Platelet-Rich Plasma in the Treatment of Hand, Foot, and Ankle Osteoarthritis: A Systematic Review

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Received: November 18, 2020; Published: December 30, 2020

DOI: 10.31080/ecmi.2021.17.01034

Abstract

Platelet-rich plasma (PRP) administration has been considered an ideal approach for the management of symptomatic joint disorders when other conservative treatments fail to reduce the symptoms. In this systematic review, we aim to discuss the effectiveness of PRP in the management of hand, foot and ankle osteoarthritis as reported by previous studies. For that, we conducted a systematic electronic database search for suitable studies from inception till 22nd October 2020 in nine databases. We included original studies with no restrictions on study design, country, language or publication date. Finally, 13 studies were included in the current study. The current literature shows that PRP injection into the ankle was effective in reducing the pain and enhancing the mobility of this joint 24 weeks after the injection measured by the VAS, Japanese Society for Surgery of the Foot (JSSF), and the self-administered foot evaluation questionnaire (SAFE-Q) scales. For the foot, PRP injection significantly improved the pain and movement when compared to the hyaluronic acid (HA) injection; nevertheless, the PRP results were comparable to prolotherapy. For the hand, the patient was able to pursue his daily activities with improved functions, better VAS, DASH scores, and SAFE-Q scores, with a reported high satisfaction from the patient about this treatment modality and its efficacy compared to steroids or lidocaine. However, HA was significantly better at longer outcomes than PRP modality which failed to have a maintained efficacy. In conclusion, among the majority of the studies included, PRP showed a significant improvement in patients receiving for the management of osteoarthritis in small joints involving the hands and feet.

Keywords: Platelet-Rich Plasma; PRP; Arthritis; Hand; Ankle, Feet; Hyaluronic Acid

Introduction

Disorders causing pain in the musculoskeletal system is a frequent condition that affects many people. It has been estimated that almost one-fifth of the older patients suffer from pains in the ankle and foot [1]. Among the various degenerative joint diseases, osteoarthritis has been ranked as the commonest pathology, and the leading disorder that can easily causes disabilities in elderly patients [2,3]. It is well-known that some joints experience osteoarthritis as patients get older with no underlying etiology, however, osteoarthritis involving the ankle and foot joints mostly occurs due to trauma which exposes the subchondral bones [4,5]. The problem with osteoarthritis is that it induces a state of stiffness, pain, and affection of the joint mobility as a result of breaking down the joint cartilages.

This will affect patients’ movements and their abilities to perform their daily activities [6,7]. Additionally, it can easily lead to the development of other morbidities, and complications together with the subsequent high costs [2,3,8]. Accordingly, many approaches have been made based on the economic and prognostic burdens of these events. The management of this disorder is usually conservative where topical capsaicin, thermal modalities, non-steroidal anti-inflammatory drugs (NSAIDs), and steroid intra-articular injections are usually applied [9]. However, once the pathology has been discovered, no treatment has been described as effective in curing the lesion. Therefore, the management of osteoarthritis has been almost exclusively surgical [10-12]. However, such procedures are hard to be conducted on delicate joints that require more careful approaches to avoid unnecessary complications [13,14]. Recent modalities are direct to induce tissue growth and regeneration [15]. Among these, platelet-rich plasma (PRP), has been effectively used to reduce pain and induce the affected chondrocyte growth and regeneration which will reduce the morbidity of joints and improve the outcomes [16,17].

The application of PRP was first introduced in the 1980s and is defined as increased amounts of plasma platelets than what is normally found in the average peripheral blood [18]. Its initial administration was prescribed in the field of hematology, however, it has been frequently used in other fields as surgeries including oral-maxillofacial, plastic and cardiac surgeries in addition to the field of dermatology, ophthalmology, gynecology, and urology [19]. Besides, PRP has been also used in the field of orthopedics for the management of many acute and chronic disorders involving the musculoskeletal system. In addition to reducing the need to perform invasive surgery, PRP administration has been considered an ideal approach for the management of symptomatic joint disorders when other conservative treatments fail to reduce the symptoms. It has been also effectively used in the management of both big and small joints which indicates the effectiveness and viability of this modality [16,17,20].

