Literature Review

Role of Platelet-Rich Plasma Application on Mesh-Tissue Integration

Peran Aplikasi Platelet-Rich Plasma pada Integrasi Mesh dengan Jaringan

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Abstract

Objective: To review the advantage of PRP use on mesh-augmented surgery.

Methods: Literature review of PRP application of mesh.

Results: The application of PRP on mesh shows potential promising outcome.

Conclusion: PRP may improve the mesh-tissue integration.

Keywords: mesh-augmented surgery, pelvic organ prolapse, platelet-rich plasma, wound healing.

Abstrak

Tujuan: *Untuk menganalisa keuntungan penggunaan PRP pada pembedahan rekonstruktif dengan mesh.*

Metode: *Kajian pustaka dari penggunaan PRP pada pembedahan rekonstruktif dengan mesh.*

Hasil: *Aplikasi PRP pada mesh menunjukkan hasil yang positif.*

Kesimpulan: *Aplikasi PRP dapat meningkatkan integrasi mesh dengan jaringan*

Kata kunci: *pembedahan rekonstruksi dengan mesh, penyembuhan luka, platelet-rich plasma, prolaps organ panggul.*

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INTRODUCTION

The prevalence of POP globally ranges from 3% - 50%, with a higher prevalence among menopausal women. In Indonesia, based on research conducted at Dr. Cipto Mangunkusumo Hospital in 2016, the prevalence of POP was 26.4%.[1-3] Mesh-augmented surgery, previously known as a procedure, to treat hernia, has now been widely used to treat pelvic organ prolapse. It gives satisfactory results with an effectiveness and recurrence rate of 76–96% and 7.4% respectively compared to the short-term success rate of anterior colporrhaphy of 35-72% and recurrence of 30%.[8] Nevertheless, mesh-related complications negatively impact women's quality of life in the form of abnormal vaginal discharge, infection, chronic pain, and extrusion. Mesh extrusion is the most common complications reported (55%) and believed to occur due to the dysfunctional wound healing process and tissue integration into the mesh.[14] Therefore, the procedure has become a focus in pelvic organ prolapse studies, one of those is the application of PRP.

Reconstructive Surgery in Pelvic Organ Prolapse

Most patients with POP have no symptoms. However, as the protrusion of the organ into the vaginal introitus progresses, the symptoms will also become more disturbing. The symptoms vary from vaginal bulging, urinary and defection

problem, sexual disorder, infection, and uterine/vaginal ulcer.[4]

POP management usually requires reconstructive surgery to restore the pelvic organs' anatomical structures. Reconstructive surgery for POP started using the native-tissue-repair (NTR) technique, utilizing only pelvic organ support tissues. Mesh-augmented surgery then employed to treat POP which offers a more durable result. However, mesh augmentation is troubled by the high rate of complications due to the dysfunctional mesh-tissue integration process.[5,6]

The mesh-augmented repair technique was first used as a treatment for inguinal hernias. The meshes used to treat hernias are generally rigid because the implantation site is on the abdominal wall tissue. This is not the case in pelvic organ prolapse, in which the mesh is placed on a highly innervated and vascularized thin vaginal mucosa.[7] There is a higher possibility of frictions in vaginal meshes due to intestinal peristalsis and sexual activity. Moreover, during the treatment of POP, the anatomical appearance may not become the most crucial outcome but rather the restoration of normal urinary, defecatory, and sexual function are. With this in mind, improving the integration of mesh for POP is essential to avoid complications such as erosion or extrusion.[8]

