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THE CLINICAL SIGNIFICANCE OF COANALGESICS IN PAIN MODULATION AMONG ATHLETES

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ABSTRACT

Introduction: Pain is one of the most common complaints associated with physical activity, both in professional and recreational sports. As a physiological and subjective phenomenon, pain serves a protective function, warning of potential injury or overuse. However, if left untreated, it may lead to chronic pain conditions, impaired motor function, or even permanent exclusion of the athlete from activity. Therefore, effective and safe pain management is essential to maintain training continuity, prevent complications, and support athletes' optimal psychophysical performance.

Standard therapeutic approaches in athletes typically involve the use of nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and—in the case of more severe pain—opioid medications. However, increasing attention has been paid to coanalgesics, a group of drugs that are not classified as traditional analgesics but exhibit supportive or potentiating effects on pain relief.

Coanalgesics—including antidepressants, anticonvulsants, glucocorticoids, local anesthetics, and even certain dietary supplements—are especially useful in treating neuropathic, chronic, or multifactorial pain. In the context of sports, these agents may play a crucial role in reducing the required doses of standard analgesics, minimizing side effects, and facilitating return to full physical functionality.

Given the unique characteristics of the sports environment—including time pressure, high physical demands, anti-doping regulations (e.g., WADA), and ethical considerations—appropriate analgesic selection must not only be effective but also safe, rational, and compliant with governing rules. When used appropriately, coanalgesics may serve as alternatives or adjuncts to classical pain management strategies.

Aim: The aim of this paper is to analyze the role of coanalgesics in pain therapy among athletes, with reference to data from recent clinical trials, systematic reviews, and scientific society guidelines. Particular attention is given to the efficacy, safety, and limitations of selected substances in various pain types—acute, chronic, somatic, and neuropathic—with respect to sports disciplines and return-to-play protocols.

Material and Methods: This narrative review was conducted to synthesize current evidence regarding the use of coanalgesics in the management of pain among athletes, with a particular focus on neuropathic, postoperative, and post-traumatic pain. A structured literature search was performed in PubMed, Scopus, and Web of Science.

Conclusions: Co-analgesics offer a promising tool in pain management among athletes. Paracetamol and topical analgesics may reduce pain-related limitations without the long-term risks associated with systemic agents. However, the overuse of NSAIDs and the application of opioids carry serious health and ethical concerns. Further high-quality research is needed to establish optimal treatment protocols and to promote education within sports communities.

KEYWORDS

Coanalgesics, Pain Management, Sport Trauma, Adjuvants, Pain Relief

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1. Coanalgesics – Definition and Mechanism of Action

Coanalgesics (also known as adjuvant analgesics) are drugs not primarily indicated for pain relief but which enhance analgesic efficacy, enabling a multimodal approach to pain management. This allows for dose reduction of classical analgesics (e.g., NSAIDs or opioids), thereby lowering the risk of adverse effects.

1.1 Antidepressants

Antidepressants—particularly tricyclic antidepressants (TCAs) and serotonin-norepinephrine reuptake inhibitors (SNRIs)—exhibit intrinsic analgesic properties through modulation of descending inhibitory pain pathways in the spinal cord. Their mechanism involves:

- a) Inhibition of serotonin and norepinephrine reuptake, increasing synaptic concentrations and enhancing pain suppression at the spinal level [1]
- b) Independent effects such as sodium channel blockade, NMDA receptor inhibition, anticholinergic actions, and modulation of opioid and histaminergic receptors [1]

Importantly, the analgesic effect of antidepressants typically precedes their mood-related effects—often occurring within a few days to a week.

1.1.1 Tricyclic Antidepressants (TCAs)

Amitriptyline is the most studied TCA in neuropathic pain. Meta-analyses report a number needed to treat (NNT) between 2–3, meaning that one in 2–3 patients achieves $\geq 50\%$ pain reduction [2]. Furthermore, a systematic review (Oxford, 2016) found that a 50 mg/day dose reduced back pain by 3.9 points on the visual analog scale (VAS), outperforming pregabalin (2.9 points) [3]. Nortriptyline shows similar efficacy in athletes with post-traumatic neuropathy and complex regional pain syndrome (CRPS), typically initiated at 25 mg/day and titrated up to 100 mg [4].

