Clinical Research

A randomized control trial of platelet-rich plasma in supporting the recovery of postpartum levator ani muscle trauma

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ABSTRACT

BACKGROUND Pelvic floor dysfunction (PFD) is mostly caused by childbirth levator ani muscle (LAM) trauma. We hypothesized that platelet-rich plasma (PRP) therapy could support the recovery of LAM in postpartum trauma.

METHODS A prospective, single-blind, randomized control study was enrolled in primigravid women from November 2016 to July 2019 at 21 health facilities in Jakarta, Indonesia. Subjects were injected with autologous PRP or placebo at LAM during perineorrhaphy after childbirth. The primary outcome was regaining LAM strength and reducing levator hiatal area at 3 months postpartum. The LAM strength was examined by perineometer (cmH_2O), and levator hiatal area was examined by transperineal ultrasound (cm^2) at antenatal and 3 months after delivery. Mann–Whitney *U* test and Wilcoxon signed-rank test were used for analysis. The study was registered in clinicaltrials.gov: NCT03021954.

RESULTS Among 240 women, 58 were eligible for analysis. There were no differences in LAM strength and levator ani hiatal area at 3 months postpartum between the two groups ($p = 0.583$ and $p = 0.185$, respectively).

CONCLUSIONS PRP therapy did not show a difference in the muscle recovery healing process.

KEYWORDS obstetric labor complication, parturition, pelvic floor disorder, platelet-rich plasma, randomized controlled trial

Pelvic floor dysfunction (PFD) is a pathological condition of pelvic floor muscle weakness, most commonly caused by a vaginal birth process.[1] More than 46% of women with a history of vaginal birth have PFD. PFD occurs due to multiple structure disruptions, including levator ani muscles (LAMs), anal sphincter, and perineum, and causes symptoms of urinary and fecal incontinence.[2] LAM defect is classified into macro- and microtrauma. Macrotrauma, also called avulsion, is a complete detachment of LAM from the inferior pubic ramus. Meanwhile, microtrauma, also called ballooning, is an over distention of the LAM. Both are two independent risk factors for PFD and lead to pelvic organ prolapse (POP) and stress urinary incontinence (SUI).[3] The prevalence of SUI 3 months after delivery in Indonesia was estimated at 20.1%, while primiparous women with vaginal delivery had a 2.1 times higher risk of developing SUI.[4] Unfortunately, postpartum SUI treatment is still limited to lifestyle and pelvic floor rehabilitation.[5] The treatment of POP mostly starts

when symptoms have already appeared, which only 5–20% of them, whereas almost half of women over 50 years of age with a history of vaginal birth have asymptomatic POP based on physical examination. Thus, early detection and treatment can help prevent patients from developing severe and symptomatic PFD. Treatment can begin with LAM defects such as microtrauma ballooning, which currently only has conservative-type pelvic floor muscle exercises as standard treatment. Optimal muscle healing and early intervention after muscle injury during vaginal birth are the keys to preventing the development of PFD and POP.

In the early muscle regeneration process, activated platelets will release cytokines and growth factors (GFs) such as platelet-derived growth factors (PDGFs), vascular endothelial growth factors (VEGFs), epidermal growth factors (EGFs), basic fibroblast growth factors (bFGFs), insulin-like growth factor-1 (IGF-1), and transforming growth factor-beta 1 (TGF-β1).[6] Those GFs are the key to tissue recovery and promising therapy. However, GFs are unstable and have a short half-life. One of the efforts to get a more stable and longer half-life is using GF, which is utilized from platelet-rich plasma (PRP). PRP is centrifugated blood with concentrated platelets and a high level of GF. When blood is centrifugated, the platelets are broken, and high amounts of GF are contained in the PRP.[7] Thus, PRP may be a promising and feasible therapy in the pelvic muscle healing process.

