



The Role and Clinical Advantages of Genicular Nerve Block Before Intra-Articular Injection of Regenerative Biomaterials in the Knee

Reza Aminnejad ^{1,2}, Sahar Kavousi Sisi³, Khatere Mokhtari^{4,*}

¹ Department of Anesthesiology and Critical Care, Qom University of Medical Sciences, Qom, Iran

² Iranian Society of Anesthesiology and Critical Care, Tehran, Iran

³ Qom University of Medical Sciences, Qom, Iran

⁴ Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran

*Corresponding Author: Department of Cell and Molecular Biology and Microbiology, Faculty of Biological Science and Technology, University of Isfahan, Isfahan, Iran.
Email: khatere_mokhtari@yahoo.com

Received: 13 August, 2025; Revised: 7 December, 2025; Accepted: 14 December, 2025

Keywords: Genicular Nerve Block, Regenerative Medicine, PRP, Stem Cell, Knee Pain, Knee Osteoarthritis

Dear Editor,

A Clinical Moment That Changed My Perspective

Knee pain steals more than movement – it steals independence, confidence, and quality of life. For many patients, regenerative injections such as stem cell or platelet-rich plasma (PRP) therapies offer a last hope before surgery. Yet, the pain of the injection itself often becomes an unexpected barrier. A patient once told me, “Doctor, I fear the injection more than the arthritis”. That statement stayed with me. In our clinical practice, we began using genicular nerve block (GNB) before intra-articular regenerative injections, and the difference has been striking. With targeted, localized analgesia, patients no longer flinch or tense during the procedure. The entire experience becomes smoother, safer, and more precise. What used to be a moment of anxiety now feels like a step toward healing. This simple pairing – GNB followed by regenerative injection – may redefine patient tolerance standards in outpatient orthopedics. If widely adopted, it has the potential to shift regenerative medicine from a feared procedure to a patient-centered, pain-controlled experience.

Why Procedural Pain Still Holds Patients Back

Every week in the clinic, I meet patients who approach the procedural table with hope – and fear. Their knees have failed them for years, and regenerative injections may be their last chance before surgery. Yet the moment the needle appears, anxiety tightens

muscles and pain overshadows the promise of healing. Pain is more than a momentary nuisance – it can disrupt biomaterial acceptance, therapy adherence, and even early rehabilitation. In our practice, preemptively blocking the genicular nerves before intra-articular regenerative injections has transformed this experience. By targeting the sensory branches of the knee, the GNB provides immediate, localized analgesia, preserving motor function and enabling smoother, more controlled procedures. Patients relax, injections are precise, and clinicians are able to perform their work – without interference from systemic analgesics.

Regenerative biomaterials aim to support joint repair by modulating the local environment, stimulating cellular activity, and enhancing tissue regeneration (1). These therapies are typically administered via intra-articular injection, a procedure that may provoke significant discomfort, particularly in patients with severe osteoarthritic changes or heightened nociceptive sensitivity. Pain management is thus critical. Genicular nerve block, a focused anesthetic technique targeting the sensory innervation of the knee, offers a minimally invasive method to reduce pain and improve procedural tolerability (2). In my experience, ignoring procedural pain has been an overlooked barrier in regenerative medicine. I believe the future of biologic therapies will depend not only on the biomaterial itself but on creating a procedural

environment that respects patient comfort, neurobiology, and psychological readiness.

What We Observed When We Added Genicular Nerve Block

The genicular nerves — specifically the superior medial, superior lateral, and inferior medial branches — provide sensory innervation to the anterior and medial aspects of the knee joint. Genicular nerve block is performed under ultrasound or fluoroscopic guidance, delivering local anesthetic near these nerve branches. Since the genicular nerves are purely sensory, this technique provides pain relief without impairing motor function.

From a clinical perspective, this small adjustment — adding a simple nerve block before injection — has reshaped how both patients and clinicians experience regenerative procedures. Incorporating a GNB before administering regenerative biomaterials offers multiple clinical advantages beyond simple pain relief. Incorporating a GNB before administering regenerative biomaterials offers several important clinical advantages. First, it provides effective analgesia by blocking afferent pain signaling from the joint, significantly reducing procedural pain and patient discomfort (3, 4). This translates into improved tolerance, allowing patients to remain relaxed during injection and enabling the clinician to perform a more precise and controlled procedure. For those who experience anxiety or heightened sensitivity, GNB reduces both physical pain and psychological stress, which in turn promotes adherence in multi-session protocols or combined regenerative-physical therapy programs (4, 5).

