



Platelet rich plasma (PRP) for vaginal tightening: A new approach

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ABSTRACT

Vaginal laxity is an anatomical deformation that can cause orgasmic dysfunction, decrease in self-esteem, worsen sexual life and quality of life in women. Although vaginal tightening has often been tried to be achieved by surgical methods, nowadays there is an increasing tendency to use non-surgical methods and to combine surgeries with non-surgical methods. These methods are non-invasive, safe, easy to apply and can be performed in private clinics as a daily outpatient procedure. A Their place in regenerative medicine is increasing day by day. Autologous platelet-rich plasma (PRP) has received more attention in cosmetic surgery, functional cosmetic genital surgery. PRP treatment stimulates neovascularization and collagen formation with the help of the growth factors that are secreted from the alfa granules of the platelets. It can be used in lichen sclerosis, vaginal atrophy, stress urinary incontinence, episiotomy scars, cervical ectopy and vaginal rejuvenation. We aimed to review the literature for PRP application in gynecology.

Keywords: Non-surgical gynecologic cosmetics; platelet-rich plasma; vaginal laxity; vaginal tightening

INTRODUCTION

Congenital differences such as labial hypertrophy, asymmetric labial growth; vaginal laxity due to obstetrical traumas, genetics, weight fluctuations; dyspareunia due to episiotomy scar, lichen sclerosis, vaginal atrophy following chemotherapy for breast cancer, genital urinary syndrome of menopause can lead to situations such as a decrease in self-esteem, sexual unsatisfaction, orgasmic dysfunction and decrease of quality of life.

Vaginal laxity as a part of natural process occurring with aging, childbirth and menopause can cause decreased introital friction, diminished arousal and orgasmic dysfunction. It can also adversely effect women's sexual health and body image.¹ This has led clinicians to seek new, safe and effective surgical or non-surgical solutions to restore the function and form of the genital area.^{2,3} Non-surgical approaches such as platelet-rich plasma (PRP), hyaluronic acid fillers, energy based devices and lipofilling

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are gaining popularity day by day due to their safe and effective outpatient application.⁴

A detailed electronic database (PubMed) search was performed for the review of studies involving PRP application. PRP, vaginal rejuvenation, vaginal laxity, vaginal tightening, female genital cosmetics were used as research terms.

PRP

It is reported in the literature that many different synthetic materials such as calcium hydroxyapatite crystals, hyaluronic acid fillers, PRP are injected into the periurethral area and vaginal walls for the treatment of sexual issues and stress urinary incontinence.⁵

PRP is a novel autologous regenerative treatment method which gained popularity in the 1980s and 1990s and used almost in all fields of surgery such as orthopedics, dentistry, plastic surgery and gynecology to promote tissue healing and regeneration.⁶⁻⁸ It is considered to be safe, low-cost, simple, natural and minimally invasive method for vaginal rejuvenation.

As the name suggests, platelet rich plasma contains a high percentage of platelets which is above that normally contained in whole blood. Autologous PRP is obtained by taking the patient's whole blood then centrifuged to remove red blood cells. Platelets have a capacity to supply and release essential growth factors and cytokines from their alpha granules to provide a regenerative stimulus that promotes repair in tissues and augments healing. It is a natural source of autologous growth factors.⁹ It contains molecules that stimulate cell proliferation and cell differentiation such as transforming growth factor- β , insulin-like growth factor, vascular endothelial growth factor, epidermal growth factor and platelet derived growth factor (PDGF) (Table 1). These molecules play an important role in inflammation reduction, collagen III synthesis, angiogenesis stimulation and as a result in tissue regeneration. PDGF has been reported to stimulate cell proliferation and is involved in wound healing.¹⁰ It is a mitogen for smooth muscle cells and fibroblasts. It plays role in angiogenesis, fibrous tissue formation and re-epithelialization which are phases of wound healing.⁷

Studies on the use of PRP in the literature are mainly urogynecology, and studies on its place in the use of vaginal laxity are limited.^{5,11,12} Moreover, most of the existing studies consist of case reports and mostly PRP is combined with other minimally invasive techniques such as lipofilling or HA.^{13,14} There are some studies investigating its effect on female sexual dysfunction and satisfaction.^{5,15} However, it can be suggested that it may also be effective in the treatment of vaginal laxity due to its tissue regeneration feature.¹⁶ It can also stimulate

collagen synthesis, neo-vascularization which can also result in repair of vaginal laxity, improvement of sexual satisfaction and increase of quality of life.^{7,10,15}

Table 1. Regenerative growth factors stored in platelet alpha granules and their functions^{8,17}

