopreservation. Evidence of improved ovarian function was noted in all who received intraovarian PRP, possibly as early as two months after treatment [10].

These encouraging results should be extended by several new publications and should also focus the injections by testing inhibin's B levels after PRP's infusion monthly because this protein is the one that gives information about eggs' quality. Also, it has to be stressed that the ideal candidates for ovarian regeneration with PRP are the following: menopausal or perimenopausal women under the age of 50 years, infertile women, who are over the age of 35 years, having low egg reserve and low AntiMullerian Hormone levels (AMH), women under the age of 35 years, who have low egg reserve and low AntiMullerian Hormone levels, and women with premature ovarian failure (POF).

## Conclusion

Conclusively, media supplementation with PRP can better support viability and growth of isolated human early preantral follicles in vitro. Through this treatment, which has no side effects because is a biological therapy, women who have not been menstruating or have undergone premature menopause will get back to the normal menstrual cycle and have a chance at pregnancy.

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