Beyond pain control, preemptive blockade of genicular nerves can optimize the regenerative environment. By minimizing acute pain responses and sympathetic activation, GNB creates local conditions that favor biomaterial integration and cellular activity. Regenerative materials often elicit a transient inflammatory response; blocking pain pathways helps smooth this phase while reducing the need for systemic analgesics or anti-inflammatory drugs that might counteract biomaterial function (6-9).

Another clinical advantage lies in the preservation of motor function. Because GNB acts only on sensory branches, patients maintain full mobility immediately after the procedure, facilitating early rehabilitation and

more natural post-procedural movement (10). The short duration of the block — lasting only a few hours — covers the procedural window without interfering with subsequent assessment or recovery (10).

Genicular nerve block is more than just a pain control tool — it serves as a bridge between diagnosis, treatment delivery, and functional recovery in patients undergoing regenerative knee therapies. This feature may be similar to the infiltration between the popliteal artery and capsule of the knee (IPACK) block feature used in patients treated with new minimally invasive modalities, which is effective in improving patient outcomes (11).

A Call for a Shift in Practice

For years, regenerative orthopedics has focused almost exclusively on what we inject — PRP formulations, stem cell sources, scaffold compositions, and biologic modifications. Yet we have paid far less attention to how we deliver these therapies and how the patient experiences the procedure itself. This imbalance has created an unnecessary gap between scientific innovation and clinical reality.

If we truly believe in the potential of biologic therapies, then we must also acknowledge a simple truth: a patient who fears the procedure is already at a disadvantage. Procedural pain is not a minor inconvenience; it shapes muscle tension, sympathetic activation, biomaterial acceptance, and even willingness to return for follow-up injections. Ignoring this barrier has kept regenerative medicine from reaching its full promise.

The routine use of a GNB before intra-articular regenerative injections represents a small but fundamental shift — one that centers patient comfort and neurobiology alongside biomaterial science. The block takes only minutes, preserves motor function, and transforms a painful, high-tension moment into a controlled, precise intervention. Most importantly, it removes the fear that prevents many patients from benefiting fully from the therapies we offer.

The question is no longer “Does GNB help?” — our clinical experience answers that clearly. The real question is: Why hasn’t this already become standard practice?

As long as regenerative medicine continues to evolve, our procedural strategies must evolve with it. Adopting pre-injection GNB is not an optional enhancement — it is

a necessary upgrade to modern, humane, patient-centered regenerative care.

Moving Forward

Genicular nerve block is a valuable adjunctive strategy in the delivery of regenerative biomaterials for knee joint therapy. Its safety, specificity, and efficacy in reducing pain make it especially useful in patients with advanced disease or high procedural sensitivity. Incorporating GNB into regenerative protocols may not only improve the procedural experience but also support the biological efficacy of emerging intra-articular therapies. Further clinical research is needed to establish standardized protocols and evaluate long-term outcomes. As regenerative medicine continues to evolve, clinicians must not only focus on what they inject but also how they deliver it. Genicular nerve block represents a small step that can make a profound difference in patient comfort, trust, and overall treatment success.

From a broader perspective, pairing GNB with regenerative injections represents more than a technical adjustment – it reflects a shift toward a more humane and biologically-informed interventional practice. We often celebrate new biomaterials, yet neglect the patient experience that determines whether those innovations succeed in real-world clinics. If regenerative medicine is to reach its full potential, procedural strategies that reduce nociception, anxiety, and sympathetic activation should become standard rather than optional.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: Study concept and design: R. A.; Drafting of the manuscript: S. K. S. and K. M.; Critical revision of the manuscript for important intellectual content: R. A.; Administrative, technical, and material support: S. K. S.; Study supervision: R. A. and S. K. S.

Conflict of Interests Statement: Reza Aminnejad is editor in chief of the Interventional Pain Medicine and Neuromodulation journal.

