Current Evidence of Platelet-Rich Blood Plasma for Pelvic Organ Prolapse: A Review

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Abstract
Objective: To review the current evidence of the potential use of Platelet-Rich Plasma (PRP) in the field of urogynecology, especially in POP cases.
Method: This review used several databases (Google Scholar, Pubmed, and Science Direct) and searched for English and Indonesian articles in the last ten years. Articles were received in the form of case reports, observational studies and clinical trials that discussed the use of Platelet-Rich Plasma in cases of Pelvic Organ Prolapse (POP).
Results: A total of three articles were included in this review.
Discussion: There were two patient studies and one in vitro study. The POP patient study showed favorable results with low recurrence rates in patients who received Platelet Rich-Plasma compared to those who did not and another study that conducted a one-year evaluation found no recurrences after the patients received Platelet Rich Plasma at the surgical site. The in vitro study showed good cell attachment and proliferation in vaginal tissue biopsies with Platelet-Rich Plasma applied to the tissue.
Conclusion: Platelet-Rich Plasma may promote tissue regeneration, hence potentially reduce recurrency after reconstruction.

Keywords: Pelvic Organ Prolapses, Platelet-Rich Blood Plasma, Urogynecology

Bukti Terkini Plasma Darah Kaya Trombosit untuk Prolaps Organ Panggul: Sebuah Kajian

Abstrak
Tujuan: Untuk meninjau bukti terkini mengenai potensi penggunaan *Platelet-Rich Plasma* di bidang uroginekologi, khususnya pada kasus POP.
Metode: Tinjauan ini menggunakan beberapa database (Google Scholar, Pubmed, dan Science Direct) dan mencari artikel berbahasa Inggris dan Indonesia dalam sepuluh tahun terakhir. Artikel yang diterima berupa laporan kasus, studi observasional, dan uji klinis yang membahas penggunaan *Platelet-Rich Plasma* pada kasus Prolaps Organ Panggul (POP).
Hasil: Sebanyak tiga artikel termasuk dalam tinjauan ini.
Diskusi: Terdapat dua studi pasien dan satu studi *in vitro*. Studi pasien POP menunjukkan hasil yang baik dengan tingkat kekambuhan yang rendah pada pasien yang menerima PRP dibandingkan dengan mereka yang tidak menerima *Platelet-Rich Plasma* dan studi lain yang melakukan evaluasi satu tahun tidak menemukan adanya kekambuhan setelah pasien menerima *Platelet-Rich Plasma* di tempat pembedahan. Studi *in vitro* menunjukkan perlekatan dan proliferasi sel yang baik pada biopsi jaringan vagina dengan *Platelet-Rich Plasma* yang diaplikasikan pada jaringan tersebut.
Kesimpulan: *Platelet-Rich Plasma* dapat meningkatkan regenerasi jaringan, sehingga berpotensi mengurangi kekambuhan setelah rekonstruksi.

Kata kunci: Platelet-Rich Blood Plasma, Prolaps Organ Panggul, Uroginekologi

Introduction

The dropping of pelvic organs into the vagina or beyond the vaginal opening is known as pelvic organ prolapse, or POP (meaning slipping or falling out of position). The urethra (ureterocele), bladder (cystocele), colon (rectocele), and small bowel are all considered to be pelvic organs.[1] Globally, about 40% of women experience POP and it is estimated to increase with age.[2] Notably, low-income countries beat a substantial burden, accounting for around 20% of global POP cases.[2] Among the 200,000 annual POP surgeries in the United States, 81% involve cystocele reconstruction, indicating its prominence compared to other types of POP.[3] Risk factors for POP include history of pregnancy, heavy physical labor, and genetic factors in the family.[4] The standard treatment for POP is surgery, for example anterior corporal reconstruction for cystocele which primarily involves tightening the anterior vaginal wall without addressing the specific defect in the apical compartement.[1,4] Consequently, there is a high incidence of post-reconstruction recurrence of POP. Research by Kayondo *et al*. published in 2022 found that 25.2% of POP cases that underwent reconstruction experienced recurrence, with 56.3% of these recurrences' involving sites other than the cystocele reconstruction site.[5]

