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Opinion

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Platelet-rich plasma in orthopaedics – to use or not to use?

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Abstract

There is a clear shift in modern medicine towards non-operative treatment or minimally invasive treatment of diseases. Orthopaedic surgery is no exception. Patients demand quick return to activity levels prior to injury and biological treatment is becoming more and more mainstream. PRP is one of the most studied orthobiologic agents in orthopaedics and is becoming more widely used. But the question is, should we encourage widespread usage of PRP at this time?

Introduction

Platelet-rich plasma (PRP) is one of the most studied orthobiologic agents. Orthobiologics are substances found in the human body that can be used to improve healing of cartilage, muscles, ligaments, tendons and fractures.[1] These agents can be directly injected in the injured structure or used as intraarticular injection thus avoiding systemic effects of drugs in conservative treatment and increasing the bioavailability of the desired treatment. In recent years, pressure on orthopaedic surgeons has risen to enable quick return to pre-injury level of activity. The former is today not only true for professional athletes but increasing elderly population also wishes to remain active. More effective and minimally invasive treatment options are actively being sought. Usage of PRP, especially in private practice, is on the rise. Should we encourage it's use or cautiously back further research?

PRP

We've all been there – a patient comes to our office either with a distinct sports related injury of the locomotor system or a degenerative disease. Wouldn't it be great if we could simply take a sample of his blood, have it processed in a laboratory and as such inject it at the site of injury, resulting in a fast, cost-effective healing of the injury? That's where PRP is supposed to come in. The appeal of PRP is it's high concentration of growth factors that are involved in the healing process. Furthermore, the components found in PRP preparations, cellular and chemical, are numerous. PRP is actually a milieu of factors that are both catabolic/anabolic and also pro-/antiinflammatory.[2] That complexity makes it difficult to reproduce precise elements in each patient and company's product.[2] A key point here is the cellular composition of PRP – increasing platelet concentrations are associated with anabolic signaling while increased leukocyte concentrations promote catabolic signaling.[3] Keeping all that in mind, it is no wonder that there is no standardized method or device for PRP production. Furthermore, injection frequency and volume vary widely among published studies. Variables include platelet concentration, leukocyte concentration, use of anticoagulants, use of platelet pre-activation factors and injection volume and frequency.[4] In order to produce PRP, blood must be drawn during each visit since it can not be stored or frozen which can also contribute to variability in composition between blood withdrawals and results.[5]

The road so far

Published reviews and meta-analyses draw variable conclusions in regard to clinical efficacy of PRP. Most of the literature reported PRP to be beneficial for a short period of time in knee osteoarthritis (OA).[6] Campbell et al. found that PRP injections in early-stage OA was an effective treatment for up to 12 months.[7] Another systematic review found that current studies are inconclusive regarding efficacy of PRP.[8] Some studies concluded that PRP is associated with improved efficacy compared with hyaluronic acid (HA) and placebo.[9] It is necessary to note that concerns exist regarding the quality of published papers and the high risk of bias.[10] The PRP treatment is not without problems. A meta-analysis of PRP papers found an increased incidence of nonspecific adverse effects among patients treated with PRP when compared to HA and placebo.[9] One review noted increased local adverse reactions associated with serial PRP injections.[7] There is also a question of leukocyte concentration in PRP preparations since increasing the concentration of leukocytes in intraarticular space can promote inflammation. A meta-analysis on randomized control trials

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comparing clinical outcomes and rates of adverse events between leukocyte-poor (LP) and leukocyte-rich (LR) PRP found 3 trials that used LP PRP which reported positive effects compared with HA. Only one trial using LR PRP reported positive effects compared to HA.[11] Polymorphonuclear neutrophils may have a negative effect on cartilage, increasing existing tissue damage.

So, what's next?

It is clear that PRP has possible benefits in treatment of musculoskeletal disorders. However, it is also clear that there is no consensus on optimal protocol of preparing PRP and products used have different compositions. That makes it extremely difficult to compare different studies and for orthopaedic societies to give recommendations regarding PRP. It is clear that there is a need to standardize preparation protocols and to make composition differences as low as possible.

Conclusion

Although advencements have been made in the field of orthobiologics, these agents are still in their beginnings. In order to make further improvements, it is necessary to define minimal standards for such treatments. Studies on PRP are a clear example of that. High number of variables require detailed preparation protocols. Future randomized trials should focus on larger sample sizes and longer follow-up times for the evidence to be more compelling. Without such studies, orthopaedic societies cannot give their recommendations on usage of PRP. Furthermore, better defined controls are also needed in order to decrease bias of the studies to a minimum level.

It is my opinion that PRP still does not warrant usage outside of controlled research environment until we have well defined protocols and reproducible studies. PRP usage is not without possible adverse effects and long-term effects of it's usage are still unclear.

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