References

1. Bahari Golamkaboudi A, Vojoudi E, Babaeian Roshani K, Porouhan P, Houshang D, Barabadi Z. Current Non-Surgical Curative Regenerative Therapies for Knee Osteoarthritis. *Stem Cell Rev Rep*. 2024;**20**(8):2104-23. [PubMed ID: 39145857]. <https://doi.org/10.1007/s12015-024-10768-6>.
2. Vilchez-Cavazos F, Gamboa Alonso AA, Simental-Mendia M, Pena-Martinez VM, Acosta-Olivo CA, Villarreal-Villarreal GA. Genicular Nerve Block for Knee Osteoarthritis: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *Clin J Pain*. 2024;**40**(10):618-24. [PubMed ID: 39143682]. <https://doi.org/10.1097/AJP.0000000000001240>.
3. Li W, Xu F, Chen F, Cao L, Bao X. Effect of Genicular Nerve Block (GNB) on Pain in Lesions of the Knee Joint: A Meta-Analysis of Randomized Controlled Trials. *J Pain Res*. 2025;**18**:511-22. [PubMed ID: 39901967]. [PubMed Central ID: PMC1789509]. <https://doi.org/10.2147/JPR.S503937>.
4. Sobel J, Oswald J. Novel Use of 3-Point Genicular Nerve Block for Acute Knee Pain in the Emergency Department. *J Emerg Med*. 2021;**61**(4):416-9. [PubMed ID: 34176690]. <https://doi.org/10.1016/j.jemermed.2021.04.012>.
5. Liu Q, Zhong Q, Tang G, Yang P, Ye L. Ultrasound-guided Genicular Nerve Block in Patients Undergoing Knee Arthroscopy: A Randomized Controlled Trial. *Sports Med Arthrosc Rev*. 2025;**33**(2):47-53. [PubMed ID: 39724016]. <https://doi.org/10.1097/JSA.0000000000000384>.
6. Aboushaar N, Serrano N. The mutually reinforcing dynamics between pain and stress: mechanisms, impacts and management strategies. *Front Pain Res*. 2024;**5**:1445280. [PubMed ID: 39624230]. [PubMed Central ID: PMC1609167]. <https://doi.org/10.3389/fpain.2024.1445280>.
7. Tong RL, Kahn UN, Grafe LA, Hitti FL, Fried NT, Corbett BF. Stress circuitry: mechanisms behind nervous and immune system communication that influence behavior. *Front Psychiatry*. 2023;**14**:1240783. [PubMed ID: 37706039]. [PubMed Central ID: PMC10495591]. <https://doi.org/10.3389/fpsyt.2023.1240783>.
8. Szoke E, Helyes Z. Molecular Links between Sensory Nerves, Inflammation, and Pain 2.0. *Int J Mol Sci*. 2023;**24**(15). [PubMed ID: 37569621]. [PubMed Central ID: PMC10418333]. <https://doi.org/10.3390/ijms241512243>.
9. Carnicer-Lombarte A, Chen ST, Malliaras GG, Barone DG. Foreign Body Reaction to Implanted Biomaterials and Its Impact in Nerve Neuroprosthetics. *Front Bioeng Biotechnol*. 2021;**9**:622524. [PubMed ID: 33937212]. [PubMed Central ID: PMC8081831]. <https://doi.org/10.3389/fbioe.2021.622524>.
10. Akesen S, Akesen B, Atici T, Gurbet A, Ermutlu C, Ozyalcin A. Comparison of efficacy between the genicular nerve block and the popliteal artery and the capsule of the posterior knee (IPACK) block for total knee replacement surgery: A prospective randomized controlled study. *Acta Orthop Traumatol Turc*. 2021;**55**(2):134-40. [PubMed ID: 33847575]. [PubMed Central ID: PMC1229621]. <https://doi.org/10.5152/j.aott.2021.20187>.
11. Aminnejad R, Aryani MR. IPACK Block as a Bridge for New Treatment Modalities of Knee Osteoarthritis. *Interv Pain Med Neuromodulation*. 2021;**1**(1). <https://doi.org/10.5812/ipmn.i15222>.