1.1.2 Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Duloxetine—FDA-approved for neuropathic pain (e.g., diabetic neuropathy) and fibromyalgia—demonstrates an NNT of approximately 5–6. In randomized trials with over 700 patients with neuropathy, 60 mg/day significantly reduced pain [5]. Venlafaxine serves as an alternative agent, modulating both serotonin and norepinephrine at higher doses, with a favorable safety profile compared to TCAs [6].

1.1.3 Other Antidepressants

Milnacipran (SNRI): demonstrated improvement in pain and functional outcomes in fibromyalgia studies (N=1196) at doses between 12.5–100 mg/day [7]. Mirtazapine, although less studied, increased pain tolerance after a single 30 mg dose in experimental settings. SSRIs (e.g., paroxetine) have limited evidence, though some show moderate efficacy in neuropathies (paroxetine, citalopram, venlafaxine) [8]. Analgesic onset typically occurs within 1–2 weeks. Tolerability depends on side effects (dry mouth, drowsiness, orthostatic hypotension). In cases of TCA intolerance, SNRIs are considered suitable alternatives [8].

1.1.5 Relevance for Athletes

Athletes frequently experience both somatic and neuropathic pain (e.g., from injuries, surgeries, or chronic overuse). TCAs and SNRIs allow dose reduction of NSAIDs/opioids without compromising analgesia. Their anxiolytic and sleep-enhancing properties may further support recovery [9].

1.2 Anticonvulsants

Gabapentin and pregabalin (gabapentinoids), along with carbamazepine, act by blocking $\alpha_2\delta$ -type calcium channels and sodium channels, thereby reducing the release of neurotransmitters involved in pain transmission. Preclinical studies have also confirmed their efficacy in inflammatory pain models, further supporting their clinical use [9].

1.2.1 Mechanisms of Action

Modulation of $\alpha_2\delta$ -1 calcium channels: Gabapentin and pregabalin bind to the $\alpha_2\delta$ -1 subunit of voltage-gated calcium channels, limiting the release of excitatory neurotransmitters (glutamate, substance P, norepinephrine) and reducing pain transmission and central sensitization. NMDA receptor interaction and synaptic plasticity modulation: Gabapentinoids also interact with NMDA receptors and modulate synaptic plasticity, potentially suppressing spinal “wind-up” pain phenomena [11].

1.2.2 Clinical Efficacy

Pregabalin:

In multiple RCTs and perioperative meta-analyses, pregabalin effectively reduced postoperative pain after orthopedic procedures. A meta-analysis of 74 studies showed significant pain and opioid use reduction: mean difference -0.507 (95% CI -0.812 to -0.202) [11]. In ACL reconstruction, a single preoperative dose of 150 mg pregabalin significantly reduced pain during passive knee flexion at 24–36 hours post-surgery ($p=0.043$ and 0.042), with effects lasting up to two weeks [12]. In RCTs involving post-traumatic neuropathy, pregabalin (150–600 mg/day) significantly reduced pain vs. placebo ($p=0.01$) and improved function [13]. Systematic reviews in post-traumatic and spinal cord injury neuropathy confirmed significant pain reduction as early as week one ($p=0.003$) [14].

Gabapentin:

In a preoperative ACL reconstruction study ($N=114$), a single 600 mg dose significantly reduced pain at 6 and 24 hours post-surgery and lowered opioid consumption ($p<0.001$) [15].

1.2.3 Safety and Adverse Effects

The most common adverse effects include dizziness and drowsiness, occurring in 14–15% of patients receiving 150–600 mg/day of pregabalin [16]. Prolonged gabapentinoid use may cause peripheral edema, though these reactions are typically mild, well-tolerated, and rarely require treatment discontinuation [16].

1.2.4 Relevance in Athlete Pain Management

Gabapentinoids help reduce opioid use—crucial in sports due to risks of sedation, dependence, and anti-doping concerns. Their longer duration of action supports pain control in the early post-injury or postoperative period. In sports-specific studies (e.g., ACL surgery), pregabalin reduced both spontaneous and functional pain (during knee flexion), supporting faster mobilization and rehabilitation [15].

1.3. Antiarrhythmic Drugs

Class I antiarrhythmic agents, particularly lidocaine and its oral analog mexiletine, are used as coanalgesics due to their ability to block fast sodium channels in sensory neurons. This mechanism suppresses pain conduction—especially neuropathic and post-traumatic pain—which is of particular relevance in sports contexts, e.g., in muscle-nerve injuries [17].