Growth factor	Function
Transforming growth factor- β	Stimulates production of collagen type I and type III, angiogenesis, undifferentiated mesenchymal cell proliferation, endothelial chemotaxis, regulates mitogenic effects of other growth factors
Insulin-like growth factor (1 and 2)	Regulates cell proliferation and differentiation, enhances bone formation, chemotactic for fibroblasts and stimulates protein synthesis
Vascular endothelial growth factor	Increases angiogenesis and vessel permeability, stimulates mitogenesis for endothelial cells
Epidermal growth factor	Accelerates re-epithelialization, increases tensile strength in wounds, regulates collagenase secretion, facilitates organization of granulation tissue
Platelet derived growth factor	Stimulates chemotaxis, cell proliferation, angiogenesis, regulates collagenase secretion and collagen synthesis
Fibroblast growth factor	Stimulates angiogenesis, promotes stem cell differentiation and cell proliferation
Connective tissue growth factor	Promotes angiogenesis, fibrosis and platelet adhesion
Platelet factor 4	Stimulates the initial influx of neutrophils into wounds
Interleukin 8	Recruitment of neutrophils and other immun cells to the site of infection, pro-inflammatory mediator

The Treatment Process

The limitation in PRP application is that the composition varies according to the device used, preparation method, preparation time, storage method and the composition of PRP varies from patient to patient.

There is no common consensus, no standard approach in terms of the anesthetic creams used, the areas where the injection is applied in the genital area, the frequency and doses of PRP injection for vaginal rejuvenation. Many clinicians have individualized their methods over time based on their own experience.

In order to induce release of a highly concentrated bolus of growth factors PRP preparations are activated. Up to 70% of

growth factor content from activated PRP can be released over 10 minutes. Roh et al.¹⁸ demonstrated that PRP activated with a low-dose mixture of thrombin and calcium significantly increased growth factor release over 7 days compared with non-activated PRP. Although due to limited data there is no agreement on whether activation is beneficial or detrimental.

There are unique strategies used to put together the PRP, such as some practitioners use a centrifuge, whilst others use a double spin method. PRP cellular composition and biomolecular characteristics vary according to the preparation protocol.¹⁹ In Giusti et al.'s²⁰ study, the optimal concentration for the stimulation of angiogenesis was 1.5×10^6 PLT/ μ L and lower or higher concentrations displayed a lower angiogenic potential.

Although PRP application can be performed easily and without complications in clinical private practices with local anesthetic cream application, some patients may prefer the procedure to be performed under anesthesia in operating room due to their anxiety. In the literature, there are various cream mixtures with different contents and ratios used for topical anesthetic effect.

In Runels et al.'s⁵ study bupivacaine, lidocaine and tetracaine cream compound with percent concentrations of 20/8/8 respectively was used. The cream was applied to the anterior vaginal wall and to the clitoris. PRP injection was performed 20 minutes after anesthetic application. Peripheral blood was centrifuged to yield 5 cc of PRP. They used either Regen® or TruPRP®. These both FDA approved systems use centrifugation to separate and concentrate PRP. They also added calcium chloride (0.5 mL) to the 5 mL of PRP isolate to activate the thrombin cascade. Injections were administered in less than 10 minutes to prevent platelet rich fibrin matrix from becoming too gelatinous for passing through a needle. Injections were given through a 27-gauge needle to the anterior vaginal wall into a space between vagina and urethra and into the clitoris. In this study, extreme sexual arousal was observed in 2 patients but these side effects only lasted 1 to 2 weeks and occurred in younger patients with minimal sexual dysfunction.

In Aguilar et al.'s¹³ study, lipofilling and injection of combined PRP and HA was applied to a 39-year-old primiparous woman who referred for sexual dysfunction. They performed the procedure under general anesthesia. They used Regen®- BCT Cellular Matrix kit. The peripheral blood was withdrawn from the patient and collected into three single use sterile tubes (4 mL per tube). 4 mL of PRP-HA mixture (2 mL of PRP for 2 mL of HA) was prepared. The tubes were centrifuged at 1500 g for 5 min. Concomitantly the fat was harvested according Coleman's technique and was then centrifuged at 1500 g for 1 min. Then fat cells were injected in the posterior vaginal wall and the injection

of the PRP-HA preparation in the perineal raphe, in the vestibular fossa and in the labius minus and majus. They reported that the total procedure took 30 min. They also reported that at 3-month follow-up the patient's symptoms improved significantly. She reported that her flatus incontinence disappeared completely.