PRP therapy has been widely studied in the field of sports medicine for muscle treatment. Rossi et al[8] reported that the use of PRP in an athlete's acute muscle injury significantly accelerated the duration of muscle recovery. Regarding these findings, we hypothesized that PRP could enhance the recovery of most skeletal muscle and cartilage injuries. However, the studies are still limited, particularly in the urogynecology field, which is also related to skeletal muscle. In the urogynecology surgery field, Atılgan and Aydın[9] reported that PRP injection into pubocervical fascia induced faster healing in cystocele surgery and prevented a recurrence. These findings gave fresh hope to other urogynecology cases, particularly in postpartum LAM trauma that was often treated when it had developed into POP, not early on. This study aimed to explore the role of PRP in enhancing LAM recovery in postpartum trauma in the form of normal levator hiatal area and LAM contraction strength.

METHODS

This was a prospective, single-blind, randomized control study. Subjects were recruited from the antenatal clinic at Primary Health Care of Setiabudi, Pancoran, Tebet, Jatinegara, Matraman, Pulo Gadung, Cakung, Gambir, Kemayoran, Senen, Cempaka Putih, and Menteng; Secondary and Tertiary Hospitals in Jakarta: Tarakan General Hospital, Pasar Minggu General Hospital, Tebet General Hospital, Rawasari Hospital, Budi Kemuliaan Hospital, Persahabatan Hospital, YPK Mandiri Mother and Child Hospital, and Evasari Awal Bros Hospital; and private midwife clinic around Jakarta, Indonesia between November 2016 and July 2019. A total sampling method was used. The minimal sample size calculated for this study was 23 subjects for each group (95% confidence interval, power 90%, $\beta = 0.10$, $\alpha = 0.05$, expected difference = 5 cm^2, subjects should have at least 5 cm^2 hiatal area difference after PRP treatment in the intervention group). With a 20% additional for anticipating loss to follow-up subjects, the minimal sample size needed was 28 for each group. Moreover, 90% was used to preserve a good study calculation.[10] A sequential numbering method was also used to maintain blinding and was done per protocol analysis.

The inclusion criteria were primigravid women aged 20–40 years in the last trimester of singleton pregnancy with normal estimated fetal weight (2,500–4,000 g), had planned vaginal delivery, agreed to take part in the research, had a clear address and telephone number that could be contacted, and provided a written informed consent. The exclusion criteria were had a history of pelvic floor muscle weakness before pregnancy, had a history of pelvic area surgery, had avulsion of the LAM based on ultrasound before and after delivery, had hemodynamic instability at delivery, had thrombocytopenia (platelets <150,000/µl) at sample recruitment, had anemia (hemoglobin <10 g/dl) at the time of sample recruitment, had sepsis, had an infection at the site of injection, used oral corticosteroids in the last 2 weeks, smoked, had cancer (hematopoietic or bone), had cesarean section delivery, had no perineorrhaphy procedure after delivery, had an acute coronary syndrome, and had rhabdomyolysis. The primary outcome measurement was the levator hiatal area examined by transperineal ultrasound (cm^2) and LAM strength examined by perineometer (cmH_2O) at antenatal, 40 days, and 3 months postpartum.

PRP preparation

Pure PRP was prepared using a PRP-double-spin (PRP-DS) method. PRP-DS method produced low leukocytes containing PRP as the centrifugation of the blood was carried out twice to avoid an over-inflammation reaction.[11]

PRP was prepared as a standard preparation protocol developed from Hayandra Lab[12] with a modification without adding a calcium activator or light activation since the preparation would be injected locally. Karina et al,[12] who studied about platelet count in PRP prepared with Hayandra Lab's protocol, found 1.3 million thrombocytes/µl in each PRP. The preparation and injection of PRP were carried out alternately at all research sites by a team of four doctors who had received training in processing PRP and could perform the same standard protocol to produce the same thrombocyte level in each PRP processing. Subjects were then explained about the procedure. All patients had blood collection during admission at the health center for childbirth. Before blood collection, they were positioned in a comfortable sitting or lying position. PRP was prepared immediately when they entered the active phase of labor. The blood sample was collected by taking eight tubes of venous blood (5 ml each). The tube was put into a centrifugation machine and rotated at 3,000 rpm for 10 min. Only one centrifuge was used per PRP production. After centrifugation was completed, plasma was taken with a sterile pipette and put into two balanced tubes, then centrifuged again at high speed for 10 min. Then, the upper plasma was removed, leaving 2.5 ml. It was then put into one tube, so the volume became 5 ml and was shaken with a sterile pipette. PRP liquid was stored in the refrigerator until the time of injection.