There is a crucial need for a method to reduce post-reconstruction recurrence. Platelet-Rich Plasma (PRP) treatment holds promise in addressing this POP problem. PRP, known for its abundance of growth factors and cytokines that facilitate tissue regeneration, has been extensively utilized in orthopedic and plastic surgery.[6] By harnessing the regenerative potential of autologous PRP, it may be possible to restore connective tissue, smooth muscle, vascularization, and innervation that provide support to compromise in POP cases. The application of PRP injection aims to strengthen ligaments and restore the natural anatomical form and support of pelvic organs, thereby reducing the risk of POP recurrence. While PRP is commonly employed in orthopedic and plastic surgery, its use in urogynecology remains relatively unexplored. This literature review aims to investigate the potential of utilizing PRP in urogynecology cases, particularly for POP.

Method

Search engines including Pubmed, Science Direct, Cochrane, and Google Scholar were employed for this literature evaluation. Platelet-Rich Plasma OR PRP OR Platelet Rich Blood AND Pelvic Organ Prolapse OR POP were the keywords used. The following criteria must be met for inclusion in the literature: (1) 10 years of publication; (2) usage of Indonesian or English; (3) complete text; and (4) articles in the form of observational studies or clinical trials. Articles that were excluded in this review are review articles. Two researchers (AMS, AH) conducted the systematic selection of articles in accordance with a number of processes, including identification, screening, and adherence with inclusion criteria. The searches conducted using journal search engines turned up a total of 724 articles. Three articles remained in this literature study after numerous selection procedures because they were pertinent.

Result

In a case report by Castellani *et al*., three patients received endoscopic Bipolar Plasmakinetic Resection (BPR) of exposed mesh and PRP gel delivery in the surgical site to fill the gap left by the resection to treat polypropylene mesh exposure following abdominal sacral colpopexy. After a year of follow-up, all women regained sexual function, and no one had a relapse of pelvic organ prolapse. This early finding demonstrated the viability of

PRP in urogynecological surgery.[7]
Medel et al.'s comparative study examined cell attachment and proliferation from vaginal tissue biopsies in postmenopausal individuals with POP and performed cell isolation in 2015. Patients who received PRP had a considerably higher attachment of POP (p=0.001). This in vitro study therefore demonstrates the potential of PRP in urogynecologic procedures and demonstrates how implantation in conjunction with PRP might decrease post-reconstruction problems.[8]A case control study was conducted in 2020 by Atilgan et al. on cystocele patients who had anterior colporrhaphy alone (Group 1) vs repair with PRP injection (Group 2).7 The Pelvic Organ Prolapse Quantification (POP-Q) and Pelvic Floor Distress Inventory (PFDI) were used to assess each group of 28 patients over a period of 48 months. For one cycle, PRP injection was done at a dosage of 4cc PRP + 0.2cc of 10% calcium chloride.

In comparison to Group 2, which received PRP therapy, there were more cystocele recurrences in Group 1 (21.4%), with both PFDI and POP-Q evaluations. This was statistically significant, with a p-value of 0.008 for PFDI evaluation and a p-value of 0.0001 for POP-Q evaluation. Five members of group 1 had reoperation, while one member of group 2 did so. This was statistically significant (p=0.001). After surgery, patients in group 2 reported feeling "better" than patients in group 1 (25 vs 21, p=0.012). In groups 1 and 2, the subjective success ratio was 75% and 89%, respectively. In this trial, neither group experienced an allergic response, and neither group experienced an infection around the incision or a hematoma.[9]