In Kim et al.'s¹⁴ study, PRP and lipofilling was applied to a 67-year-old patient for vaginal atrophy and lichen sclerosis. Autologous fat was harvested from the abdomen and mixed with autologous PRP. PRP was prepared by double-spin centrifugation using a SmartPreP® APC-30. A total of 36 cc of autologous fat was mixed 4 cc of autologous PRP. One month after injection her symptoms were resolved.

In another study, four sessions of PRP were administered to the anterior vaginal wall of 52 female patients with sexual dysfunction and orgasmic disorder.¹⁵ A local anesthesia cream which contained lidocaine 2.5% and prilocaine 2.5% was applied around the clitoris and the vaginal lower one-third of the region half an hour before the procedure. The collected blood was centrifuged at 3200 rpm for eight minutes. Calcium chloride (0.5 mL) was used for activation. PRP of 4 cc was administered around the clitoris in the direction of clock positions of 12,3, 6 and 9, each with 1 cc, 2 cc subcutaneously; right/left of paraurethral vaginal wall. The administration was continued once every four weeks for four months. An increase in the satisfaction of the patients were observed in this study.

Contrary to what can be seen in calcium Hydroxyapatite Crystals or HA fillers in the literature, complications such as granuloma formation, infection or local tissue necrosis have not been reported if the procedure is performed by an expert clinician and if FDA-approved kits that are used for preparation of PRP.^{5,21} Also there are no reports of allergic reaction due to PRP injection.

PRP application is not recommended in individuals who are taking antiplatelet therapy or who can not delay this treatment, and individuals using non-steroidal anti-inflammatory drugs (NSAIDs), reversible cyclo-oxygenase inhibitors, and anti-hyperglycemic pioglitazone, since these medications may significantly reduce the improvement potential of PRP treatment.⁸ In addition to these, the use of systemic immunosuppressants such as glucocorticoids, blood dyscrasias and antibiotic use due to infection can be counted as medical contraindications. Being unable to tolerate injection therapies or afford to undergo a potential series of injections may be non-medical contraindications.

Patients should be informed that they may experience discomfort, swelling and redness in the injection areas after the procedure. These complaints often disappear within a few days. In addition, the information that they can easily return to their

daily routines after the procedure and that they will not need to rest can be given before the procedure. If only PRP application is performed as a rejuvenation procedure than sexual intercourse, heavy exercise and using tampon are not recommended for only 1 week after the procedure. Also they should avoid using NSAIDs for 2 to 6 weeks after the procedure. They can use acetaminophen as an alternative to NSAIDs as painkiller.

DISCUSSION

As stated in Shaw et al.'s²² guideline no: 423, healthcare providers should educate women about female anatomy and anatomical variations. It is stated that most women who seek genital cosmetic surgery have normal genitalia, and up to 87% are reassured by counselling.²² However, we can offer both surgical and non-surgical methods to the patient in cases such as vaginal laxity that can disrupt the person's sexual life and self-confidence.¹

Although methods such as vaginoplasty, perineoplasty, colpoperineoplasty are preferred in vaginal tightening, non-surgical methods such as HA, PRP fillers, lipofilling and energy based devices have become more preferred among both patients and healthcare providers today.^{4,23-25} Some frequent outcomes encompass enhancement in vaginal tightness, decreased stress urinary incontinence, and elevated sexual function.¹³⁻¹⁵ These consequences may additionally be transient or permanent, relying on the method and the patient's recuperation process.

While PRP is used in many fields of medicine due to its positive effect on wound healing, its use in urogynecology and vaginal rejuvenation, either alone or in combination with methods such as HA and lipofilling, has begun to enter the literature.^{5,6,9,11}

Its autologous nature, the low complication rate, ease of preparation and application, and outpatient applicability suggest that PRP application will increase its popularity in many areas of gynecology such as vaginal rejuvenation, urogynecology in the coming days. However, differences in preparation and application techniques, variability in cell numbers and the scarcity of studies in the literature indicate that our knowledge in this area is still limited and more prospective randomized studies are needed.^{15,19}

CONCLUSION

PRP application in vaginal laxity and rejuvenation is a safe, simple and minimally invasive method, both alone and in combination with surgical approaches due to its accelerated wound healing effect. More prospective randomized studies are

needed in gynecological practice in order to reach a consensus on the preparation and administration and the optimal cell amount.

ETHICS

Peer-review: Externally peer-reviewed.

Contributions

Concept: G.S., A.A.S.; Design: G.S., E.Ö., A.A.S.; Literature Search: E.Ö.; Writing: G.S., E.Ö.

DISCLOSURES

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