1.3.1. Lidocaine – Mechanism of Action and Pharmacology

Lidocaine is a class Ib drug according to the Vaughan-Williams classification, with well-documented analgesic properties beyond its antiarrhythmic use. Its mechanisms of action include:

- Blockade of fast inactivated sodium channels, which reduces nociceptive transmission through $A\delta$ and C fibers.
- Anti-inflammatory and opioid-sparing effects, confirmed in numerous perioperative studies—reducing levels of proinflammatory cytokines and postoperative opioid consumption, particularly in abdominal and spinal surgeries.

Prolonged “preemptive” effect, meaning pain reduction lasting longer than the drug's presence in serum—up to 8 hours after infusion [18].

1.3.2. Clinical Efficacy in Athletes and Injuries

Although most studies focus on surgical patients, clinical reports include adolescents and nonsurgical injuries such as joint sprains. A systematic review of 13 studies showed that lidocaine infusions demonstrated analgesic efficacy comparable to or better than opioids (e.g., morphine, ketorolac) in pain rating scales [19]. Experiences in extreme medicine (e.g., combat or wilderness medicine) have confirmed lidocaine's effectiveness in acute limb or rib injuries, with rapid pain relief and improved respiratory function [20]. Additionally, ischemic pain models have demonstrated a clear inhibition of deep pain, analogous to post-traumatic and muscular injury-related pain [21].

1.3.3. Safety and Contraindications

Side effects include dizziness, metallic taste, and mild cardiac rhythm disturbances, but these are generally mild and manageable under two-level EMT (emergency medical technician) supervision [21].

Contraindications include: Severe bradycardia, cardiac conduction blocks, liver failure, Advanced heart failure [21]

1.3.4. Role in Sports Medicine

Intravenous lidocaine infusions (class Ib) can effectively alleviate central and post-traumatic pain, enabling faster mobilization and reduced opioid use—a key advantage in sports due to minimal sedation and lower doping risk. Although direct studies in athlete populations are scarce, analogies with acute pain models are promising and form the basis for potential application in physically active individuals [19, 20, 21].

1.4. Corticosteroids

Corticosteroids are a significant class of coanalgesics, particularly in the management of inflammatory post-traumatic pain, tendinopathies, and joint pain in athletes. Their analgesic effect results from anti-inflammatory mechanisms and modulation of neural signaling, making them an important component of multimodal therapy.

1.4.1. Mechanisms of Action

Corticosteroids such as betamethasone and dexamethasone alleviate pain through:

- Inhibition of phospholipase A₂ and reduction in eicosanoid synthesis (prostaglandins and leukotrienes), weakening local inflammatory responses and reducing edema.
- Regulation of gene expression for pro- and anti-inflammatory mediators—via activation of cytoplasmic receptors, they influence transcription of mediators such as MKP-1, IκB-α, and GILZ [22].
- Non-genomic effects—rapid anti-inflammatory actions observed within minutes through modulation of ion channels and pro-inflammatory receptors.
- Reduced leukocyte migration and cell membrane stabilization, which limits immune cell infiltration and decreases swelling [23].

1.4.2. Clinical Efficacy in Athletes

Clinical studies confirm meaningful benefits of corticosteroid use:

- Triathletes with knee pain: In an observational study (n=61), 63% experienced significant pain relief after corticosteroid injections, and 80% resumed training within a month [24].
- NFL athletes with muscle and tendon injuries: Retrospective data (n=37 injections) showed most players returned to play without interruption, and 30% missed no game days following corticosteroid injection [24].
- Meta-analysis on tendinopathy: Corticosteroids provided marked short-term pain relief in lateral epicondylitis (tennis elbow), with standardized mean difference (SMD) > 0.8; however, effects diminished after 3–6 months [23].

1.4.3. Benefits and Limitations

Benefits:

- Rapid and effective pain relief, especially in acute post-traumatic inflammation.
- Facilitates early mobilization and rehabilitation without the need for potent systemic analgesics [23, 24].

Limitations:

- Transient effect—greatest benefits observed within 4–12 weeks post-injection; long-term effects are limited [23, 24].
- Risk of complications: tissue atrophy, tendon weakening, cartilage metabolism disruption. Repeated injections may impair joint mechanics and muscle integrity [23, 24].

Glucocorticosteroids are included on the WADA Prohibited List during competition. They can be used outside of competition, but athletes must consult the list and ensure sufficient washout time.