In general, mesh products are divided into synthetic and biological mesh.[9,10] Biological mesh can be derived from human, bovine, or porcine tissue, which has been decellularized to release the collagen matrix.[9,10] This biologically derived material is also more prone to degradation and has a weaker structure, increasing the risk of recurrence.[12] Several types of biological mesh include allograft, xenograft, and autograft.[12,13] There are two synthetic mesh types used in urogynecology, namely absorbable and non-absorbable materials. The absorbable mesh was developed to reduce long-term complications and help postoperative fibroblast activity; however, this mesh showed weaker scar tissue formation, causing high recurrence rates. Non-absorbable mesh is reported to have suitable mechanical properties and long-term stability, making it easy to modify intraoperatively. Polypropylene (PP) mesh is a synthetic mesh commonly used in urogynecology to repair POP and stress urinary incontinence (SUI).[13] This mesh has varying flexibilities, diverse inflammatory responses, is easy to manipulate, and relatively inexpensive. In order to improve the quality of the mesh, polypropylene mesh has been currently designed with a lighter material that can increase the inflammatory response, reduce mesh contraction, and improve tissue integration.[14] This mesh appears to be more durable, non-toxic, and has low antigenicity.[14]

Wound Healing Process in Mesh Implantation

Wound healing is a physiological process involving three concurrent phases: hemostasis/inflammation, proliferation, and remodeling. The inflammatory phase begins with hemostasis and chemotaxis; proinflammatory cytokines will activate the tissue's neutrophils and other immune cells. The processes of angiogenesis, re-epithelialization, collagen formation, and wound contraction occur in the proliferative phase.[15-17]

Implantation of the mesh will trigger a foreign body reaction associated with the wound healing process. The reaction plays an essential role in the tissue-mesh integration, which is characterized by one of the three stereotypical reactions; tolerance, destruction, and rejection or removal of the implanted material.[11,16] Foreign body reaction is a complex defense mechanism that will trigger infiltration of various foreign-body giant cells, macrophages, fibroblasts, and angiogenesis in the mesh-implanted tissue.[17] The infiltration of fibroblast will cause new collagen deposition. Moreover, angiogenesis will allow tissue remodeling thus scar tissue will not replace the mesh. Subsequently, mesh-host tissue integration will take place along with the deposition of new collagen until resorption of the mesh begins. The integrated mesh will last for several years after implantation, whereas non-integrated mesh will be degraded within 2-3 months. However, exaggerated inflammation response can lead to excessive scarring, mesh encapsulation, and degradation.[10,12]

Dysfunctional tissue reaction is more profound in menopausal women due to the low estrogen level. Estrogen favors wound healing process and has a vital role in both stages of hemostasis/inflammatory, proliferation, and remodeling by reducing wound size, increasing collagen deposition by controlling the amount of collagen I and III in the remodeling phase, and strengthening the tissue. Estrogen could also increase angiogenesis and re-epithelialization-epithelialization by increasing the mitotic rate of epidermal cells. Low estrogen levels in animal models of rabbits in a study showed inhibition of

the wound healing process.[12,14]

This phenomenon was observed in experiments performing bilateral oophorectomy on menopausal rabbits. Their results showed that in menopausal tissue, the wound healing process occurred slower than that in premenopausal tissue. In addition to that, histological findings revealed more significant neovascularization, accumulation and maturation of granulation tissue, collagen deposition, and re-epithelialization processes during the first 35 days following the surgery. They also found an increased in acute and chronic inflammatory response. This phenomenon seemed to happen due to increased response of neutrophil elastase and fibronectin degradation, which resulted in delayed wound healing and scar contraction.[12,16]

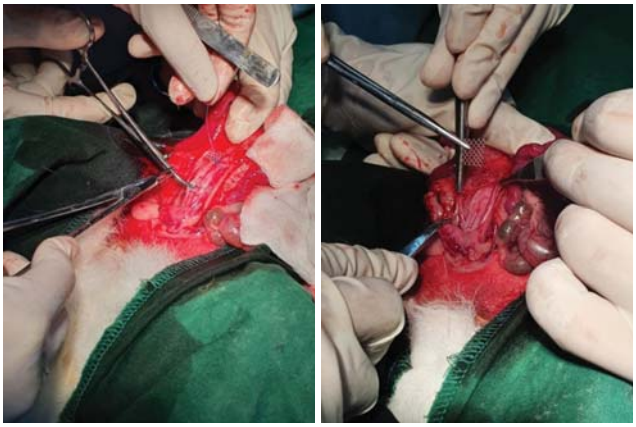

Figure 1. Mesh implantation in rabbits' vagina[25]

