INTRODUCTION
Platelet-rich plasma (PRP) is a modern treatment that has gained worldwide acceptance. PRP was introduced in the early 1950s, and is used in many areas of medicine today. The use of PRP is beneficial and may be even more important in the future. The most common indications were tendon damage (77%), osteoarthritis (68%), muscle damage (57%) and cartilage damage (51%). It is a purified autologous blood product with a higher platelet concentration than whole blood. It is rich in various cytokines and growth factors and has been shown to initiate and enhance healing by stimulating cell migration, cell proliferation, angiogenesis, and matrix synthesis.

BIOMEMOLECULAR OF PLATELET IN NON-HEMOSTATIC FUNCTION
Platelets are involved in many non-hemostatic processes. Interestingly, platelets also convey different meanings depending on the stimulus that activates them. Alpha particles contain many substances that have exactly the opposite effect. So it means a specific mechanism that releases the unique specific content of the particle.

Physicochemical properties of PRP can stimulate cell proliferation, migration, cell migration, cell proliferation, angiogenesis, and matrix synthesis.
PROCESSING METHOD OF PRP

The first volume of whole blood extract is 51 ml (from 8 to 450 ml). There are two steps for spinning. The first spin combination is 3200 rpm for 15 minutes. The average speed for second spin was 3300 rpm (range 200 to 4500 rpm) with an average spin time of 10 minutes (range 2 to 25 minutes). The time interval between processing and intrasite injection was reported for only 27 studies (mean and standard deviation = 14 ± 33 hours with a median of 1 hour). A conical bottom tube is more preferred than a flat bottom tube because the platelet recovery rate will be higher in the flat type before the two above rates are balanced while the conical one dominates.6,9 2-6 ml of platelet-rich plasma is extracted and activated with thrombin to induce the release of platelet growth factor and fibrinogen through thrombin to induce the release of platelet growth factors and polymerisation of fibrinogen into fibre.

A synergistic effect is observed on platelet proteins and plasma.7

A meta analysis study by Chahla et al. (2017) demonstrated that platelet concentrations in initial blood samples were reported in 23 studies with a mean of 381 ± 391 x 10^4 platelets / mL and a median of 234 ± 10^4 platelets / mL. End-stage platelet counts were reported in 27 studies, with a mean count of 1,473 ± 2,211 x 10^4 platelets / mL with a median of 962 x 10^4 platelets / mL. In 57 studies, an increase in platelet counts in starting blood samples was reported, with a median of 5 times (range, 1.2 to 10 times). 59 studies reported a median terminal volume of PRP of 5 mL (range, 2-30 mL) (Figure 1).9

Despite these extensive studies, the optimal dose range for PRP has not been established. One possible explanation for this tolerance is marked individual variability in blood levels of platelet cells and growth factors. Therefore, there is still a need to develop standardized PRP formulation regimens, and accurate composition is critical for evaluating its efficacy as a therapeutic for musculoskeletal disorders.10

Figure 1. Preparation Method of PRP

Figure 2. Histograms of studies reporting a fold increase in platelet count by body part in 57 studies and final PRP volume by body part in 59 studies (Chahla et al., 2017).
CURRENT PRP PRACTICE AND ITS EFFECTIVENESS

Rotator Cuff Injury
The most common cause of pain and disability due to shoulder injuries is a partial or slight rupture of the rotator cuff. Surgical treatment of tears can improve the patient’s outcome, but there are risks of postoperative infection, delayed recovery, shoulder stiffness, and damage to other parts of the tendon. PRP is considered an effective treatment for rotator cuff tears and is less invasive than surgical treatment. Improve pain scales, shoulder function and tear size. Several studies have investigated how the use of PRP during arthroscopic rotator cuff repair (RCR) can improve and accelerate the repair process. There several meta-analysis studies performed by Lin TM et al. (2020) and Hamid MS et al. (2021) show that in the short term (3-6 weeks) and medium-term (12 weeks), the effectiveness of PRP injection and group of control was indistinguishable in terms of outcomes (pain scale reduction and functional improvements). PRP injection also led to significant long-term (> 24 weeks) pain relief (SMD: 0.42, 95% CI: 0.12-0.72, without heterogeneity). Nevertheless, functional improvement in the long term, PRP injection was not more effective than the control group (SMD: 1.20, 95% CI: -0.20-2.59, with heterogeneity). However, side effects were found in only one study reported by Schwitzgubel et al. (2019), for example frozen shoulder extension and tears. Therefore, PRP can still be considered as a safe treatment option for tendinopathy of the rotator cuff. Constant scores (Visual Analog Scale for pain (VAS), UCLA Score (UCLA), Simple Shoulder Test (SST), Recurrence Rerate Rate, American Shoulder and Elbow Surgeon (ASES)) were significantly better in patients receiving PRP rich in leukocytes compared to the PRP group with low leukocytes. Patients treated with PRP gel reported higher Constant scores than the control group, whereas patients treated with non-gel PRP did not report higher scores on VAS. Regardless of the PRP formulation (PRP for low leukocytes: OR, 0.36, PRP rich in leukocytes: OR, 0.32) or the use of a gel (without gel: OR, 0.42, gel: OR, 0.17), the chance of return to long term retear has reduced.

