Meta-analysis

Does Platelet-Rich Plasma Lead to Earlier Return to Sport When Compared With Conservative Treatment in Acute Muscle Injuries? A Systematic Review and Meta-analysis

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Purpose: To compare the time to return to sport and reinjury rate after platelet-rich plasma (PRP) injection versus control therapy (i.e., physiotherapy or placebo injection) in patients with acute grade I or II muscle strains. **Methods:** All eligible studies comparing PRP against a control in the treatment of acute (≤7 days) grade I or II muscle strains were identified. The primary outcome was time to return to play. The secondary outcome was the rate of reinjury at a minimum of 6 months of follow-up. Subgroup analysis was performed to examine the efficacy of PRP in hamstring muscle strains alone. The checklist to evaluate a report of a nonpharmacologic trial (CLEAR-NPT) was used to assess the quality of studies. **Results:** Five randomized controlled trials including a total of 268 patients with grade I and II acute muscle injuries were eligible for review. The pooled results revealed a significantly earlier return to sport for the PRP group when compared with the control group (mean difference, −5.57 days [95% confidence interval, −9.57 to −1.58]; $P = .006$). Subgroup analysis showed no difference in time to return to sport when comparing PRP and control therapy in grade I and II hamstring muscle strains alone ($P = .19$). No significant difference was noted in the rate of reinjury between the 2 groups ($P = .50$) at a minimum of 6 months of follow-up. **Conclusions:** Evidence from the current literature, although limited, suggests that the use of PRP may result in an earlier return to sport among patients with acute grade I or II muscle strains without significantly increasing the risk of reinjury at 6 months of follow-up. However, no difference in time to return to sport was revealed when specifically evaluating those with a grade I or II hamstring muscle strain. **Level of Evidence:** Level II, meta-analysis of level I and II studies.

Acute muscle injuries are among the most common sports injuries suffered by professional and recreational athletes.[1,2] The majority of these injuries involve the hamstrings, adductors, quadriceps, and calf muscles.[1,3] More than 90% of sports-related muscle injuries are either contusions or strains, whereas lacerations are relatively uncommon.[4] Contusions occur as a result of a sudden, heavy extrinsic compressive force (i.e., direct blow), whereas muscle strains occur when muscle fibers are exposed to an excessive intrinsic tensile force.[5] Muscle strains have traditionally been classified as mild, moderate, or severe. Mild (grade I) strains result from a tear of only a few muscle fibers, whereas moderate strains (grade II) represent greater damage to the muscle with incomplete tearing of the fibers. Severe (grade III) strains occur when the tear extends across the entire cross section of muscle, resulting in complete loss of function.[6]

Data from various sports including basketball,[7] rugby,[8] soccer,[1] and football[9] show that muscle strains account for approximately 10% to 31% of all injuries. Ekstrand et al.[1] found that each season 37% of soccer players missed training or competition as a result of

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The authors report that they have no conflicts of interest in the authorship and publication of this article. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Received October 30, 2016; accepted June 20, 2017.

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0749-8063/161027/$36.00

http://dx.doi.org/10.1016/j.arthro.2017.06.039

muscle injuries, with an average of 90 days and 15 matches missed per club per season from hamstring injuries alone.[10] Considering the fact that the average cost of an injury to a first-team soccer player is approximately €500,000, this represents a significant financial burden to the team.[11] Moreover, a study of elite Australian football players determined the cost of hamstring strain injuries during the 2009 season to be approximately $1.5 million, which represented 1.2% of the league's salary cap.[12]

Despite an apparent growing incidence of muscle injuries,[13] there remains a lack of consensus regarding the optimal management, because of a lack of high-quality scientific evidence.[14] Current management of these injuries includes rest, ice, compression, elevation,[15] nonsteroidal anti-inflammatory drugs,[16] physiotherapy,[17] and injection therapy with corticosteroid,[18] autologous blood products[19,20] such as platelet-rich plasma (PRP), and Traumeel/Actovegin.[20,21] Traumeel is a homeopathic anti-inflammatory drug with extracts of arnica, calendula, and chamomile, while Actovegin is a deproteinized diasylate from bovine blood thought to have muscle-regenerating properties.[20]

The growing use of PRP injections for the treatment of soft tissue injuries including rotator cuff tears,[22,23] Achilles tendinopathy,[24] lateral epicondylitis,[25] patellar tendinopathy,[26] and now muscle injuries[13] has garnered significant attention in the sports medicine community and mainstream media. The term *PRP* is used to describe autologous blood products generated from the centrifugation of whole blood to yield a concentration of platelets above baseline levels.[27] The rationale behind its use in the treatment of soft tissue injuries is derived from animal studies, which have shown that the elevated level of platelets and resultant release of growth factors allows for accelerated regeneration and enhanced healing of muscle.[13] Despite its promising effects and increasing popularity, there remains very little clinical evidence to support the use of PRP injections in acute muscle injuries.

The purpose of the study was to compare the time to return to sport and reinjury rate after PRP injection versus control therapy (i.e., physiotherapy or placebo injection) in patients with acute grade I or II muscle strains. We hypothesized that the use of PRP injections may lead to earlier return to sport without increasing the risk of reinjury in these patients.

Methods

We conducted a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Eligibility Criteria

We identified all published randomized or quasi-randomized controlled trials (RCTs) fulfilling the following eligibility criteria: the study evaluated the clinical efficacy of PRP or similarly defined preparations (e.g., platelet-enriched plasma, platelet-rich growth factors, autologous conditioned serum, or thrombocyte-rich plasma) against a control (e.g., placebo or physiotherapy) in the treatment of acute ($\leq$7 days) grade I or II muscle strains. There were no age or language restrictions. We excluded case series, review, technique, and basic science articles that did not report patient-specific data. Studies with less than 6 months of follow-up were excluded when evaluating the rate of reinjury.

Literature Search

Two investigators independently performed a systematic search of the electronic databases MEDLINE, EMBASE, and PubMed. A keyword search including a combination of the following medical subject headings (MeSH) was performed: *muscle strain*, *muscle injury*, and *thrombocyte rich plasma*. The search was conducted during the week of August 8, 2016, and articles were retrieved from database inception to the search date. Additional studies were detected by searching the reference lists of eligible studies. The complete search strategy used for EMBASE is displayed in Appendix Table 1 (available at www.arthroscopyjournal.org).

Study Selection

Two independent reviewers screened the titles and abstracts from our initial search for eligibility. If any ambiguity or uncertainty was encountered, the study was included until full-text review could be performed. Any disagreement between the 2 reviewers during full-text review was resolved through mediation with a third reviewer (senior author) until consensus was reached.

Data Extraction

Two reviewers independently extracted relevant data from all eligible studies into a standardized collection form using spreadsheet software. Data collected included general study information (author, year of publication, study design), study population data (sample size, mean or median age, gender), treatment information (intervention and control protocol), PRP characteristics (manufacturer, number of injections, volume used, leukocyte content), follow-up data (mean duration, rate), and outcome measures used.

Assessment of Risk of Bias in Eligible Studies

The checklist to evaluate a report of a nonpharmacologic trial (CLEAR-NPT)[28] was used to assess the methodologic quality of eligible RCTs. The CLEAR-NPT is a validated checklist that evaluates the adequacy of 10 key elements of a nonpharmacologic RCT.[28] Two