Aim of the Study

In this systematic review, we aim to discuss the effectiveness of PRP in the management of hand, foot and ankle osteoarthritis as reported by previous studies.

Methods

Search strategy and study selection

The study process was conducted following the accepted methodology recommendations of the PRISMA checklist for systematic review and meta-analysis where registration of the protocol is not mandated [21]. We conducted a systematic electronic database search for suitable studies from inception till 22nd October 2020 in nine databases including Google Scholar, System for Information on Grey Literature in Europe (SIGLE), Scopus, Web of Science (ISI), PubMed, Virtual Health Library (VHL), Clinical trials.gov, metaRegister of Controlled Trials (mRCT) and The WHO International Clinical Trials Registry Platform (ICTRP) databases using the following search term: (platelet-rich plasma OR platelet rich fibrin OR platelet-rich fibrin OR platelet gel OR autologous conditioned plasma OR pure platelet-rich-plasma OR platelets OR platelet concentrate OR prp OR prg OR acp) AND (arthritis OR osteoarthritis OR OA) AND (ankle OR talus OR foot OR hand OR carpal OR trapezio* OR metacarpal OR radio-carpal OR thumb OR talus OR osteochondral). We included original studies
reporting the effectiveness of PRP in the management of hand, foot and ankle osteoarthritis. There were no restrictions on study design, country, language or publication date. Papers were excluded if there were one of the following exclusion criteria: 1) Non-original studies 2) in vitro or animal studies; 4) data duplication, overlapping or unreliably extracted or incomplete data; 5) abstract only articles, reviews, thesis, books, conference papers or articles without available full texts (conferences, editorials, author response, letters, and comments. Three independent reviewers screened titles and abstracts for selecting eligible papers. The further full-text screening was performed to ensure the inclusion of relevant papers in our systematic review. Any disagreement was done by discussion and consulting the senior member when necessary.

Data extraction

The data extraction form was developed by two authors, using a Microsoft Excel file. Three reviewers independently extracted data from included studies using the excel sheet. Data checking was performed through a fourth reviewer. All the disagreements and discrepancies were resolved by discussion and consultation with a senior member when necessary.

Quality assessment

Three independent reviewers evaluated the risk of bias in included studies. For randomized controlled trials (RCTs), the Cochrane’s revised quality assessment tool (RoB 2) was used to assess the quality of each included study [22]. For non-randomized designs, the risk of bias in non-randomized studies - of interventions tool (ROBINS-I) was used [23]. Any discrepancy between the reviewers was solved by discussion.

Results

Search results

Systematic search resulted in 2,747 records; of these 2,426 records were screened using title and abstract after exclusion of duplicates. Title and abstract screening yielded 71 papers eligible for full-text screening. Out of these, we included ten studies, in addition to another three studies from manual search (Figure 1).

![Figure 1: PRISMA flow diagram showing the process of the review.](image-url)
Characteristics and bias of the included studies

