Ovarian Rejuvenation

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Along with the global modernization, the number of advance aged women with diminished ovarian reserve tends to increase. Platelets-rich-plasma has been recently implemented to reproductive treatment for ovarian rejuvenation. Although several studies suggested that intraovarian injection PRP resulted in live births in poor prognostic infertile patients, the current understanding of the autologous PRP activities in the ovaries, as well as the long-term effectiveness of this approach are at an incipient stage. The extension of this novel intervention in clinical practice requires more serious evaluations with better designed studies.

add on treatment diminished ovarian reserve platelet-rich-plasma premature-ovarian-insufficiency

1. Introduction

Along with the global modernization, women tend to delay their childbearing due to professional investment and seeking better living conditions. Recent data revealed a significant rise in the mean age of first-time mothers, ranging between the third and fourth decade [1][2]. This is associated with ovarian aging, which is a physiological process characterized by declining oocyte quantity and quality—an unsolved problem in reproductive medicine. Premature ovarian insufficiency (POI), a condition characterized by a premature decline of ovarian function occurring before the age of 40, has risen from 1% to nearly 2% in the last few decades [3][4]. These changes placed a requirement of implementation therapeutic strategies for these low prognostic infertile women. Indeed, many innovative approaches have been proposed to fulfill the desire of aforementioned patients to have genetically related offspring.

Platelet-rich plasma (PRP), derived from peripheral blood, consists of a high number of platelets (about 1,000,000 of platelets/μL in 5 mL of plasma)[5][6]. The alpha granules of activated platelets release a variety of growth factors including platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-I), basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), and pro-inflammatory cytokines (IL-1β and IL-6)[5][7]. PRP has been shown to enhance effectively the regeneration and healing of human tissue[8][9][10][11].

In reproductive medicine, PRP was first used to enhance endometrial thickness in patients attempting in vitro fertilization (IVF) treatment[12]. Several subsequent reports revealed that that intraovarian injection of PRP

promoted the follicle growth and improved the treatment outcome in poor prognostic infertile women, resulting in several live births without complications.

3. The Hypothesized Mechanism of PRP in Ovarian "Rejuvenation"

Given the roles of the bioactive factors presented in PRP in folliculogenesis, the intraovarian injection of PRP is supposed to improve follicular growth. Thus, it is rational to hypothesize that autologous PRP intraovarian infusion treatment could "rejuvenate" the dysfunctional ovarian tissue.

In cyclophosphamide-induced ovarian failure rats, PRP treatment increased the ovarian cortex volume, pre-antral follicles number, and antral follicle diameter[13]. In another study, histopathological studies presented that receiving PRP treatments improved not only the quantity but also quality of follicles in all stages in mice ovaries. In comparison to the control group, the PRP-treated group had an evidently lower number of atretic follicles[14]. In bovine ovaries, a study presented that the serum progesterone concentrations were increased in four of the five cows treated with PRP, followed by four pregnancies after artificial insemination. Meanwhile, there were no recorded variation in progesterone concentration and pregnancies in the control group[15]. Another study suggested that latent follicles and in vivo embryo production could be stimulated by PRP treatment[16]. In an in vitro study, PRP culture could increase the viability and the development of isolated human primordial and primary follicles[17].

Considering the angiogenic features of platelet-derived cytokines, PRP is also expected to ameliorate the aging ovaries by increasing the neovascularization. Studies reported that the molecular network promoting angiogenesis was significantly disrupted in patients presenting with ovarian dysfunction[18][19]. An increase of vascularization in ovary enhances its blood nourishment, contributing to the follicular growth and oocyte quality, resulting in higher fertilization and developmental potentials[20]. Moreover, enhancing oxygen perfusion improves intrafollicular oxygen and better ooplasm quality, leading to the recovery of mitochondrial function that drives a higher possibility to produce an ongoing pregnancy[21]. Numerous publications reported that PRP could improve neoangiogenesis in different clinical situations, especially in regenerative medicine[22][23][24]. At the level of ovary, PRP was revealed to prevent effectively of ischemia and reperfusion damage by studying ovarian torsion in a rat model. PRP decreased the mean total oxidant status, oxidative stress index, and histopathological scores[25]. In POI rats' ovaries, the PRP injection induced ovarian tissue vascularization via an increase of alpha-smooth muscle actin in the small arteries [14].

3. Conclusions

In conclusion, published literature presented that PRP intraovarian infusion could be a beneficial add-on treatment in the reproductive field. However, the current understanding of the autologous PRP activities in the ovaries, as

well as long-term effectiveness of this approach are at an incipient stage. The extension of this novel intervention in clinical practice requires more serious evaluations with better designed studies.

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