

News from Good Life

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Sincerely,
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Managing Osteoarthritic Pain with Topical NSAIDs

Osteoarthritis (OA) is a leading cause of pain and disability worldwide. Due to the rapid aging of the world's population, OA of the hands, knees and lower back is expected to be one of the major challenges to maintaining physical function and quality of life in the elderly. Topical NSAIDs are expected to be at the forefront of providing relief from osteoarthritic pain while avoiding systemic exposure – an important consideration in a patient population with frequent co-morbidities and age-related decline in renal and hepatic function.



Best available evidence indicates that topical NSAIDs have a moderate effect on relief of osteoarthritic pain, comparable to that of oral NSAIDs but with a better risk-to-benefit ratio. International clinical practice guidelines recommend topical NSAIDs on par with or ahead of oral NSAIDs for pain management in patients with knee and hand osteoarthritis, and as the first-line choice in persons aged ≥ 75 years.

Primary symptoms of OA include joint pain, stiffness and movement limitation with occasional effusion and variable degrees of local inflammation. Treatment goals are to manage pain, reduce inflammation and maintain joint function. NSAIDs are central to the pharmacological management of OA. However, frequent or prolonged use of oral NSAIDs in chronic conditions such as OA raises tolerability and safety concerns, especially in more vulnerable populations such as the elderly and those with predisposing co-morbidities including high cardiovascular risk, type 2 diabetes and renal dysfunction. Oral NSAIDs are associated with age- and dose-related risks of gastrointestinal, cardiovascular, renal and hepatic adverse events.

Topical NSAIDs operate under the same mechanism of action as oral NSAIDs but with

localized absorption and effect. Topical NSAIDs provide analgesic concentrations at the site of pain/inflammation, while avoiding systemic distribution of drug at physiologically active levels.

Systematic reviews and meta-analyses reporting on the efficacy and safety of topical NSAIDs found that most evidence exists for topical ketoprofen and diclofenac. "Topical NSAIDs are effective and should be recommended as a first-line intervention for mild to moderate pain associated with musculoskeletal disorders."

The National Institute for Health and Clinical Excellence (2014) recommends that for hand and knee OA, topical NSAIDs should be considered for pain relief ahead of oral NSAIDs, COX-2 inhibitors or opioids. The Osteoarthritis Research Society International reported topical NSAIDs are appropriate to treat knee OA in patients with or without co-morbidities.

In the treatment of acute musculoskeletal pain (e.g., sprains, strains and overuse injuries) in adults, topical NSAIDs were found to provide significantly higher rates of clinical success (more patients with $\geq 50\%$ pain reduction) than topical placebo during short-term use (less than 7 days), with an efficacy comparable to that of oral NSAIDs. Topical NSAIDs were well tolerated during short-term use.

The balance of lipophilic and hydrophilic components in gel-based formulations allows for faster diffusion across the skin and greater absorption in local tissues when compared with ointments and creams. Gels have better cosmetic acceptability since they spread and vanish more readily and are devoid of fatty components that leave a greasy residue. When assessed for ease of application, rate of penetration, after-feel and scent, ketoprofen gel scored higher than diclofenac and piroxicam.

[Pain Manag. \(2018\) 8\(2\), 115–128](#)

Clinical Benefits of Low-Dose Naltrexone for Sjogren's

Sjogren's Syndrome is a chronic autoimmune disorder that causes inflammation of the lacrimal and salivary glands, resulting in dryness of the eyes and mouth. In addition, fatigue and musculoskeletal pain, often described as aching, is very common. Treatment directed toward alleviating the fatigue and pain associated with Sjogren's is currently very limited.

Low-Dose Naltrexone (LDN) has pain-relieving and anti-inflammatory properties. Limited studies have shown benefit in helping relieve the pain in patients with fibromyalgia and improving disease activity in autoimmune conditions such as inflammatory bowel disease and multiple sclerosis. As a result, it seems reasonable that the medication might be useful in Sjogren's.

A case report describes a 47-year-old female with suspected Sjogren's based on long-standing dry eyes, dry mouth, joint pain, fatigue, elevated measures of inflammation, and a positive rheumatoid factor. She failed standard therapy but improved clinically with LDN. She initially had a negative rheumatoid factor, but her erythrocyte sedimentation rate (ESR) was 48 to 61 (normal is less than 20 mm/h). Her C-reactive protein (CRP) was 1.74 (normal is less than 0.80 mg/dl). Four years later,

when she saw a second rheumatologist, her rheumatoid factor was 69 IU/ml (normal is less than 14 IU/ml). Her antinuclear antibody (ANA) and Sjogren antibodies (SS-A and SS-B) were absent. ESR was 48 and CRP was 1.42. Medications taken daily to help with symptoms of Sjogren's Syndrome and fibromyalgia included Lexapro®, Restasis®, meloxicam 15 mg, vitamin D3, magnesium, tramadol 100 mg daily PRN, Salagen® 5 mg TID PRN, and hydroxychloroquine 400 mg daily. Her exam demonstrated widespread trigger points affecting both sides of her body, above and below her waist.

About two years later, she saw the author of this case report, with complaints of fatigue, severe musculoskeletal pain, as well as dryness of her eyes and mouth. She elected to try compounded low-dose naltrexone (LDN), and started at 1.5 mg daily with instructions to increase the medication weekly by 1.5 mg. Two weeks after starting the medication, she was taking 3 mg daily and stated that she felt terrific. Her lab was remarkable for a normal ESR of 25 and a CRP of 2.33.

During subsequent followup visits, she felt well but complained of neuropathic pain and increased achiness, and had widespread tender points. In place of meloxicam, she was given a short course of corticosteroids with symptomatic improvement. After hydroxychloroquine was discontinued due to a prolonged QTc interval, her ESR and CRP decreased. LDN was increased to 4.5 mg and the patient noted significant relief from fatigue and pain within two weeks but no significant change in her dry eyes or mouth. She continued to do well on low-dose naltrexone four months after stopping hydroxychloroquine, and her clinical improvement was associated with an improvement in her inflammatory markers.

Overall, LDN is well-tolerated. Side effects include but are not limited to vivid dreams (most patients take the medication in the evening, but morning dosing of the medication may help with this issue). LDN should not be used in patients who are currently receiving opioid analgesics as it may reduce pain relief, and there is a possibility of acute opioid withdrawal. Patients taking thyroid replacement may require a lower amount of thyroid medication so periodic monitoring is indicated. The elevation of liver enzymes is a potential risk with naltrexone treatment but is uncommon with LDN. Other potential side effects may include but are not limited to gastrointestinal disturbances, such as stomach cramps and diarrhea, agitation, anxiety, flu-like symptoms, and headaches. The most common starting dose is 0.5 mg daily in the evening and increased weekly up to a target dose of 4.5 mg. LDN should be stopped at a minimum of 24-72 hours prior to the time narcotics may be needed for pain relief for a scheduled surgical procedure.

[Cureus. 2019 Mar 11;11\(3\):e4225.](#)

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