



- **FACT SHEET No. 18**

WHO Analgesic Ladder: Is It Appropriate for Joint Pain? From NSAIDs to Opioids

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In 1986, the World Health Organization (WHO) established the first recommendations to trigger the treatment of cancer pain. These recommendations, which were insufficient, were based on the WHO “pain ladder,” a stepwise approach to the use of analgesics depending on pain severity. The regimen considered in a parallel manner the severity of pain and the presumed efficacy of analgesics. The WHO stratified three steps in this approach of analgesic drugs: Step I using non-opioid analgesics (acetaminophen or non-steroidal anti-inflammatory drugs—NSAIDs), Step II with “weak” opioids (hydrocodone, codeine, or tramadol), and Step III with “strong” opioids (morphine, hydromorphone, oxycodone, fentanyl, or methadone). Additional drugs (adjuvants) were to be used to decrease anxiety.

This therapeutic step-by-step approach has led many to propose non-opioid analgesics for patients in mild pain, weak opioids for patients with moderate pain, and strong opioids for those with severe pain. The WHO recommendations suggested prescribing a Step II analgesic if treatment with a Step I analgesic was ineffective and a Step III analgesic in cases in which pain persisted despite a Step II analgesic. This approach was then extrapolated to non-cancer pain, including articular pain. In acute articular pain, the severity of pain may justify starting immediately with a weak or strong opioid to reduce pain quickly and switching later to a non-opioid analgesic if the pain subsides.

In 2015, the scientific community discussed this approach and suggested other classifications based on clinical efficacy or pain mechanisms. A mechanistic approach is probably more appropriate. David Lussier and Pierre Beaulieu proposed a new rational taxonomy in the book *Pharmacology of Pain* (IASP,



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2010) based on both pain mechanisms and the molecular targets of the analgesics. Concerning chronic pain, nociceptive inflammatory pain could be treated by reducing inflammation with steroids or NSAIDs, non-inflammatory nociceptive pain by opioid and non-opioid analgesics, and neuropathic pain by antidepressants or anticonvulsants, including specific drugs in certain rheumatologic clinical situations, such as colchicine to treat gout. A different approach from the WHO analgesic ladder allows the physician to treat pain according to the clinical reality and avoid being locked into a therapeutic escalation of stronger drugs.

Osteoarthritis is a major cause of pain in elderly patients, who often take multiple medications with common comorbidities that must be considered when choosing the analgesic. Previously published guidelines and the recently OARSI (Osteoarthritis Research Society International) recommendations defined appropriate treatments as acetaminophen, NSAIDs, and duloxetine based on comorbidities. Treatments that were considered not appropriate included opioid analgesics. Opioid analgesics should be prescribed only for patients with refractory osteoarthritis pain or with contraindications to the recommended treatments or for patients waiting for orthopedic surgery or when surgery is not possible.

Pain in osteoarthritis has a variety of characteristics suggesting different underlying mechanisms. Some patients describe their pain as neuropathic pain with suspected peripheral or central sensitization. In this sub-phenotype of patients, the treatment could be aimed at either reducing peripheral and central sensitization or enhancing descending inhibitory activity (i.e., anticonvulsants, antidepressants, or capsaicin).

In inflammatory rheumatic diseases, optimal pain treatments are NSAIDs and corticosteroids. Opioid and non-opioid analgesics are preferentially prescribed for mechanical pain induced by articular destruction. Now, biotherapies are also part of the therapeutic approaches against pain in inflammatory rheumatic diseases and may be considered at least as anti-nociceptive analgesics. Concerning microcrystalline arthritis, optimal treatment requires NSAIDs, colchicine, or corticosteroids based on the EULAR (European League Against Rheumatism) recommendations for calcium pyrophosphate deposition and the third initiative for gout.

In fibromyalgia, non-opioid and weak opioid analgesics only lead to a modest relief of pain. Although assessment of pain is often high in these patients and should theoretically lead to a prescription of strong opioids based on the WHO ladder, there is no evidence of efficacy, and physicians should consider other treatment options. The recommended treatments are more often modulators of descending inhibition.

Finally, the WHO analgesic ladder is not appropriate for acute or chronic joint pain management. The future challenge is to better characterize the different mechanisms of joint pain and to adapt the drugs according to their molecular targets.

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