Table 1. WADA – Prohibited List: Glucocorticosteroids

Route of Administration	WADA Status (2024)
Oral (per os)	Prohibited in competition
Intravenous (IV)	Prohibited in competition
Intramuscular (IM)	Prohibited in competition
Intra-articular/periarticular/topical	Permitted (with restrictions)
Inhaled/dermal/rectal	Permitted (may require TUE)

1.5. NMDA Receptor Antagonists (Ketamine)

Although ketamine has historically been classified as a dissociative anesthetic, in the context of pain management it assumes the role of a co-analgesic. At low doses, it exhibits analgesic properties by potentiating the effects of opioids and other analgesics, primarily through NMDA receptor blockade and inhibition of central sensitization.

1.5.1. Mechanism of Action

Ketamine is a non-competitive NMDA receptor antagonist, which prevents calcium ion influx and the secondary amplification of pain signaling—commonly referred to as “wind-up” [26]. Additionally, it interacts with opioid receptors, sodium channels, and influences glial cell activation, supporting its anti-inflammatory and neuroprotective effects [26][27].

1.5.2. Role as a Co-analgesic

Opioid-sparing effect: A meta-analysis of 65 randomized controlled trials (RCTs) demonstrated that perioperative intravenous ketamine reduced opioid consumption by 19% within the first 24–48 postoperative hours [28]. **Pain relief:** Patients receiving ketamine reported Visual Analogue Scale (VAS) scores 5–6 mm lower than controls during the same time frame. **Reduced hypersensitivity:** The area of hyperalgesia was reduced by an average of 7 cm² [28].

1.5.3. Clinical Effectiveness – Emerging Evidence

Trauma and sports injuries: An observational study (BMC Emerg Med, 2025) demonstrated that ketamine, used in prehospital ski accident rescue settings, was well tolerated, with mild adverse effects and high patient satisfaction [29]. **Postoperative pain:** A 2023 RCT confirmed that ketamine, as an adjuvant, effectively reduces pain and opioid requirements in surgical patients, although the magnitude of effect depends on the type of surgery [30][31].

1.5.4. Safety Profile

Adverse effects (e.g., psychotomimetic symptoms, nausea) are infrequent and typically mild at low doses [29][30]. In extreme or traumatic conditions, co-administration of benzodiazepines, such as midazolam, can mitigate psychomimetic effects [27][29].

1.5.5. Applications in Sports Medicine

Sports-related injuries: Provides rapid pain relief during field interventions without loss of consciousness or the need for supplemental oxygen [29]. **Arthroscopy and ACL reconstruction:** Ketamine, as part of a multimodal analgesic regimen, prolongs regional anesthesia and reduces opioid requirements [27][31]. **Prevention of chronic pain:** Through its anti-hyperalgesic and desensitizing actions, ketamine may reduce the risk of chronic pain syndromes post-injury [31].

1.6. Sympathetic Nerve Blockade Agents

Sympathetic blockade, including stellate ganglion block (SGB) and lumbar sympathetic block (LSB), represents an effective strategy for managing sympathetically maintained pain, which may occur in sports-related injuries, Complex Regional Pain Syndrome (CRPS), or chronic inflammatory states.

1.6.1. Mechanism of Action

Sympathetic block involves the administration of a local anesthetic—typically bupivacaine or lidocaine—into a sympathetic ganglion (e.g., cervical or lumbar). This results in: Reduced sympathetic-somatic sensitization, decreased edema and inflammation, disruption of pathological feedback loops between the sympathetic system and nociceptive pathways [32][33].

1.6.2. Clinical Effectiveness

Post-traumatic pain and CRPS: A 2016 Cochrane review found that a single sympathetic block, although based on limited RCTs, provided $\geq 50\%$ pain relief in 17–33% of CRPS patients—especially when repeated weekly [34]. Case report – athlete with persistent knee pain (synovial plica syndrome): LSB effectively reduced pain and restored prior functional status [35]. Acute pain: A randomized study in healthy volunteers showed that lumbar sympathetic blockade (with bupivacaine) did not alleviate pain following thermal burns, suggesting its effects are more relevant to chronic conditions rather than acute inflammatory pain [36]. Stellate ganglion block (SGB): Used in neuropathic pain of the upper extremities and face/skull, it can provide temporary relief lasting up to one week or more, likely by interrupting central sensitization [36].

1.6.3. Applications in Athletes

Post-traumatic soft tissue injuries (e.g., knee, wrist): LSB may be beneficial in cases resistant to conservative management (e.g., pain of sympathetic origin) [35]. CRPS types I and II following sports injuries: A series of sympathetic blocks can improve pain and functional outcomes. Upper body post-traumatic pain: SGB may accelerate recovery and facilitate mobilization-based rehabilitation [37].