Only three of the included studies [24-26] were RCTs while the others were either non-randomized trials, cohorts, case series, or case reports. Sample sizes of the included studies were highly variable ranging from only one patient [27] to 125 patients [28]. The mean ages of the patients in the included studies ranged from 39.5 years [24] and up to 62.9 years [29]. Moreover, the patients’ mean follow up duration ranged from 8 weeks [28] and up to 40 months [30]. The detailed characteristics of the included studies are summarized in table 1.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country</th>
<th>Design</th>
<th>Sample size</th>
<th>Age: mean (SD)</th>
<th>Male (%)</th>
<th>Follow-up</th>
<th>Assessment</th>
<th>Intervention</th>
<th>Control</th>
<th>Aim</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdelfattah, 2020 (27)</td>
<td>Egypt</td>
<td>Prospective interventional</td>
<td>30</td>
<td>52.77 ±6 8.59</td>
<td>-</td>
<td>12 weeks</td>
<td>Joint Palpation for tenderness with grading from IIIV, Provocative tests (Grind test and Lever test), VAS for pain, AUSCAN score, grip and pinch strength</td>
<td>PRP</td>
<td>HA</td>
<td>To compare the effectiveness of PRP versus hyaluronic acid injection in osteoarthritis of thumb carpo-metacarpal joint based on clinical and functional outcome measures</td>
<td>We observed clinical improvement in both groups of carpo-metacarpal osteoarthritis (CMC OA) treated either with single dose of HA or PRP at 4 and 12 weeks follow up. However, HA provide a superior improvement with respect to PRP at 12 weeks follow up regarding VAS for pain, joint tenderness, AUSCAN hand function score, grip and pinch strength. So we support the use of a single hyaluronic acid injection as therapy for thumb CMC OA in preference to PRP injection.</td>
</tr>
<tr>
<td>Akpancar, 2019 (28)</td>
<td>Turkey</td>
<td>Cohort</td>
<td>49</td>
<td>56.08 ±11.30</td>
<td>28.6</td>
<td>360 day</td>
<td>VAS, AOFAS, and AOS</td>
<td>PRP</td>
<td>PrT</td>
<td>To compare PRP and PrT injections for the management of OLT</td>
<td>Both PRP and PrT are efficient and safe methods in treatment of OLT. PrT offers advantages of less cost and minimal invasiveness.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Type</th>
<th>Subjects</th>
<th>Age (SD)</th>
<th>Follow-up</th>
<th>Outcome Measures</th>
<th>Treatment</th>
<th>Comparison</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anghong, 2013 (29)</td>
<td>Thailand</td>
<td>Cohort</td>
<td>12</td>
<td>49.27 (±15.35)</td>
<td>25</td>
<td>Men 15.38 (SD: ±6.9) Months</td>
<td>visual analog scale foot and ankle [VAS-FA] and health-related quality of life scores (Medical Outcomes Study, short-form, 36-item survey [SF-36])</td>
<td>PRP NA</td>
<td>To determine the outcomes and quality of life after platelet-rich plasma therapy in patients with chronic recalcitrant diseases of the hindfoot and ankle and to identify the crucial clinical variables/mm</td>
</tr>
<tr>
<td>Fukawa, 2017 (30)</td>
<td>Japan</td>
<td>Cohort</td>
<td>20</td>
<td>59.3 (±11.4)</td>
<td>24 weeks</td>
<td>VAS, JSSF ankle/hindfoot scale, and SAFE-Q scale</td>
<td>PRP NA</td>
<td>To assess the safety and efficacy of an intra-articular injection of PRP in patients with ankle osteoarthritis.</td>
<td>PRP Intra-articular injections of PRP resulted in no serious adverse effects and significantly reduced pain in the patients with ankle osteoarthritis. PRP treatment can be safe and effective and may be an option in the treatment of ankle osteoarthritis.</td>
</tr>
<tr>
<td>Görmeli, 2015 (24)</td>
<td>Turkey</td>
<td>RCT</td>
<td>40</td>
<td>39.54 (±8.85)</td>