Randomization and subjects' allocation

At the antenatal visit, the subjects were given informed consent and recorded to the subject list. Permuted block randomization was performed with computerization after the minimal sample was met. The randomization was done by a third observer to maintain balanced and blinded subject allocation into the intervention and control groups. The intervention group received 1% lidocaine injection and autologous PRP injection at LAM during perineal repair, while the control group only received infiltrated 1% lidocaine injection (as a placebo).

Blinding procedure

All subjects were not informed which intervention was given. The examiner of pre-intervention and post-intervention measurements and the birth assistant were blinded. We did not blind the doctors who gave the injection and did the perineal repair since 1% lidocaine and PRP had a different appearance. It was not possible to keep blindness of the doctor team who gave the injection. Nonetheless, the examination and injection were done by different doctors to maintain the blinding process.

Control *versus* intervention groups

All deliveries in both groups were assisted by certified healthcare providers with a national standardized procedure. The perineal repair and injection were performed by our trained doctors and supervised by a urogynecologist. All doctors were previously standardized to handle the perineal repair and injections. A 1% lidocaine infiltration was injected into all subjects for the analgesic procedure before perineal repair. During perineal repair, the intervention group was injected 5–10 ml PRP (not exceeding 10 ml) in three sites and injections, two injections at both origin or insertion of LAM (left and right side) intramuscularly, and one injection at perineorrhaphy area. To identify the puncture site at LAM, an index finger was placed parallel to the urethra with the fingertip on the bladder neck level and its palmar surface pressed the posterior/dorsal of the pubic symphysis to identify the origin and insertion site of LAM.[13] The finger palpated muscle between the urethra medially and the origin or insertion of the puborectalis muscle laterally. Aseptic and antiseptic procedures were performed before the injection. We did not give additional saline in the control group since PRP was injected in a small volume and considered would not have a significant difference, while additional saline might interfere with the natural healing process.

Follow-up and outcome measurement

All subjects were given the national standard postpartum therapy and controlled by certified healthcare providers. They underwent the measurement of levator hiatal area and LAM strength at 40 days postpartum to explore the partial healing process and at 3 months postpartum to explore the complete healing process. The measurement

was performed with the same device used in the pre-intervention examination. The numerical measurement of the examinations was considered the primary outcome. The examination was performed by different certified urogynecologists. Levator hiatal area that measured ≥25 cm^2 during valsalva was considered widened or ballooning. However, the LAM that had any attachment defect with levator-urethral gap length ≥2.5 cm at tomographic ultrasound imaging feature during levator contraction was considered as avulsion.[14] Subjects with avulsion were excluded since the reattachment in avulsion was little known, possibly only scar formation.[15] We also examined LAM strength using a perineometer and digital palpation of LAM tone based on a Modified Oxford Grading Scale assessment with an interval limit from 0 (no contraction) to 5 (strong contraction).[16] All subjects were interviewed in each follow-up visit whether any side effects occurred, and the visual analog scale was used for pain assessment. They were also examined for any sign of allergy and infection at the injection sites. All side effects were recorded until 3 months postpartum.

Statistical analysis

The data were analyzed using SPSS software version 25.0 (IBM Corp., USA). Data distribution was tested for normality using Kolmogorov–Smirnov test and analyzed using Mann–Whitney *U* test for comparative study between groups (independent analysis) and Wilcoxon signed-rank test for a comparative study before and after intervention in each group (dependent analysis). Variables were expressed as mean (standard deviation [SD]) or median (interquartile range [IQR]) according to the data distribution and categorical variables as a percentage (%). A $p<0.05$ was considered statistically significant.