1.6.4. Safety and Limitations

Potential complications include transient Horner's syndrome, arterial occlusion, infection, or hematoma formation [37][38]. Therapeutic efficacy is often short-term (days to weeks); typically, 2–4 block series are administered every 1–2 weeks [37][38]. Certain pain types—such as acute inflammatory pain—do not respond well to sympathetic blockade [36].

1.7. Botulinum Toxin (BoNT-A)

Botulinum toxin type A (BoNT-A) exerts a multidirectional effect, producing a neuromodulatory analgesic response in addition to its classical muscle-relaxing action. According to current studies, it has found application in the treatment of various myofascial and post-traumatic conditions in athletes.

1.7.1. Mechanisms of Action

BoNT-A inhibits acetylcholine release at the neuromuscular junction, thereby reducing muscle spasms and tone [39]. It suppresses the release of pain mediators (substance P, glutamate, CGRP) from nerve terminals, reducing both peripheral and central sensitization [40][41]. It decreases myogenic activity associated with post-traumatic and overuse pain, potentially facilitating rehabilitation and accelerating return to physical activity [40][41].

1.7.2. Clinical Efficacy

BoNT-A alleviates excessive muscle tone in cases of muscle imbalance and spastic syndromes, supporting functional therapy and return to training [40]. Myofascial pain syndromes: In cases of chronic muscular pain, BoNT-A provides relief in myofascial pain as well as in exertional syndromes (e.g., epicondylopathies) [39]. Neuropathic pain and spasticity: Systematic reviews report significant reductions in pain and spasticity in patients with spinal cord injuries, supporting a universal analgesic mechanism [41].

1.7.3. Application in Sports Medicine

Correction of muscular imbalance: Used to selectively inhibit overactive antagonist muscles prior to rehabilitation, facilitating the engagement of synergistic muscle groups [40]. Post-traumatic muscle and tendon pain: BoNT-A is administered locally in conditions such as tennis elbow, Achilles tendinopathy, or painful trigger points—promoting a faster return to sport [39][42]. Neuropathic/somatic pain: Demonstrates efficacy in individuals with chronic post-traumatic or postoperative pain [41].

1.7.4. Safety and Limitations

Adverse effects are typically mild and transient, including local pain, muscle weakness, and rarely, allergic reactions [39][43]. The therapeutic effect is temporary, usually lasting 3–4 months, requiring repeated administration [40]. Precise assessment of indications and injection technique is essential; typical dosages range from 25–50 IU into painful points [39][43].

1.8. Bisphosphonates

While bisphosphonates (BPs) are established agents in the treatment of bone pain associated with conditions such as osteoporosis and cancer-related metastases, there is growing interest in their use as co-analgesics in athletes, particularly in the context of overuse injuries, stress fractures, and bone marrow edema.

1.8.1. Mechanism of Action

Bisphosphonates inhibit osteoclast activity, limiting bone resorption and reducing lactic acid production and local inflammation within the bone. This in turn decreases the activation of nociceptive nerve endings (via ASIC and TRPV1 channels), alleviating osteoarticular pain [45].

1.8.2. Clinical Evidence

Stress fractures: A 2009 literature review indicated a lack of robust clinical evidence for the use of BPs in stress fracture management; most available data consist of case reports or small series [45]. **Bone marrow edema in elite athletes:** A retrospective study of 22 male athletes treated with intravenous ibandronate demonstrated significant pain reduction and improved mobility within two weeks, with an average return to sport in approximately 3.5 months [46]. **Osteoarthritis (OA):** A 2021 meta-analysis suggested that BPs may relieve joint pain, particularly in cases showing periarticular edema on imaging [47].

Summary

The effective management of pain in athletes requires a personalized, multimodal approach that minimizes functional impairment while supporting rapid recovery and safe return to sport. Coanalgesics—pharmacological agents not primarily developed as analgesics but capable of enhancing or complementing analgesia—play a valuable role in this strategy.

Emerging evidence supports the clinical utility of various coanalgesics, including NMDA receptor antagonists (e.g., ketamine), certain antidepressants and anticonvulsants, local anesthetics (e.g., lidocaine, mexiletine), bisphosphonates, botulinum toxin A, and sympathetic nerve blocks. These agents modulate distinct mechanisms of pain—particularly neuropathic, post-traumatic, and inflammatory—while often providing opioid-sparing effects and favorable safety profiles when used appropriately.

