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## Editorial

# Emerging role of orthobiologics for the management of knee osteoarthritis

Ashim Gupta<sup>1,2,3,4,5\*</sup>, Karun Jain<sup>6</sup>

<sup>1</sup>Regenerative Orthopaedics, Noida, Uttar Pradesh, India

<sup>2</sup>Future Biologics, Lawrenceville, Georgia, India

<sup>3</sup>BioIntegrate, Lawrenceville, Georgia, USA

<sup>4</sup>South Texas Orthopaedic Research Institute (STORI Inc.), Laredo, Texas, USA

<sup>5</sup>Indian Stem Cell Study Group (ISCSG) Association, Lucknow, Uttar Pradesh, India

<sup>6</sup>Shri Mahaveer Ortho Clinic, New Delhi, Delhi, India



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Knee osteoarthritis (OA) is typically managed via non-pharmacological approaches, pharmacological agents, and surgical intervention, in advanced stages or when traditional modalities have been unsuccessful.<sup>1</sup> These conventional modalities have shortcomings, constantly aiming to alleviate symptoms instead of concentrating on causing pathophysiology.<sup>1</sup> Recently, the use of autologous and allogenic source-derived orthobiologics for the management of knee OA have significantly increased.<sup>1–4</sup> Here, we are providing an overview of evidence-based basis, based on latest level-I study or other types of clinical studies, in absence of level-I evidence, for the clinical use of these orthobiologics in knee OA patients.

Lately, autologous peripheral blood-derived orthobiologics, including platelet-rich plasma (PRP), platelet lysate, autologous conditioned serum, Gold-induced cytokine, autologous conditioned plasma, plasma-rich in growth factors, growth factor concentrate, autologous protein solution, platelet-rich fibrin and hyperacute serum, have been investigated for the management of knee OA. Among these, PRP has been most extensively promoted, yet its efficacy remains controversial.<sup>2</sup> Xiong et al.,<sup>2</sup> in a recent systematic review and meta-analysis, investigated 24 RCTs

with 1,344 patients and reported significant improvements in the Visual Analogue Scale (VAS), Knee Injury and Osteoarthritis Outcome Score (KOOS), Western Ontario and McMaster Universities Arthritis Index (WOMAC) and International Knee Documentation Committee (IKDC) scores in the PRP group compared to the controls (saline and/or hyaluronic acid (HA)).

Belk et al.<sup>3</sup> investigated 27 level-I studies comparing efficacies of PRP (n=1,042), bone marrow aspirate concentrate (BMAC, n=226) and HA (n=1,128), and reported significant improvements in the VAS, WOMAC and IKDC scores in the PRP or BMAC group compared to the HA. No significant differences were obtained between the PRP and BMAC groups.

Boada-Pladellorens et al.<sup>4</sup> investigated the efficacy of stromal vascular fraction (SVF), most widely used adipose tissue derivative, in 9 clinical studies (RCTs, non-RCTs, cohort studies, case series) with 239 participants (274 knees) and reported improvements in VAS, KOOS and WOMAC scores, and anatomical structures (assessed via MRI).

Aratikatla et al.<sup>1</sup> investigated allogenic perinatal tissue-derived formulations, including amniotic tissue and umbilical cord, and reported significant improvements for various patient-reported outcome measures (PROMs), including VAS, KOOS, WOMAC and IKDC.

\* Corresponding author.

E-mail address: [ashim6786@gmail.com](mailto:ashim6786@gmail.com) (A. Gupta).

In addition to the above-mentioned orthobiologics, mesenchymal stem cells (MSCs) isolated from both autologous and allogenic sources have been widely explored. Copp et al.<sup>5</sup> investigated 15 RCTs (9-autologous MSCs (bone marrow- and adipose-derived), 6-allogenic MSCs (bone marrow-, adipose-, Wharton's Jelly- and placenta-derived)) with 610 patients and reported significant improvements in various PROMs, including VAS, KOOS and WOMAC compared to the baseline and control(s).

The aforementioned studies have flaws, including lack of standardized formulation protocols, variability in dose and number of dosages used, harvest site morbidity (for BMAC and SVF), small cohort size, and short- to mid-term follow-up. Despite these, administration of these orthobiologics have the potential to reduce pain and improve function in knee OA patients. Nonetheless, more adequately powered, multi-center, prospective, double-blind, randomized controlled trials with longer follow-up are merited to establish long-term efficacy of these orthobiologics in knee OA patients and justify their routine clinical use.

### Conflict of Interests

The authors declare that they have no competing interests.

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### Author Contributions

Ashim Gupta conceptualized this study and wrote the initial manuscript draft. Ashim Gupta and Karun Jain reviewed and critically edited this manuscript and have read and approved the submitted manuscript.


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### Author biography

**Ashim Gupta**, Founder and President, CEO, Chief Science Officer, and Professor  <https://orcid.org/0000-0003-1224-2755>

**Karun Jain**, Founder and Orthopaedic Surgeon

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