Discussion

Platelet-Rich Blood Plasma

A product made from autologous blood called Platelet-Rich Blood Plasma (PRP) has platelet concentrations that are two to three times higher than typical.[10] PRP, a plasma product made from a patient's own blood, is intended to boost platelet numbers and concentrations of molecular mediators, which have therapeutic benefits by eliminating undesirable components like red blood cells.[11] The benefits of PRP include enhancing clinical circumstances in various illness settings through the process of selective enrichment of growth factors and anti-inflammatory cytokines.[12] PRP's capacity to control a number of processes that impact tissue healing, such as inflammation or cell activation, is supported by several studies on its use in regenerative medicine.[13] Platelets release proteins in exosomes, which are extracellular vesicles, in addition to releasing free proteins to the desired place. Exosomes have regenerative benefits, much to PRP.[14,15] Research by Lana *et al*[16] discovered that the release of pro- and anti-inflammatory chemicals by leukocytes in PRP plays a significant role in the inflammation that precedes tissue regeneration. They discovered that platelets and activated neutrophils work better together to promote tissue healing. The importance of monocyte plasticity for a non-inflammatory and reparative role in tissue healing was also mentioned. Intra-articular autologous Platelet-Rich Plasma (PRP) has gained popularity as a secure and effective biotechnological option for the treatment of a variety of illnesses for more than ten years.[17] The first step in preparation is blood collection, which is accomplished by venous puncture. The sample is then centrifuged, and the plasma that has been enhanced with platelets is extracted. It will be possible to create a PRP preparation that is rich in growth factors, cytokines, chemokines, and cell adhesion molecules.[10]

Potential Mechanism of Action of PRP for Pelvic Organ Prolapse

PRP stimulates the migration and

multiplication of fibroblasts, which quickly regenerate connective tissue. PRP is utilized in urogynecology for site-specific prolapse repair with good functional and anatomical results because of the benefit of this impact. The key outcome of using PRP is a low recurrence rate. Additionally, PRP injection has a greater impact on the Pelvic Floor Distress Inventory scale's assessment of the prolapse symptoms' decrease. As a result, administering platelet-rich plasma may be an effective alternative therapy to stop pelvic organ prolapse recurrence. Additionally, preliminary research has indicated that PRP can work as a source of growth factors to quicken the healing of tendons and ligaments.[18]

Vascular Endothelial Growth Factor (VEGF), Insulin Growth Factor I (IGF-I), Platelet Derived Growth Factor (PDGF), Hepatocyte Growth Factor (HGF), Transforming Growth Factor Beta (TGF-b), and Fibroblast Growth Factor (FGF) are among the growth factors found in PRP and are thought to be involved in the pathophysiology of ligament reconstruction.[19] Fig.1 illustrates the distinct functions that each growth factor performs.[20] In more recent research, it was utilized to treat vaginal mesh exposure following abdominal sacrocolpopexy, and in vitro autologous PRP encouraged the adhesion of human vaginal fibroblasts to vaginal implants and boosted their healing potential in vaginal prolapse surgery.[21,22] It hasn't, however, been applied to cystocele repair. Because a cystocele is a protrusion of the bladder through the anterior vaginal wall, well-developed pubovesical fascial support would stop recurrence.

Safety and Adverse Effect

PRP currently has no known negative effects. In the 48-month follow-up period of Atilgan and Aydin's investigation on the effects of PRP on the treatment of cystocele, no adverse effects were seen after PRP injection.[9] Uncertainty persists over the advised number of PRP administration repetition sessions.[23] From one study to the next, the quantity and