Osteoarthritis
Osteoarthritis (OA) is a widespread and common degenerative disease involving joint damage, inadequate healing response and progressive deterioration of joint structure, usually affecting the knee or hip joint. This is a serious public health problem worldwide and is expected to increase rapidly as the population ages and obesity rates increase. OA is the most common musculoskeletal disorder in elderly patients, with a prevalence of 10% in the world population over the age of 60. The knee is often symptomatic and can lead to pain, disability and high health costs. New non-surgical treatments, including replacement of intra-articular viscosity and PRP injections, have been proposed to treat the early stages of osteoarthritis to provide symptomatic relief and delayed surgery. The experimental study also showed that in the one-month follow-up study, significantly lower levels of interleukin (IL)-6 and tumor necrosis factor (TNF)-α were observed in the PRP group compared to the hyaluronic acid group (p <0.05). One study found that a total of 10 billion platelets in the PRP formula are needed for long-term protection of cartilage for up to a year in people with moderate osteoarthritis of the knee. The application of PRP in cases of early knee OA (Kellgren-Lawrence grade II) is probably valid. A meta-analysis study by Dai WL et al. (2016) showed that at 12 months post-injection, PRP was associated with significant reductions in pain (WOMAC pain score, mean difference -2.83) and function (WOMAC functional score, mean difference -12.53; WOMAC total score is better than Hyaluronic acid. WOMAC pain and function scores after 12 months exceeded the clinically important minimal difference (-0.79 for WOMAC pain and -2.85 for WOMAC function). Compared with control saline solution, PRP injection appeared to be more effective in controlling and relieving pain in terms of WOMAC pain score and functional improvement (WOMAC Functional Score) at 6 and 12 months post-injection. The study also found that PRP did not increase the risk of side effects compared to HA and saline. In addition, the meta-analysis of Nie LY et al. (2021) showed no difference in the efficacy of platelet-rich plasma (PRP) injections in the treatment of knee OA and between low-leukocyte PRP (LP-PRP) and leukocyte-rich PRP (LR-PRP). A meta-analysis by Garcia et al. (2020) and Medina et al. (2021) showed that the use of PRP for the treatment of OA, intra-articular hip disorders, including acetabular syndrome (FAIS), and labial pathology has shown reductions in pain and outcomes in patients for up to one year. However, there is no statistically difference at short-term VAS scores (less than 2 months, P=0.27), mid-term (4 to 6 months, P=0.85), or long-term follow-up (12 months, P=0.42). At medium-term follow-up, PRP can be helpful and safe for people with Hip OA. However, the benefits of other procedures such as hyaluronic acid are not clear.