Ethical statement

This study had been reviewed by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia (No: 993/UN2.F1/ETIK/2016). The data were analyzed anonymously to maintain confidentiality.

RESULTS

Of 240 primigravid women initially enrolled the study, 58 were dropped out because 53 had moved back to their hometown and could not come to the clinic, and 5 had avulsion. Moreover, 23 subjects had microtrauma ballooning (23/63, 37%), with 11 had already been detected antenatally (11/63, 17%). A total of 58 subjects successfully followed the examination until the end of the study (Figure 1).

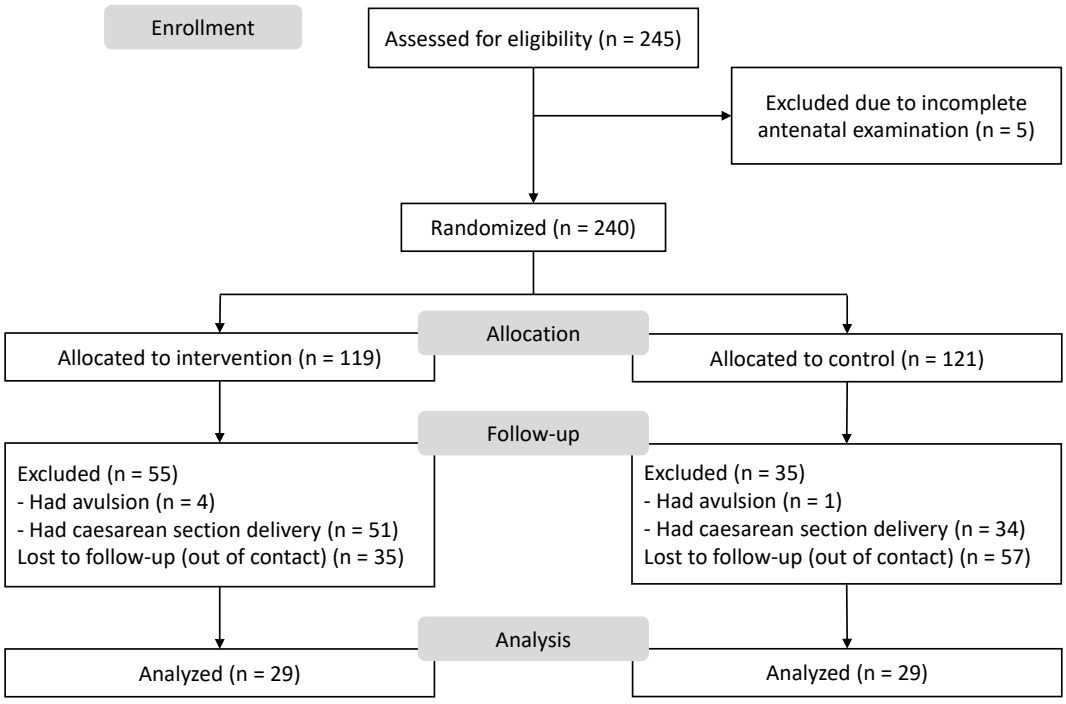

Figure 1. Flow diagram of subject recruitment

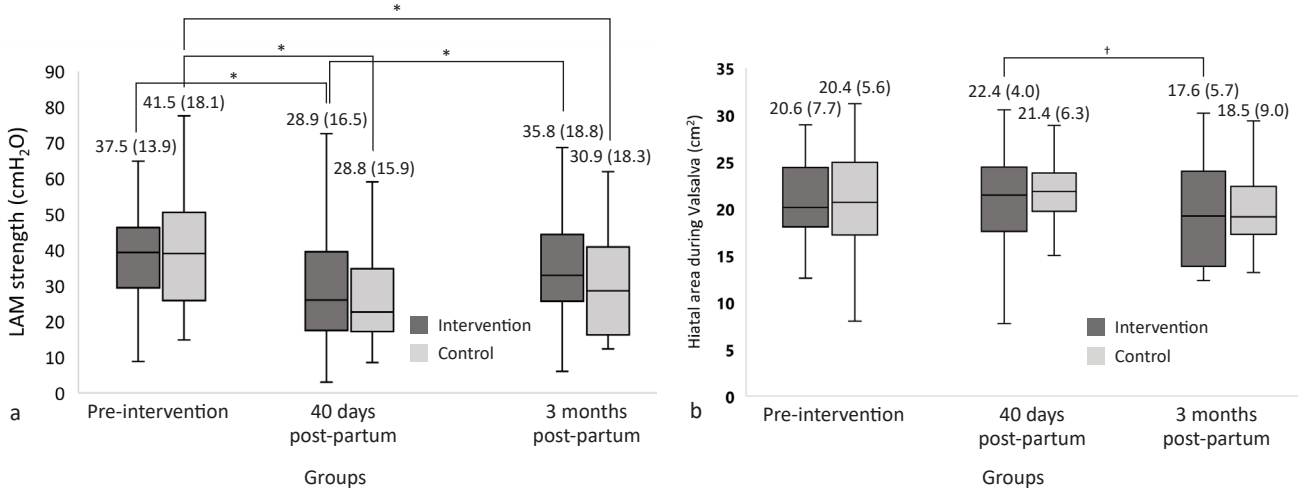

Figure 2. Outcome measurement in the intervention and control groups. (a) LAM strength (cmH_2O) presented in mean (SD); (b) hiatal area measurement presented in median (IQR). IQR=interquartile range; LAM=levator ani muscle; SD=standard deviation
*Dependent *t*-test, $p \leq 0.001$; †Mann–Whitney *U* test, $p = 0.004$

Pre-intervention and subject characteristics

Each intervention and control group consisted of 29 subjects. The median (IQR) ages of subjects were 31 (6) years in the intervention group and 25 (5) years in the control group ($p = 0.001$). There was no significant difference in infant birth weight between groups (intervention group = 3.042 [SD = 436] g; control group = 3.100 [SD = 460] g; $p = 0.333$), and no fetal macrosomia in all subjects. There were also no differences in the incidence of prolonged second-stage labor (>120 min) ($p = 0.640$), the use of vacuum ($p = 0.389$), and the episiotomy