Many factors could affect the mesh-host tissue integration. These factors will work together during each phases to determine the degree of integration between the mesh and tissue. In previous studies, these factors were inflammatory response, fibroblast proliferation, angiogenesis, and infection. Moreover, the integration of implanted meshes and healing process depend on the intrinsic mesh characteristics such as the primary material, filament structure, and pore size.[17]

Various mesh materials have been used to repair disorders of the pelvic floor. Based previous studies, it can be concluded that polypropylene (PP) mesh has an appropriate biomechanical property and is adequate to repair pelvic floor abnormalities.[18] Polypropylene mesh is also the gold standard material for treating urogynecology cases. It poses a lower risk of inflammation than other materials.[12,17] Previous studies found that PP mesh could induce milder foreign body reactions than other synthetic materials, while polyester mesh showed a more significant foreign body reaction.[12,17]

Platelet-Rich Plasma Roles in Mesh-Host Tissue Integration

Platelet-Rich Plasma (PRP) is known to contain several growth factors such as Interleukin 6, Interleukin 8 (IL-6, IL-8), and vascular endothelial cell growth factor (VEGF), all of which could accelerate the wound healing process by lowering inflammatory response while also increasing angiogenesis and collagen deposition.[19] The exact mechanism of PRP's role in the wound healing process, especially in postmenopausal/ hypoestrogenic conditions, has not been fully understood yet.

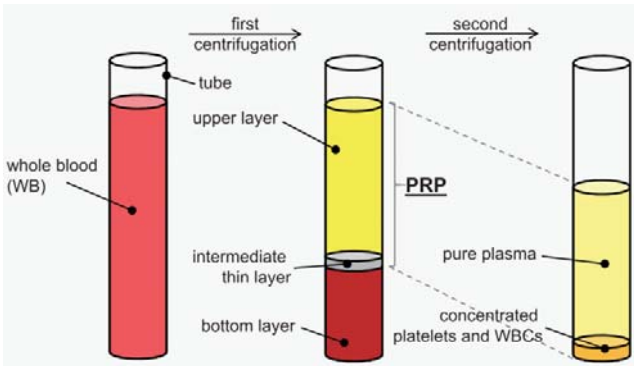

Figure 2. Platelet-rich plasma (PRP) preparation[20]

Studies on the effect of PRP on mesh-host tissue integration are scarce, and each has its limitations. Several studies showed a significant decrease in the expression of proinflammatory cytokines IL-17 and IL-1β with increased CD-31 expression and collagen deposition in the meshes implanted with PRP compared to those without PRP. The addition of PRP to the surface of the mesh implanted in adult rabbits decreased the number of inflammatory cells on the 30th-day post-implantation. However, this study was using non-hypoestrogenic adult rabbits, even though POP is more prevalent in menopausal women.[21] Another study showed that PP meshes coated with PRP had lower inflammatory infiltration within 30 days after mesh implantation than those without PRP. There was also an increase in collagen III deposition at 90 days after implantation.[22] Another in vitro study was conducted on 7 different types of mesh combined with PRP. The result showed that after 6 weeks of mesh implantation combined with PRP, reduced adhesion was observed in all meshes, and biocompatibility of

the mesh had improved. Moreover, mesh coated with PRP showed less severe adhesion, reduced hernia recurrence, increased angiogenesis, increased neovascularization, and improved mesh integrity.[23]

The results of a study conducted by Dimitri et al. on autologous plasma utilization in treating POP and SUI showed that this procedure was relatively safe and did not increase perioperative complications.[24] They also performed a separate analysis on the presence of growth factors in PRP and showed a significant increase in PDGF, VEGF, TGF-b1, and EGF compared to the concentrations in whole blood. Platelet-derived growth factors play an essential role in the early phase of wound healing. The application of PRP to damaged tissues plays a role in USL regeneration by modulating tissue healing. These studies have shown that PRP can improve tendon and ligament healing. Therefore, PRP application has a promising role to improve mesh-tissue integration and further research is needed.[25]

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