Elbow Ulnar Collateral Ligament
Elbow injuries to the ulnar ligament (UCL) are most commonly diagnosed among professional baseball players because of repeated valgus pressure back onto the elbow during the injury. The diagnosis of UCL injury was confirmed by history, physical examination and radiography. Magnetic resonance imaging (MRI) is currently the standard imaging method for diagnosing UCL injuries. Kato et al. (2019) A follow-up study showed that 26 of 30 athletes were able to return to their pre-injury level of game within 6 months of surgery, with a median time of 12.4 weeks (range: 10-18 weeks). The median follow-up period was 54.2 weeks (range: 26-148). The average VAS and DASH scores rose from 53.5 to 17.2 and from 81.7 to 24.2, respectively. The mean ulnar-humeral joint distance decreased from 3.81 mm to 3.45 mm with valgus pressure. The DASH average improved from 83.8 to 17.8 and from 77.5 to 36.7 in proximal and distal tears. The mean ulnar-humeral joint distance with valgus pressure decreased from 3.64 to 3.21 mm and from 4.14 to 3.92 mm in proximal and distal tears. Otherwise, a retrospective study by Chauhan et al. (2019), the use of PRP in professional baseball players has been exacerbated as part of a standard non-surgical treatment program. In addition, no significant differences were observed in physical examination findings or performance measures between these
patients. Comparing MRI findings, athletes without adequate non-surgical treatment had distal dissections and those without had proximal fractures. After age adjustment, location and evidence of chronic MRI changes, the risk of failure of non-surgical treatment for distal segment rupture was 12.40 times higher. Long-term follow-up with a mean follow-up of 12 years with standard deviation of 2 years, the total return per game was 85%. There were no significant differences between matched pairs of studies in any performance measure, with an overall recurrence rate of injury 11.1%. Recommendations for PRP preparation have not yet been established, more extensive research and long-term follow-up for the same type of products are needed, and the best recommendations should be made regardless of the condition of elbow pathologies.\(^{31,32}\)

**Lateral Elbow Epicondylitis (Tennis Elbow)**

Lateral epicondylitis (LE), described in 1883 as “tennis elbow” (TE), is the most common pathological condition of the elbow joint. Epidemiological studies describe a prevalence of 1% to 3% in the general population. The report describes the data as 10 percent female.\(^{33}\) In the past, TE was considered an inflammation. But recent studies have shown that only a few inflammatory cells exist. The most common reported mechanisms are microtears and recurrent degeneration of the extensor carpi radialis brevis (ECRB) due to overwork of the muscles. Recently, micro-instability of posterolateral aspect has been suggested as a possible cause for TE.\(^{33}\) A meta-analysis study by Arirachakaran et al (2016) showed that PRP injections significantly improved VAS and DASH scores compared to corticosteroids. PRP exhibited much better VAS compared to autologous blood injection. Autologous blood for automatic injection carries a greater risk of side effects. Compared with corticosteroids, the relative risk was 1.78.\(^{33}\) Gaspar et al. (2017) have shown that PRP injections are an effective treatment for resistant LE with continuous improvement in pain, strength and function with median follow-up of at least 3 years in a follow-up study.\(^{34}\)

**Medial Elbow Epicondylitis (Golfer Elbow)**

Medial epicondylitis (ME) is less common but resembles lateral epicondylitis. Commonly referred to as “golfer’s elbow” (GE), its incidence is estimated at 1% of the general population. ME was more associated with work activity than exercise, and forced activity was a more significant risk factor than simple repetitive tasks. Although some studies have shown that conservative treatment is the most successful in reducing inflammation and reducing pain, a substantial proportion of ME patients require surgery compared with LE patients (12% and 4%, respectively). MEs must be classified as Type 1 and Type 2. Type 1, which does not involve the ulnar nerve, has a more successful outcome with nonoperative management than type 2, which requires surgery.\(^{32}\) Varshney et al (2017) conducted a study in which 83 patients with elbow pathologies were randomly divided into two groups (53 patients treated with corticosteroid injections and 33 patients treated with PRP). Reported a 91% improvement in VAS pain score 6 months after PRP injection compared to a 42.2% improvement in the steroid injection group. A limitation of this study is the lack of reports with different results for lateral and medial elbow epicondylitis.\(^{33}\) Boland et al. (2021) conducted a prospective follow-up study in obstinate type 1 MS. After 3.9 years of follow-up, the study showed a statistically significant improvement in time to full mobility (ROM) (42.3 days for PRP vs. 96.1 day for PRP). for surgery, p <0.01) and time for painless condition (56.2 days for PRP and 108.0 days for surgery, p<0.01). Positive results of 80% were found in patients receiving PRP alone and in 94% of patients undergoing surgery. No significant difference was found in the return of activity rates.\(^{36}\) The PRP used in the ME study was inadequate, and PRP therapy was not yet established.