procedure ($p = 1.000$) between groups. Episiotomy was performed in 72.4% of subjects. The median (IQR) of the hiatal area during valsalva in the pre-intervention measurement was not significantly different between groups (intervention group = 20.6 [7.7] cm^2; control group = 20.4 [5.6] cm^2; $p = 0.957$). Likewise, the mean of LAM strength was not significantly different between groups (intervention group = 37.5 [13.9] cmH_2O; control group = 41.5 [18.1] cmH_2O; $p = 0.621$).

Levator hiatal area during valsalva and levator ani strength post-intervention

The levator hiatal area during valsalva and LAM strength in the independent group analysis had insignificant results ($p = 0.583$ and $p = 0.185$, respectively). However, the dependent analysis showed a significant tightening of the levator hiatal area in the intervention group after 40 days postpartum ($p = 0.004$) and better improvement after 3 months postpartum compared with the control group even though it was not statistically significant (20.6 [IQR = 7.7] to 17.6 [IQR = 5.7] cm^2 *versus* 20.4 [IQR = 5.6] to 18.5 [IQR = 9.0] cm^2). The LAM strength was significantly different between the control and intervention groups. The LAM strength in the intervention group showed a significant decrease after 40 days postpartum ($p \leq 0.001$) but significantly increased again after 3 months postpartum ($p \leq 0.001$), even almost equal to the pre-intervention strength (37.5 [SD = 13.9] to 35.8 [SD = 18.8] cmH_2O; $p = 0.29$). On the contrary, in the control group, the LAM muscle was significantly decreased after 40 days ($p = 0.208$) and 3 months postpartum ($p = 0.001$) (Figure 2).

