MUSCULOSKELETAL PAIN
IASP Special Interest Group

FACT SHEET

Pharmacological Treatment of Musculoskeletal Pain

- **Vasileios Georgopoulos, PhD, PT:** Post-doctorate Research Fellow, Pain Centre Versus Arthritis, Academic Rheumatology, University of Nottingham Clinical Sciences Building, City Hospital, Hucknall Road, Nottingham, NG3 5DU, UK. Advanced Physiotherapist Practitioner, Primary Integrated Community Services, Ash Tree Court, Nottingham Business Park, Nottingham, NG8 6PY, UK.
- **David Andrew Walsh, PhD, FRCP:** AProgramme Director UKRI/Versus Arthritis Advanced Pain Discovery Platform and co-director Pain Centre Versus Arthritis, Academic Rheumatology, University of Nottingham. Nottingham, UK. Honorary Consultant Rheumatologist, Sherwood Forest Hospitals NHS Foundation Trust, UK.

Musculoskeletal pain management should accommodate patient choice, sensory and emotional aspects of pain, its diverse mechanisms in both peripheral and central nervous systems, and its context, including diagnosis, disability and co-morbidities, emotions, and past experiences.

Musculoskeletal disorders may broadly be classified as inflammatory (characterised by specific immune responses, as in rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis), or non-inflammatory (e.g. osteoarthritis, neck or low back pain). Mechanisms also differ between acute and chronic pain. People with chronic musculoskeletal conditions often continue to experience acute pain. Acute pain on a background of chronic musculoskeletal disease may respond differently to treatment than in a healthy, usually pain-free individual. All patients should consider tailored pharmacological and non-pharmacological management strategies that can help pain irrespective of diagnosis, alongside diagnosis-specific medications.

Pharmacological Treatment of Inflammatory Pain

In conditions that are characterised by specific immune responses, pain may be predominantly driven by inflammation within musculoskeletal tissues. In these cases, pharmacological immune suppression may reduce pain more effectively, and with lower risk than do less targeted strategies. Immune suppression in rheumatoid or psoriatic arthritis may, furthermore, reduce progressive joint damage (i.e., using `disease modifying anti-rheumatic drugs' (DMARDs)), and therefore protect against longer term pain and functional decline. Immunosuppressive therapies that can relieve pain in inflammatory arthritis include methotrexate, biologic agents targeting tumour necrosis factor or other cytokines or immune cells, and targeted synthetic agents such as inhibitors of Janus Kinase pathways [1]. Each of these also can retard joint damage. However, all may take weeks or months to achieve maximum benefit, and more rapid anti-inflammatory strategies are required to bridge between diagnosis and stable maintenance therapy. Rapid relief can be achieved with non-steroidal anti-inflammatory drugs (NSAIDs), which may be more effective for inflammatory musculoskeletal pain than are paracetamol (acetaminophen) or even so-called `strong painkillers' such as opioids [2]. Glucocorticoids administered orally, intramuscular, intravenous, or intra-articular, also provide rapid analgesic benefit in active inflammatory arthritis. Pain relief from glucocorticoids can be useful to bridge until DMARDs take effect, but tends to wain over 6 to 12 weeks, even with continued use. Co-morbidities such as diabetes mellitus, cardiovascular disease or osteoporosis can hinder or preclude glucocorticoid use.

Pharmacological Treatment of Pain in Osteoarthritis

NSAIDs are also recommended for pharmacological management of osteoarthritis, particularly during acute pain flares. Topical NSAIDs may be helpful for knee or hand osteoarthritis but may not penetrate deeper joints such as hips. Topical capsaicin may also be helpful for hand or knee osteoarthritis [3]. Some guidelines recommend NSAIDs as first-line oral analgesics for osteoarthritis, either non-selective agents (e.g. ibuprofen, naproxen) or COX-2 selective inhibitors (e.g. celecoxib) [4]. NSAIDs increases risks of upper gastrointestinal blood loss, which can be reduced by concurrent use of a proton pump inhibitor (e.g. omeprazole). Despite a narrow therapeutic window, and little evidence of efficacy, paracetamol continues to be commonly used for osteoarthritis pain [5]. Intra-articular glucocorticoid injections

may reduce osteoarthritis knee pain for, on average, 6 weeks, but oral glucocorticoids and immunosuppressive agents used in rheumatoid arthritis have not shown analgesic benefit in osteoarthritis. Most current guidelines recommend against the use of opioids for pain in osteoarthritis, due to lack of long-term efficacy and significant risk of adverse events.

Pharmacological Treatment of Spinal Pain

Pharmacological management of back or neck pain differs between acute (<3 months) and chronic pain. NSAIDs have evidence of analgesic benefit for acute spinal pain, whereas several systematic reviews have failed to find more than placebo benefit from paracetamol and weak opioids may have second-line value in acute spinal pain, if NSAIDs are ineffective or contra-indicated [6]. Only NSAIDs have robust evidence for sustained analgesic benefit in chronic spinal pain, although effect sizes may not be large [7].

Pharmacological Treatment of Nociplastic Pain

Inadequate symptom relief from anti-inflammatory treatments, and duration of pain beyond the expected natural recovery timeframe, should lead to review of pain mechanisms and consideration of other treatment options. Chronic musculoskeletal pain that appears disproportionate to any observable injury or disease (e.g. fibromyalgia) may be classified as chronic primary pain [8]. When there is evidence of pain hypersensitivity (e.g. allodynia) musculoskeletal pain may satisfy IASP criteria for nociplastic pain [9]. Some anti-depressant medications, such as tricyclics (e.g. amitriptyline, nortriptyline) or serotonin and noradrenaline reuptake inhibitors (SNRIs, e.g. duloxetine, milnacipran) have some evidence of analgesic benefit. However, their use for musculoskeletal pain is mostly 'off-label.' SNRIs may be considered for chronic primary pain [10] after shared and informed decision-making. Negative or inconclusive evidence has generally led most guidelines to recommend against using gabapentinoids (gabapentin, pregabalin), antipsychotics, ketamine, or benzodiazepines (diazepam) for any type of musculoskeletal pain, acute or chronic, primary, or secondary. Current guidelines recommend that NSAIDs, opioids, and paracetamol should not be initiated for patients with nociplastic pain and should be carefully deprescribed in chronic primary pain.

References

1. Radu, A.-F. and S.G. Bungau, Management of rheumatoid arthritis: an overview. Cells, 2021. 10(11): p. 2857.
2. NICE, Rheumatoid arthritis in adults: diagnosis and management. National Institute for Health and Care Excellence: London, UK, 2018.
3. Kolasinski, S.L., et al., 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis & rheumatology, 2020. 72(2): p. 220-233.
4. Arden, N.K., et al., Non-surgical management of knee osteoarthritis: comparison of ESCEO and OARSI 2019 guidelines. Nature Reviews Rheumatology, 2021. 17(1): p. 59-66.
5. Bannuru, R.R., et al., OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis and cartilage, 2019. 27(11): p. 1578-1589.
6. van der Gaag, W.H., et al., Non steroidal anti inflammatory drugs for acute low back pain. Cochrane Database of Systematic Reviews, 2020. 2020(4).
7. NICE, Low Back Pain and Sciatica in Over 16s: Assessment and Management. 2016.
8. Treede, R.-D., et al., Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). pain, 2019. 160(1): p. 19-27.
9. Kosek, E., et al., Chronic nociplastic pain affecting the musculoskeletal system: clinical criteria and grading system. Pain, 2021. 162(11): p. 2629-2634.
10. NICE Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain. 2021.