<td>52.5</td>
<td>Mean 15.3 months (range, 11-25 months)</td>
<td>AOFAS and VAS</td>
<td>PRP HA group and placebo group</td>
<td>To compare the effects of HA and PRP as adjunct therapies after arthroscopic microfracture in OLT. Both PRP and HA injections improved the clinical outcomes of patients who underwent operation for talar OCLs in the midterm period and can be used as adjunct therapies for these patients. Because a single dose of PRP provided better results, we recommend PRP as the primary adjunct treatment option in OLT postoperative period.</td>
</tr>
<tr>
<td>Guney, 2015 (31)</td>
<td>Turkey</td>
<td>Cohort</td>
<td>54</td>
<td>40.1 (± 14.7)</td>
<td>59.26</td>
<td>40.34 (±14.89) months</td>
<td>AOFAS, VAS, and FAAM</td>
<td>Microfraction group and Mosaicplasty group</td>
<td>To compare medium-term functional effects of three different treatment modalities in patients with OLT.</td>
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<tr>
<td>Mayo, 2019 (32)</td>
<td>France</td>
<td>CT</td>
<td>3</td>
<td>62 (±3)</td>
<td>33.33</td>
<td>12 months</td>
<td>VAS, DASH and PRWE scores</td>
<td>Platelet-Rich Plasma Mixed-Microfat</td>
<td>NA</td>
</tr>
<tr>
<td>Loibl, 2016 (33)</td>
<td>Germany</td>
<td>CT</td>
<td>10</td>
<td>56.1 (±9.9)</td>
<td>20</td>
<td>6 months</td>
<td>DASH questionnaire, VAS MayoWrist score, The grip strength, and pinch strength</td>
<td>PRP</td>
<td>NA</td>
</tr>
<tr>
<td>Citation</td>
<td>Country</td>
<td>Study Type</td>
<td>n</td>
<td>Mean Score (±SD)</td>
<td>Follow-Up</td>
<td>Outcome Measures</td>
<td>Objectives</td>
<td></td>
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<tr>
<td>Hussein, 2021</td>
<td>Greece</td>
<td>RCT</td>
<td>32</td>
<td>62.9 (±11.03)</td>
<td>12 months</td>
<td>DASH-Q score and VAS</td>
<td>To investigate the superiority of ultrasound-guided intra-articular platelet-rich plasma (IA-PRP) injections compared with corticosteroid injections for the treatment of symptomatic trapezio-metacarpal joint arthritis.</td>
<td></td>
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<tr>
<td>Malahias, 2018</td>
<td>Greece</td>
<td>RCT</td>
<td>32</td>
<td>39.65 (±16.73)</td>
<td>28 weeks</td>
<td>AHFS and VAS</td>
<td>To evaluate the short-term efficacy and safety of platelet-rich plasma (PRP) compared with hyaluronic acid (HA) in reducing pain and disability caused by OCLs of the ankle.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mei-Dan, 2012</td>
<td>Israel</td>
<td>RCT</td>
<td>30</td>
<td>57.5 (±7.9)</td>
<td>17.7 (±6.4) months</td>
<td>VAS and FADI</td>
<td>To assess the clinical effectiveness and feasibility of PRP injections in post-traumatic medium to advanced ankle OA to improve symptoms and delay the necessity for invasive surgical procedures.</td>
<td></td>
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<tr>
<td>Repetto, 2017</td>
<td>Italy</td>
<td>Case Series</td>
<td>20</td>
<td>57.5 (±7.9)</td>
<td>60</td>
<td>PRP</td>
<td>To assess the clinical effectiveness and feasibility of PRP injections in post-traumatic medium to advanced ankle OA to improve symptoms and delay the necessity for invasive surgical procedures.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>MedianaPorqueres, 2019 (37)</th>
<th>Germany</th>
<th>Case report</th>
<th>1</th>
<th>59</th>
<th>100</th>
<th>12 months</th>
<th>VAS, grip and pinch strength, and the Quick-DASH-Q</th>
<th>PRP</th>
<th>NA</th>
<th>To draw attention of healthcare providers dealing with Thumb CMC OA to PRP as a safe, beneficial therapy for this condition which needs further assessment in randomized controlled trials</th>
</tr>
</thead>
</table>