Side effect

No subject reported any adverse effects, signs of infection, and allergy during intervention and follow-up until 3 months postpartum.

DISCUSSION

In this study, PRP did not improve LAM strength and levator hiatal area at 3 months postpartum. Although age differences did not affect PRP on muscle healing,[17] there were improvement in the recovery of LAM in both groups. In all cases, the area of the levator hiatal in the intervention and control groups became larger at 40 days postpartum before going smaller at 3 months postpartum. Pregnancy itself contributed to pelvic floor anatomy changes through hormonal and mechanical changes. The levator hiatal area and distensibility of the levator hiatus were increased. These conditions may have a role in developing PFD.[18]

At the initial measurement before childbirth, the levator hiatal area during valsalva in the intervention group was larger than the control group, but it became smaller at 3 months postpartum (Figure 2).

LAM overdistention in a vaginal delivery causes a significant distention of muscle and pudendal nerve.[19] This condition may cause permanent nerve damage. At the beginning of the healing process, thrombocytes release GFs (for coagulation, inflammation, and angiogenesis). Activated GFs contained in PRP have a major role in accelerating the healing process of LAM. These GFs (PDGF, VEGF, EGF, bFGF, IGF-1, and TGF-β1) help muscle cells, vascular, and connective tissue muscle healing by suppressing inflammatory mediator and synthesizing regenerative protein.[7]

Subjects in both groups had decreased pelvic muscle strength at 3 months after childbirth. However, the LAM contraction strength in the intervention group came back into nearly their strength before childbirth, compared with before childbirth and 3 months postpartum, and revealed no significant difference (p = 0.29). This shows that the healing process nearly reaches its initial strength. However, the pelvic strength in the control group was significantly decreased at 3 months postpartum compared with before childbirth (p = 0.001), showing a non-optimal healing process to reach the initial strength (Figure 2).

Atılgan and Aydın[9] performed a PRP therapy for cystocele repair, and the injection was administered to the pubocervical fascia. They obtained satisfactory results, such as low cystocele recurrence rate, reduced patient symptoms assessed from the low score of the pelvic floor distress inventory questionnaire, and a higher level of patient global impression of improvement questionnaire in evaluating patient satisfaction. Cochrane review by Maher et al[20] stated that high-grade cystocele cases had a high recurrence rate. Improvement of cystocele symptoms indicates increased muscle strength, which supports the pelvic organs. The effect of PRP, which can increase the recruitment, proliferation, and differentiation of cells involved in the tissue regeneration process, provides an advantage in the muscle healing process compared with the non-PRP injection group.

The effect of PRP has also been shown to increase the healing of skeletal muscles, especially tendons. Zhang et al,[21] who conducted *in vitro* culture trials of PRP-clot releasate (PRCR) using rabbit tendon, found an increase in tendon stem cells (TSCs) in tenocytes. There was a change in the shape and number of fibroblast phenotypes, and TSC did not stimulate differentiation into non-tenocyte cells (adipocytes, chondrocytes, and osteocytes) that would produce fat, mucoid, and calcified tissue. These cells are frequently seen in chronic tendon injuries (tendinopathy). These findings were confirmed by de Mos et al[22] who performed an *in vitro* trial of human hamstring tendons aged 13–15 years. Samples were taken while hamstring tendon release was performed, then cultured for 14 days with PRCR. There was a progressive increase in the number of new collagen cells at 4, 7, and up to 14 days of culture. In addition, there was an increase in VEGF-A, where the increase in VEGF is an intrinsic mechanism of the angiogenesis process, which is part of tissue recovery. Based on these *in vitro* studies, the *in vivo* use of PRP in humans with tendon injuries could be safely administered and stimulate collagen proliferation and production.[23]

Wu et al,[24] in the field of orthopedics, performed an intra-articular injection of PRP in patients with osteoarthritis and proved a significant increase in knee strength, which reduced the level of pain, stiffness, and disability of the patient. However, they still suggested additional muscle training to improve muscle recovery. Although positive results were found in several studies on skeletal muscle recovery, this study found a negative result for PRP therapy on LAM healing process. However, PRP therapy could maintain pelvic floor muscle contraction strength back to near the pre-birth state.