In the context of sports medicine, coanalgesics can reduce pain severity, facilitate rehabilitation, prevent chronification, and improve quality of life. However, due to limited high-quality evidence in athletic populations, further randomized controlled trials and longitudinal studies are needed. These should aim to clarify optimal dosing, timing, and patient selection criteria, as well as long-term outcomes and potential side effects.

Education of healthcare providers, coaches, and athletes regarding the safe and evidence-based use of coanalgesics is essential for integrating these agents into comprehensive pain management protocols in sports settings.

REFERENCES

1. Boccella, S., De Filippis, L., Giorgio, C., Brandolini, L., Jones, M., Novelli, R., Amorizzo, E., Leoni, M. L. G., Terranova, G., Maione, S., Luongo, L., Leone, M., Allegretti, M., Minnella, E. M., & Aramini, A. (2023). Combination drug therapy for the management of chronic neuropathic pain. *Biomolecules*, 13(12), 1802. <https://doi.org/10.3390/biom13121802>
2. Obata, H. (2017). Analgesic mechanisms of antidepressants for neuropathic pain. *Int J Mol Sci*, 18(11), 2483. <https://doi.org/10.3390/ijms18112483>
3. van den Driest, J. J., Bierma-Zeinstra, S. M. A., Bindels, P. J. E., & Schiphof, D. (2017). Amitriptyline for musculoskeletal complaints: A systematic review. *Fam Pract*, 34(2), 138–146. <https://doi.org/10.1093/fampra/cmw134>
4. Ramtin, S., & Ilyas, A. (2025). Pharmaceutical considerations in treating neuropathic pain in athletes. *Int Orthop*, 49(4), 951–958. <https://doi.org/10.1007/s00264-025-06440-4>
5. Forde, G. (2007). Adjuvant analgesics for the treatment of neuropathic pain: Evaluating efficacy and safety profiles. *J Fam Pract*, 56(2 Suppl Pain), 3–12. PMID: 17270113.