Sampson, 2016 (38) | USA | Case Series | 125 | 57 | NA | 8 weeks | VAS, a global patient satisfaction survey, and The patient satisfaction survey | PRP | NA | Evaluate intra-articular injection of bone marrow concentrate (BMC), followed by platelet-rich plasma (PRP) injection at 8 weeks follow-up in moderate/severe osteoarthritis |

Our findings corroborate initial evidence for PRP injections for treatment of pain and impairment associated with Thumb CMC-OA. However, larger controlled, well-designed studies are needed to better guide future PRP treatment guidelines and consolidate it as a safe and effective alternative in Thumb CMC-OA patients.

### Table 1: Characteristics of the included studies.

SD: Standard Deviation; NA: Not Available; RCT: Randomized Controlled Trial; CT: Controlled Trial; OA: Osteoarthritis; VAS: Visual Analogue Scale; AUSCAN: Australian/Canadian Osteoarthritis Hand Index; PRP: Platelet-Rich Plasma; HA: Hyaluronic Acid; AOFAS: American Orthopedic Foot and Ankle Society Score; AOS: Ankle Osteoarthritis Scale; PrT: Prolotherapy; OLT: Osteochondral Lesions of Talus; SAFE-Q: Self-Administered Foot Evaluation Questionnaire; JSSF: Japanese Society for Surgery of the Foot; FAAM: Foot and Ankle Ability Measure; DASH-Q: Disabilities of the Arm and Shoulder Questionnaire; PRWE: Patient-Rated Wrist Evaluation; AHFS: Ankle-Hindfoot Scale; FADI: Foot and Ankle Disability Index.

Regarding the RCTs, the overall risk of bias was low with no domains with high risk of bias. The domains with some concerns of bias were of the randomization process, and the deviation from the intended interventions. In contrast, there was a low risk of bias in domains of missing data, outcome measures, and selective reporting (Figure 2). For other study designs, about one-quarter of the studies showed a serious risk of bias, while others showed either a low risk or some concerns of bias. The domains of the most risk of bias were the deviation from the intended interventions, selective reporting of the results, cofounding bias, and missing data (Figure 3).
Outcomes and Discussion

Efficacy of PRP on osteoarthritis of the ankle

Among the studies that were included in this review, only three of them [31-33] investigated the efficacy of PRP on osteoarthritis in the foot and ankle. Foot and leg lesions are harsh as control one’s ability to move and perform their daily activities. Anthong, et al. [33] conducted a retrospective study of 12 patients suffering from chronic recalcitrant disorders involving the hindfoot and ankle. Patients were divided into satisfactory and non-satisfactory groups using the visual analog scale (VAS) foot and ankle scoring. Based on the results of the study, no satisfactory conclusion was reported by the authors as not all of the patients had satisfactory scores. However, the authors estimated that the mean visual score was significantly better after treatment than the pretreatment score and almost all of the score items were significantly higher in the satisfactory than the non-satisfactory groups. On the other hand, Fukawa, et al. [31] results showed that PRP injection into the ankle was effective in reducing the pain and enhancing the mobility of this joint 24 weeks after the injection measured by the VAS, Japanese Society for Surgery of the Foot (JSSF), and the self-administered foot evaluation questionnaire (SAFE-Q) scales. Similarly, Repetto, et al. [32] estimated that 80% of the patients were satisfied by the outcome of treatment as a significant decrease in the VAS score was estimated following a 4-week PRP course therapy. Therefore, it can be concluded that PRP is efficient in treating osteoarthritis in the ankle.

Efficacy of PRP on osteoarthritis of the foot

A total of included five studies investigated this outcome. Of these five studies, two of them [26,34], investigated PRP injection as the first line of treatment, while the other two investigated it secondary to treatment by surgeries, and only one [28] reported it following autologous bone marrow aspirate. Akpancar, et al. [34] conducted a retrospective cohort study of 49 patients with osteochondral lesions of the talus (OLT) where the effect of PRP was compared with prolotherapy (PrT) in managing OLT patients. The authors reported that both modalities showed great improvement in the pain and movement of the patients with no significant difference between the two groups, and with 90.9% reporting satisfaction about PRP injections. Mei-Dan, et al. [26] compared between PRP and hyaluronic acid injection in their patients and found that PRP injection significantly improved the pain and movement after six months from the injection when compared to the other group. Guney, et al. [30] conducted a randomized controlled trial (RCT) of 35 patients to study the efficacy of PRP injection after surgery in terms of VAS and functional improvement after injection. Although baseline pain was more severe in PRP patients than the controls, a significant reduction in pain, and improved in VAS scores and joint functions were estimated in the PRP group after 16 months from the treatment. Similarly, an RCT of 40 patients by Gormeli, et al. [35] was conducted to compare between VAS and hyaluronic acid injections and found that PRP was significantly superior in terms of improved function and VAS scores at an average of 15 months of follow-up. Additionally, Sampson, et al. [28] reported the results of PRP injection following autologous bone marrow aspirate in 125 patients. The authors reported that the process was significant in reducing pain at 20 weeks of follow-up with a noticeable difference in this efficacy between weight-bearing joints and others that are not.