Since most cases were obtained without postpartum levator ani trauma (macro or micro), where 57% (36/63) had normal muscle, the wound healing of the two groups did not seem different. In cases without trauma, we thought the LAM physiologically could heal spontaneously without PRP. Dietz et al[3] stated that there were two types of levator hiatal trauma called avulsion (major trauma) and ballooning (minor trauma) of the levator hiatal. These were two independent risk factors in the incidence of POP. Moreover, ballooning of the levator hiatal can be a risk factor for the traumatic avulsion of the LAM. Nevertheless, no other similar studies have compared the PRP therapy effect on LAM healing. PRP therapy on LAM trauma is expected to give better results than non-LAM trauma for future studies, thus providing a similar result to other studies on PRP.

This study had several limitations. Most of the subjects had normal pelvic floor muscles after giving birth. Involving subjects with pelvic floor muscle trauma (ballooning or avulsion trauma) in future studies could give a different result for PRP therapy. Due to limited resources, we could not make a similar appearance of a placebo to blind the doctors and give the exact same treatment between the control and intervention groups. Furthermore, we only educated each subject to do pelvic floor muscle training without monitoring it. Future studies might need to improve these limitations for better evidence. Since PRP therapy is autologous blood with a high amount of platelet, there were no side effects reported after PRP injection in this study. A similar result was also found in a study in India that there was no major adverse effect of PRP injection for both short- and long-term follow-up.[25,26] In conclusion, PRP therapy has not been showing differences in accelerating LAM recovery.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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REFERENCES