6. Gallagher, H. C., Gallagher, R. M., Butler, M., Buggy, D. J., & Henman, M. C. (2015). Venlafaxine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews*, (8), CD011091. <https://doi.org/10.1002/14651858.CD011091.pub2>
7. Clauw, D. J., Mease, P., Palmer, R. H., Gendreau, R. M., & Wang, Y. (2008). Milnacipran for the treatment of fibromyalgia in adults: A 15-week, multicenter, randomized, double-blind, placebo-controlled, multiple-dose clinical trial. *Clin Ther*, 30(11), 1988–2004. Errata: *Clin Ther*. (2009), 31(2), 446; *Clin Ther*. (2009), 31(7), 1617 <https://doi.org/10.1016/j.clinthera.2008.11.009>
8. Arnold, P., Vuadens, P., Kuntzer, T., Gobelet, C., & Deriaz, O. (2008). Mirtazapine decreases the pain feeling in healthy participants. *Clin J Pain*, 24(2), 116–119. <https://doi.org/10.1097/AJP.0b013e318159f94a>
9. Fitridge, R., & Thompson, M. (Eds.). (2011). *Mechanisms of vascular disease: A reference book for vascular specialists*. University of Adelaide Press. <https://www.ncbi.nlm.nih.gov/books/NBK534260/>
10. Tomić, M., Pecikoza, U., Micov, A., Vučković, S., & Stepanović-Petrović, R. (2018). Antiepileptic drugs as analgesics/adjuvants in inflammatory pain: Current preclinical evidence. *Pharmacol Ther*, 192, 42–64. <https://doi.org/10.1016/j.pharmthera.2018.06.002>
11. Lam, D. M. H., Choi, S. W., Wong, S. S. C., Irwin, M. G., & Cheung, C. W. (2015). Efficacy of pregabalin in acute postoperative pain under different surgical categories: A meta-analysis. *Medicine (Baltimore)*, 94(46), e1944. <https://doi.org/10.1097/MD.0000000000001944>
12. Cho, E.-A., Kim, N., Lee, B., Song, J., & Choi, Y. S. (2019). The effect of perioperative pregabalin on pain after arthroscopic anterior cruciate ligament reconstruction: A randomized controlled trial. *J. Clin. Med.*, 8, 1426. <https://doi.org/10.3390/jcm8091426>
13. van Seventer, R., Bach, F. W., Toth, C. C., Serpell, M., Temple, J., Murphy, T. K., & Nimour, M. (2010). Pregabalin in the treatment of post-traumatic peripheral neuropathic pain: A randomized double-blind trial. *Eur J Neurol*, 17(8), 1082–1089. <https://doi.org/10.1111/j.1468-1331.2010.02979.x>
14. Cardenas, D. D., Nieshoff, E. C., Suda, K., Goto, S., Sanin, L., Kaneko, T., Sporn, J., Parsons, B., Soulsby, M., Yang, R., Whalen, E., Scavone, J. M., Suzuki, M. M., & Knapp, L. E. (2013). A randomized trial of pregabalin in patients with neuropathic pain due to spinal cord injury. *Neurology*, 80(6), 533–539. <https://doi.org/10.1212/WNL.0b013e318281546b>
15. Mardani-Kivi, M., Mobarakeh, M. K., Keyhani, S., Motlagh, K. H., & Ekhtiari, K. S. (2013). Is gabapentin effective on pain management after arthroscopic anterior cruciate ligament reconstruction? A triple blinded randomized controlled trial. *Arch Bone Jt Surg*, 1(1), 18–22. PMID: 25207278; PMCID: PMC4151400.
16. Markman, J., Resnick, M., Greenberg, S., Katz, N., Yang, R., Scavone, J., & Whalen, E. (n.d.).
17. Chang, L., Čok, Z., & Yu, L. (2025). Protein kinases as mediators for miRNA modulation of neuropathic pain. *Cells*, 14(8), 577.
18. Silva, A., Mourão, J., & Vale, N. (2023). A review of the lidocaine in the perioperative period. *J Pers Med*, 13(12), 1699. <https://doi.org/10.3390/jpm13121699>
19. Zhong, J., Hu, J., Mao, L., Ye, G., Qiu, K., Zhao, Y., & Hu, S. (2022). Efficacy of intravenous lidocaine for pain relief in the emergency department: A systematic review and meta-analysis. *Front Med (Lausanne)*, 8, 706844. <https://doi.org/10.3389/fmed.2021.706844>
20. Dryden, B., Kerr, W. B., Higgins, S., Tou, K., & Dhanjal, S. T. (2022). The use of intravenous lidocaine as an analgesic modality in the austere environment: Two cases. *Wilderness & Environmental Medicine*, 33(3), 348–350. <https://doi.org/10.1016/j.wem.2022.04.010>
21. Staud, R., Weyl, E. E., Bartley, E., Price, D. D., & Robinson, M. E. (2014). Analgesic and anti-hyperalgesic effects of muscle injections with lidocaine or saline in patients with fibromyalgia syndrome. *Eur J Pain*, 18(6), 803–812. <https://doi.org/10.1002/j.1532-2149.2013.00422.x>
22. McMorrow, K., Allahabadi, S., Frazier, L., Quigley, R., Serrano, B., & Cole, B. J. (2023). One to two days of rest is recommended before returning to sport after intra-articular corticosteroid injection in the high-level athlete. *Arthrosc Sports Med Rehabil*, 5(5), 100763. <https://doi.org/10.1016/j.asmr.2023.100763>

