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EDITORIAL

Autologous peripheral blood-derived orthobiologics: Different types and their effectiveness in managing knee osteoarthritis

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Abstract

Knees are the most commonly impacted weight-bearing joints in osteoarthritis (OA), affecting millions of people worldwide. With increasing life spans and obesity rates, the incidence of knee OA will further increase, leading to a significant increase in the economic burden. Conventional treatment modalities utilized to manage knee OA have limitations. Over the last decade, the role of various autologous peripheral blood-derived orthobiologics (APBOs) for the treatment of knee OA has been extensively investigated. This editorial provided an overview and focused on defining and shedding light on the current state of evidence based on the most recent published clinical studies concerning the use of APBO for the management of knee OA. While numerous studies have demonstrated promising results for these preparations, a notable gap exists in the comparative analysis of these diverse formulations. This absence of head-to-head studies poses a considerable challenge for physicians/surgeons in determining the optimal preparation for managing knee OA and achieving sustained long-term results. Thus, more adequately powered, multicenter, prospective, double-blind, randomized controlled trials with longer follow-ups are needed to establish the long-term efficacy and to aid physicians/surgeons in determining the optimal APBO for the management of knee OA.

Key Words: Knee osteoarthritis; Platelet-rich plasma; Platelet lysate; Autologous conditioned serum; Gold-induced cytokine; Plasma rich in growth factors; Growth factor concentrate; Autologous protein solution; Platelet-rich fibrin; Hyperacute serum

Core Tip: This editorial briefly defined various autologous peripheral blood-derived orthobiologics (APBO) being explored and assessed their current state of evidence based on the most recently published clinical study for the management of knee osteoarthritis (OA). The present literature demonstrates the potential of these APBOs in reducing pain and improving function in knee OA patients; thus, they can be utilized in patients who are refractory to conservative treatment modalities. Yet, more adequately powered clinical trials with longer follow-up and comparative studies are required to establish the long-term efficacy and determine the most optimal APBO for the management of knee OA, respectively.

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INTRODUCTION

Osteoarthritis (OA) of the knee is conventionally managed using non-pharmacological methods, pharmacological agents, and surgery in later stages or when conservative options have failed[1]. These therapies have limitations, like continuously trying to lessen symptoms rather than focusing on the underlying etiology[1]. Recently, there has been considerable interest in the utilization of autologous peripheral blood-derived orthobiologics (APBO) for the management of knee OA[2-11]. Here, we provided an overview while focusing on defining and reporting evidence-based assessments based on the most recent level I clinical studies as well as other levels of clinical evidence for clinical utilization of these APBOs for the management of knee OA.

APBO

Platelet-rich plasma (PRP) is the most commonly used orthobiologic, and still its efficacy remains debatable, which is attributed to patient variables, absence of standardized formulation protocol, *etc*[1,2]. In addition, there is limited literature regarding the most apt PRP formulation[1]. Gupta *et al*[1] in a recent editorial concluded that clinical outcomes obtained with either leukocyte-rich or leukocyte-poor PRP are similar at the 12-mo follow-up in knee OA patients. Conversely, Xiong *et al*[2] in an up-to-date systematic review and meta-analysis reported that leukocyte-poor PRP was significantly effective in reducing pain in knee OA patients, whereas leukocyte-rich PRP was not. These contentious outcomes have led researchers and clinicians to explore alternative APBOs for the management of knee OA[3-11]. Different types of APBOs along with the most recent clinical evidence are summarized in Table 1.

CONCLUSION

The most recent clinical studies described in Table 1 are not without shortcomings. They include variability in the formulation protocols, small cohort sizes, short-term to mid-term follow-up, *etc*. This variability can lead to inconsistencies in the composition and efficacy of the final product. The short-term to mid-term follow-up periods may not provide sufficient insight into the long-term effectiveness and safety of these treatments. Moreover, there is inadequate literature comparing the efficacy of one APBO to another. This further adds to the dilemma of physicians/surgeons in deciding the most appropriate APBO for the management of knee OA. Despite these constraints, the results from included clinical studies demonstrated the ability of various APBOs in decreasing pain and enhancing function in knee OA patients. Nonetheless, shared standardized formulation protocols for these APBOs must be created to ensure repeatability and reproducibility of outcomes associated with the use of these orthobiologics. In addition, further sufficiently powered, multicenter, prospective, randomized controlled trials with lengthier follow-ups are warranted to determine long-term efficacy and to aid physicians/surgeons in identifying the ideal APBO for managing knee OA along with justifying their routine clinical use.