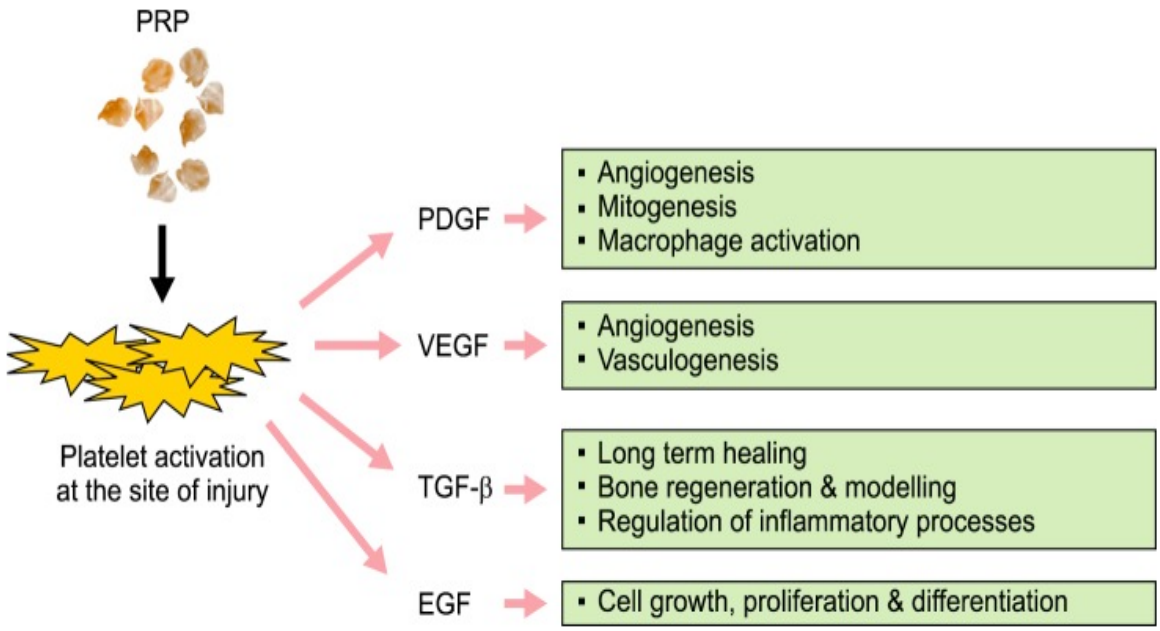

Figure 1 Action Mechanism of Platelet-Rich Blood Plasma.[20]

frequency of repeated doses varied. PRP injection into the pubocervical fascia during anterior vaginal wall prolapse repair may be a useful alternative to avoid cystocele recurrence given the risks associated with mesh implants in cystocele. For a variety of urogynecological treatments, larger randomized controlled trials are required to prove their effectiveness and safety.[9,24]

In any of the investigations, there were no grave side effects discovered. Minimal adverse effects, including short and bearable discomfort during treatment, a moderate headache, little itching, and transient erythema and edema of the treated region, were seen in trials employing PRP for hair growth. After PRP treatment, there were no significant side effects like scarring, infection, panniculitis, hematomas, or allergic reactions. Patients were able to resume their regular daily activities without the need for antibiotics to prevent infection, and most of them were able to go back to work the next day.[25]

Conclusion

Post-reconstruction PRP therapy in POP cases is likely to reduce the risk of post-reconstruction recurrence. PRP plays a role in rapidly reshaping connective tissue by stimulating fibroblast migration and proliferation. The reduction in prolapse symptoms ascertained by Pelvic Floor Distress Inventory scale was more significant with PRP administration. Thus, administration of platelet-rich plasma may be a good alternative treatment to prevent POP recurrence. The weakness of this literature review is that only one article directly examined the difference between reconstruction alone and reconstruction combined with PRP therapy, so it cannot be generalized to a wider population. The strength of the evidence found that three articles open the opportunity for PRP therapy as a solution to reduce the recurrence rate in POP cases, thus providing new therapeutic potential in the field of urogynecology. Recommendations for future research to further examine the potential of PRP for POP cases are either preclinical studies, observational studies, or clinical trials to determine the safety and efficacy of giving PRP after reconstruction of POP.

Conflict Of Interest

All authors declare that there is no conflict of interest

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