**Acute Muscle Injury**

Muscle injuries account for a third of sports injuries. The incidence of strain in the hamstrings is 15%. Thigh muscle injuries are common in endurance sports such as football, rugby, hockey, and running, and are associated with repetitive, slow, explosive movements. Although there is no absolute and universal treatment plan has been established, it generally includes pharmacological interventions such as conservative treatment, therapeutic exercise, electrotherapy, massage, mobility, and nonsteroidal anti-inflammatory drugs. Nowadays PRP is believed to promote healing, it is increasingly being used as a biologic supplement for muscle injuries.\(^{37,38}\) Basic scientific research has shown that platelet-rich plasma has many positive effects in vitro and in vivo on different cells of the musculoskeletal system, such as muscle cells, tenocytes, and chondrocytes. Meta-analysis by Jeyakumar et al. (2017) and Kunze et al. (2019) also reported improved functional and structural performance, reduced fibrosis, and enhanced muscle regeneration in PRP-treated muscles compared to control muscles. However, the quality of the literature on basic science and clinical research remains limited. Therefore, in clinical studies, the effect is not as pronounced as in basic scientific research.\(^{39,40}\) A meta-analysis by Grassi et al (2018) found that in 6 studies of 374 patients, the time to return to exercise, as estimated in all 6 studies, was significantly shorter in patients treated with PRP, with a mean difference of 7.17. Repetitive injury and complications were similar in both groups. There were no differences in pain, imaging, strength, ROM, and muscle function.\(^{38}\) A systematic review by Nasser AM et al. (2021) showed, at very low levels of evidence, that autologous whole blood versus injection of platelet-rich plasma did not differ in bodily function and mid-term quality of life.\(^{41}\) Seow et al. (2021) show a total of 10 studies were conducted in the PRP group, involving 207 patients with posterior femoral muscle injury and 149 patients in the control group. At the same time, the recovery time between platelet-rich plasma and physical therapy and physical therapy did not favor PRP over physical therapy (mean difference, 5.67 days). The mean incidence of postoperative pain, discomfort, and sciatic nerve irritation complications was 5.2% ± 2.9%.\(^{42}\) More high-quality, large cohort studies are needed to better support or disprove the consensus of systematic reviews and meta-analyses.
Achilles Tendinopathy

Chronic achilles tendinopathy, is a common cause of pain in recreational and competitive athletes. Achilles tendinopathy, often considered an overuse syndrome, causes significant pain and swelling in the area where blood pressure drops 2 to 6 centimeters near the tibial insertion. Conservative treatment usually begins with rest, activity changes, physical therapy, shoe changes, and eccentric exercise. If symptoms do not resolve after 6 months of conservative treatment, more invasive treatment options may be considered. PRP injections have emerged as an alternative treatment for Achilles tendinopathy, which is not resistant to conservative treatment. PRP contains growth factors to speed healing and speed recovery from this condition. Many studies have been carried out in recent years. However, whether PRP has a beneficial effect in chronic Achilles tendinopathy remains controversial.\(^5,\^6\) A systematic study by Madhi et al. (2020) found that the mean VISA-A scores of patients increased from 41.2 points to 70.12 points after PRP treatment, and the mean difference between VISA-A scores was 28.9 points, which was significant compared to other non-operative treatment method.\(^6\) According to a study by Krogh et al. (2016), tendon thickness increased slightly by 0.5 mm after 3 months of follow-up, while Albano et al. (2017) also showed a statistically significant reduction in mean VAS before treatment (6.4 ± 1.4) and after 6 months (1.8 ± 1.7), increased tendon thickness was also observed in magnetic resonance imaging and ultrasound.\(^4,\^5\) Limited evidence supports the conclusion that PRP is no better than other treatments. These results still need to be validated by a large number of heterogeneous randomized controlled studies.\(^46^-^49\)

CONCLUSIONS

In biological theory, the use of platelet-rich plasma in orthopedic clinical practice is important to accelerate and enhance the healing process of musculoskeletal injuries. However, the majority of published literature is secondary and tertiary evidence. Future studies could provide important information about the optimal concentrations of growth factors, platelets and leukocytes required for the desired effect in many specific tissues, as well as the appropriate method of administration and timing of drug application.

CONFLICT OF INTEREST

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REFERENCES