Table 1 A brief description of different types of autologous peripheral blood-derived orthobiologics and associated recent clinical evidence evaluating their efficacy for the management of knee osteoarthritis

APBOs	Ref.	Description	Most recent clinical evidence
PRP	Xiong *et al*[2]	PRP is derived from whole blood and is rich in platelets, can be LR or LP, is poor in erythrocytes, and can be activated using external activators	An up-to-date systematic review and meta-analysis examined 24 RCTs with 1344 patients and reported significant improvements in the VAS, KOOS, WOMAC, and IKDC scores in the PRP group compared to the controls (saline and/or HA)
PL	Hosseini *et al*[3]	PL is derived from PRP and formulated *via* a double freeze/thaw cycle	A recent RCT involving 50 patients reported significant improvements in VAS, WOMAC, and ROM scores at the 6-mo follow-up in the PL group compared to the baseline and PRP group
ACS	Raeissadat *et al*[4]	ACS is formulated by incubating whole blood with $CrSO_4$-coated glass beads	A recent meta-analysis investigated eight clinical studies involving 439 patients with at least 3 mo of follow-up and reported significant improvements in VAS and WOMAC scores post-treatment with ACS compared to the baseline
GOLDIC	Tulpule *et al*[5]	GOLDIC is a type of ACS and involves incubating whole blood with gold particles	A recent prospective study involving 65 patients (106 knees) reported significant improvements in VAS and WOMAC scores at the 12-mo follow-up in patients treated with serial injections of GOLDIC compared to the baseline
PRGF	Ríos Luna *et al*[6]	PRGF is formulated by activating erythrocyte poor and LP-PRP with $CaCl_2$	A recent retrospective observational study involving 79 patients (85 knees) reported significant improvements in the KOOS score at the 11-mo follow-up post-administration of PRGF compared to the baseline
GFC	Saraf *et al*[7]	GFC is an acellular formulation prepared by incubating whole blood with an external platelet activator	A recent RCT involving 58 participants reported significant improvements in VAS and WOMAC scores at the 12-mo follow-up in patients treated with serial injections of GFC compared to the control
APS	Kuwasawa *et al*[8]	APS is derived from and formulated by exposing LR-PRP to polyacrylamide beads	A recent retrospective study assessed 148 knees and reported significant improvement in the KOOS score at the 12-mo follow-up post-injection of APS compared to the baseline
PRF	Cheeva-Akrapan and Turajane[9]	PRF is derived from whole blood, formulated without the use of an anticoagulant, and consists of autologous platelets and a LR fibrin matrix	A recent prospective cohort study involving 368 participants reported that nearly 80% of patients had their surgery postponed over 3 yr following the administration of PRP supplemented with PRF, supporting its utility in treating osteoarthritis patients for long-term effects
HS	Olmos Calvo *et al*[10]	HS is formulated by mechanically releasing, *via* pressing or centrifugation, growth factors and cytokines from the PRF clot	A recent clinical study involving 24 patients reported significant improvements in Lysholm-Tegner, VAS, and KOOS scores at the 6-mo follow-up in patients treated with serial injections of HS compared to the baseline
ACP	Korpershoek *et al*[11]	ACP is a single-spin LP-PRP formulation	A recent real-world prospective case series involving 260 patients (307 knees) reported significant improvement in KOOS and NPRS at the 12-mo follow-up compared to the baseline after administration of 3 weekly intra-articular injections of ACP. Interestingly, despite a statistically significant outcome for the KOOS score, the MCID was not accomplished

ACP: Autologous conditioned plasma; ACS: Autologous conditioned serum; APBOs: Autologous peripheral blood-derived orthobiologics; APS: Autologous protein solution; GFC: Growth factor concentrate; GOLDIC: Gold-induced cytokine; HA: Hyaluronic acid; HS: Hyperacute serum; IKDC: International knee documentation committee; KOOS: Knee injury and osteoarthritis outcome score; LP: Leukocyte-poor; LR: Leukocyte-rich; MCID: Minimally clinically important difference; NPRS: Numeric pain rating scale; PL: Platelet lysate; PRF: Platelet-rich fibrin; PRGF: Plasma-rich in growth factors; PRP: Platelet-rich plasma; RCT: Randomized controlled trial; ROM: Range of motion; VAS: Visual analogue scale; WOMAC: Western Ontario and McMaster Universities arthritis index.

FOOTNOTES

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