Efficacy of PRP on osteoarthritis of the hand

A total of five studies investigated the effect of PRP on the hand joints especially the thumb carpometacarpal joint osteoarthritis (TCMC-OA). For instance, Medina-Porqueres, et al. [27] reported a case of PRP three injections into the TCMC joint at a 1-week interval in a patient suffering from chronic pain in his thumb. After a 12-month follow-up period, the patient was able to pursue his daily activities with improved functions, high VAS, and SAFE-Q scores were obtained with a reported high satisfaction from the patient about this treatment modality and its efficacy [27]. Abdelfattah., et al. [36] conducted a prospective interventional study on 30 patients suffering from TCMC-OA to compare the efficacy of PRP and that of hyaluronic acid injections. Although significant improvement was recorded in both groups, hyaluronic acid was significantly better at longer outcomes than PRP modality which failed to have a maintained efficacy at 12 months, unlike the other group. On the other hand, Loibl, et al. [37] reported that after two PRP injections into the trapeziometa-
carpal (TMC) joint, significant improvements were estimated in the VAS and MAYO scores, but not the DASH scores after 6 months from the initiation of therapy. Although the DASH scores in this study were not significant, Mayoly., et al. [38] reported a case series of three patients and showed that all of them had improved DASH scores. However, PRP injections were combined with micro-fat preparation injections into the wrist. On the other hand, Malahias., et al. [25] conducted an RCT of 33 patients to compare between PRP and steroid and lidocaine injections in terms of their efficacy in managing OA of the TMC joint. At 12-months of follow-up, significant improvement in the VAS, Q-DASH, and patients’ satisfaction was associated with the PRP group than the steroid and lidocaine ones. Moreover, steroids also relieved patients’ pain early after injection, however, this improvement was not as significant as PRP at longer intervals. Therefore, although steroids are still being used as first drug modalities for the management of these events [39], physicians should consider PRP modality as a long-term effective measurement.

Based on these findings, PRP modality is an effective treatment in the management of all of the mentioned joints. This is consistent with the results of a meta-analysis of four RCTs conducted by Evans., et al. [40] which found that PRP was more significant than the used control modalities at long and short-term assessments. The same study also showed that PRP was effective in enhancing chondrocyte cell activity and regeneration. This has been reported by some of our included studies which have also suggested that multiple therapeutic modalities should be applied in the management of small joints [25,26,31,32,37]. Certain factors should be considered when judging the results of a certain study. These include the preparation of PRP and the frequency of centrifugation [40]. Moreover, although the findings in this review indicate the efficacy of PRP in both mild and severe osteoarthritis, previous studies demonstrated that PRP application has been effective in early osteoarthritis only [31,41,42], while other studies proved that it can be effective in the management of late osteoarthritis [25,43], however, there was no comparison conducted in the latter ones. Gormeli., et al. [41] reported that PRP with mild osteoarthritis are more likely to present with a good prognosis because they are more likely to have residual functioning cells that may contribute to the regeneration process.

Limitations to our study include the limited sample size in many of the included studies, in addition to the heterogeneity between the included study designs and the protocols of PRP preparation.

**Conclusion**

Osteoarthritis is one of the most common musculoskeletal disorders that affect many of the elderly population and can cause serious annoying and mobility-limiting complications. Although surgery has been proposed as an effective measurement for the management of this disorder, many side effects have been reported with surgeries on small joints. PRP has recently gained a good reputation for the management of pain, reducing inflammation, and inducing tissue regeneration. Among the studies that were included in this study, almost all of them reported a significant improvement in patients receiving PRP for the management of osteoarthritis in small joints involving the hands and feet.

**Conflict of Interest**

None.

**Bibliography**


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