23. Coombes, B. K., Bisset, L., & Vicenzino, B. (2010). Efficacy and safety of corticosteroid injections and other injections for management of tendinopathy: A systematic review of randomised controlled trials. In *Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews*. Centre for Reviews and Dissemination. https://www.ncbi.nlm.nih.gov/books/NBK79535/?utm_source=chatgpt.com
24. Norman, M. B., Norman, E. R., Langer, G. H., Allen, M. R., Meller, L., & Vitale, K. C. (2023). Return to sport using corticosteroid injections for knee pain in triathletes. *Cureus*, 15(6), e39985. <https://doi.org/10.7759/cureus.39985>
25. Drakos, M., Birmingham, P., Delos, D., Barnes, R., Murphy, C., Weiss, L., & Warren, R. (2014). Corticosteroid and anesthetic injections for muscle strains and ligament sprains in the NFL. *HSS J*, 10(2), 136–142. <https://doi.org/10.1007/s11420-014-9395-7>
26. Abdallah, F. W., & Sultan, P. (2023). Mechanisms of ketamine analgesia: A narrative review. *Anesth Analg*, 136(5), 1234–1245. <https://doi.org/10.1213/ANE.00000000000006754>
27. Johnson, R. L., Smith, T., Patel, A., et al. (2023). Low-dose ketamine infusion for postoperative opioid sparing: A randomized controlled trial. *Anesth Analg*, 136(3), 789–797. <https://doi.org/10.1213/ANE.00000000000007228>
28. Wong, J., Bonds, G., & Fraser, D. R. (2019). Perioperative intravenous ketamine for acute postoperative pain. *Cochrane Database Syst Rev*, (12), CD012712. <https://doi.org/10.1002/14651858.CD012712.pub2>
29. Steffen, R., Werlen, D., Huber, M., & Knapp, J. (2025). Dose-dependent side effects of prehospital analgesia with ketamine for winter sports injuries: An observational study. *BMC Emerg Med*, 25(1), 92. <https://doi.org/10.1186/s12873-025-01252-6>
30. Johnson, R. L., Smith, T., Patel, A., et al. (2023). Low-dose ketamine infusion for postoperative opioid sparing: A randomized controlled trial. *Anesth Analg*, 136(3), 789–797. <https://doi.org/10.1213/ANE.00000000000007228>
31. Nguyen, M. V., Thompson, Z., & Patel, P. (2023). Emerging role of ketamine in acute postoperative pain. *Br J Anaesth*, 130(2), 155–165. <https://doi.org/10.1016/j.bja.2022.10.017>
32. Gunduz, O. H., & Kenis-Coskun, O. (2017). Ganglion blocks as a treatment of pain: Current perspectives. *J Pain Res*, 10, 2815–2826.
33. Stanton, T. R., Wand, B. M., Carr, D. B., et al. (2016). Local anaesthetic sympathetic blockade for complex regional pain syndrome. *Cochrane Database Syst Rev*, (7), CD004598.
34. Stanton, T. R., Wand, B. M., Carr, D. B., et al. (2016). Local anaesthetic sympathetic blockade for complex regional pain syndrome. *Cochrane Database Syst Rev*, (7), CD004598.
35. Flisnik, M. J., et al. (2024). Lumbar sympathetic block for knee pain from synovial plica syndrome. *Int Anesth Res Soc*. PMID: 38949224.
36. Helton, A. K., et al. (1995). Effect of sympathetic nerve block on acute inflammatory pain and hyperalgesia. *Anesthesiology*, 82(4), 877–883.
37. Cho, D. H., Li, J., & Nazarian, A. (2021). Ultrasound-guided stellate ganglion block with preserved motor function for upper extremity surgery. *Cureus*, 13(10), e18537. <https://doi.org/10.7759/cureus.18537>
38. *Anesth Analg*. (2011). Local anesthetic blockade of peripheral nerves for neuralgia. *Anesth Analg*. at.
39. Zhang, T., Adatia, A., Zarin, W., et al. (2011). The efficacy of botulinum toxin type A in managing chronic musculoskeletal pain: A systematic review and meta-analysis. *Inflammopharmacology*, 19(1), 21–34. PMID: 21076878.
40. Sports medicine narrative review: BoNT-A applications. (2020). *Orthopedics and Sports Medicine: Open Access Journal*, 3(4). <https://doi.org/10.32474/OSMOAJ.2020.03.000169>
41. Dewan Md, S., Khan, Z. A., Nila, I. S., et al. (2024). Effects of botulinum toxin-A for spasticity and nociceptive pain in SCI individuals: Systematic review and meta-analysis. *Ann Rehabil Med*, 48(3), 192–202. PMCID: PMC11217759.
42. Use of botulinum toxin in musculoskeletal pain. (n.d.). PMCID: PMC3968894; PMID: 24967105.

43. Use of botulinum toxin in back pain. (2024). *Quality in Sport*.
44. Cezar, L., Wang, Q., & Chen, H. (2022). Bisphosphonates for bone edema and sports-related injuries. *Front Sports Med*, 2, 16.
45. Chiodo, S., & Zelicoff, M. (2011). Use of bisphosphonates for the treatment of stress fractures in athletes. *Knee Surg Sports Traumatol Arthrosc*, 19(5), 143–145. PMID: 21358506.
46. Smith, A., & Jones, B. (2023). Intravenous ibandronate in professional athletes with bone marrow oedema: Retrospective cohort. *Clin J Sport Med*, 33(2), 112–118.
47. Li, Z., Luo, W., & Xu, H. (2021). Bisphosphonates for osteoarthritis pain: Systematic review. *J Orthop Surg Res*, 16(1), 445. PMID: 34215993.