1. Pangastuti N, Sari DC, Santoso BI, Agustiningsih D, Emilia O. [Risk factors for pelvic organ prolapse in women with history of vaginal delivery in Yogyakarta]. Maj Kedokt Bandung. 2018;50(2):102–8. Indonesian.
2. Davila GW, Ghoniem GM, Wexner SD, editors. Pelvic floor dysfunction: a multidisciplinary approach. London: Springer; 2006.
3. Dietz HP, Franco AV, Shek KL, Kirby A. Avulsion injury and levator hiatal ballooning: two independent risk factors for prolapse? An observational study. Acta Obstet Gynecol Scand. 2012;91(2):211–4.
4. Fakhrizal E, Priyatini T, Santoso BI, Junizaf J, Moegni F, Djusad S, et al. Prevalence and risk factors of persistent stress urinary incontinence at three months postpartum in Indonesian women. Med J Indones. 2016;25(3):163–70.
5. Sénat MV, Sentilhes L, Battut A, Benhamou D, Bydlowski S, Chantry A, et al. Postpartum practice: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). Eur J Obstet Gynecol Reprod Biol. 2016;202:1–8.
6. Wroblewski AP, Mejia HA, Wright VJ. Application of platelet-rich plasma to enhance tissue repair. Oper Tech Orthop. 2010;20(2):98–105.
7. Dhurat R, Sukesh M. Principles and methods of preparation of platelet-rich plasma: a review and author's perspective. J Cutan Aesthet Surg. 2014;7(4):189–97.
8. Rossi LA, Molina Rómoli AR, Bertona Altieri BA, Burgos Flor JA, Scordo WE, Elizondo CM. Does platelet-rich plasma decrease time to return to sports in acute muscle tear? A randomized controlled trial. Knee Surg Sports Traumatol Arthrosc. 2017;25(10):3319–25.
9. Atılgan AE, Aydın A. Cystocele repair with platelet-rich plasma. Indian J Surg. 2021;83:726–30.
10. Teare MD, Dimairo M, Shephard N, Hayman A, Whitehead A, Walters SJ. Sample size requirements to estimate key design parameters from external pilot randomised controlled trials: a simulation study. Trials. 2014;15:264.
11. Lana JF, Huber SC, Purita J, Tambeli CH, Santos GS, Paulus C, et al. Leukocyte-rich PRP versus leukocyte-poor PRP - The role of monocyte/macrophage function in the healing cascade. J Clin Orthop Trauma. 2019;10(Suppl 1):S7–12.
12. Karina K, Ekaputri K, Biben JA, Purwoko RH, Sibuea TP, Astuti SL, et al. Evaluating the safety of intravenous delivery of autologous activated platelet-rich plasma. J Health Sci. 2021;11(2):61–5.
13. Dietz HP. Pelvic floor muscle trauma. Expert Rev Obstet Gynecol. 2010;5(4):479–92.
14. Memon HU, Blomquist JL, Dietz HP, Pierce CB, Weinstein MM, Handa VL. Comparison of levator ani muscle avulsion injury after forceps-assisted and vacuum-assisted vaginal childbirth. Obstet Gynecol. 2015;125(5):1080–7.
15. Shek KL, Chantarasorn V, Langer S, Dietz HP. Does levator trauma 'heal'? Ultrasound Obstet Gynecol. 2012;40(5):570–5.
16. Schüssler B, Laycock J, Norton PA, Stanton SL. Pelvic floor re-education: principles and Practice. 1st ed. London: Springer; 1994. p. 190.
17. Trevisson B, Becerro-de-Bengoa-Vallejo R, Sevillano D, González N, Losa-Iglesias M, López-López D, et al. Age-based inter-subject variability in platelet and white blood cell concentrations of platelet-rich plasma prepared using a new application to blood separation system. Int Wound J. 2022;19(2):362–9.
18. van Veelen GA, Schweitzer KJ, van der Vaart CH. Ultrasound imaging of the pelvic floor: changes in anatomy during and after first pregnancy. Ultrasound Obstet Gynecol. 2014;44(4):476–80.
19. Petros P. The female pelvic floor: unction, dysfunction and management according to the integral theory. 2nd ed. Germany: Springer Berlin Heidelberg; 2007. p. 260.
20. Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Brown J. Surgery for women with anterior compartment prolapse. Cochrane Database Syst Rev. 2016;11(11):CD004014.
21. Zhang J, Wang JH. Platelet-rich plasma releasate promotes differentiation of tendon stem cells into active tenocytes. Am J Sports Med. 2010;38(12):2477–86.
22. de Mos M, van der Windt AE, Jahr H, van Schie HT, Weinans H, Verhaar JA, et al. Can platelet-rich plasma enhance tendon repair? A cell culture study. Am J Sports Med. 2008;36(6):1171–8.
23. Middleton KK, Barro V, Muller B, Terada S, Fu FH. Evaluation of the effects of platelet-rich plasma (PRP) therapy involved in the healing of sports-related soft tissue injuries. Iowa Orthop J. 2012;32:150–63.
24. Wu YT, Hsu KC, Li TY, Chang CK, Chen LC. Effects of platelet-rich plasma on pain and muscle strength in patients with knee osteoarthritis. Am J Phys Med Rehabil. 2018;97(4):248–54.
25. Gupta PK, Acharya A, Khanna V, Roy S, Khillan K, Sambandam SN. PRP versus steroids in a deadlock for efficacy: long-term stability versus short-term intensity-results from a randomised trial. Musculoskelet Surg. 2020;104(3):285–94.
26. Alam M, Hughart R, Champlain A, Geisler A, Paghdal K, Whiting D, et al. Effect of platelet-rich plasma injection for rejuvenation of photoaged facial skin: a randomized clinical trial. JAMA Dermatol. 2018;154(12):1447–52.