**TABLE 394-1 PHARMACOLOGIC TREATMENT FOR OSTEOARTHRITIS**

| Treatment | Dosage | Comments |
|---|---|---|
| Acetaminophen | Up to 1 g tid | Prolongs half-life of warfarin. Make sure patient is not taking other treatments containing acetaminophen to avoid hepatic toxicity. |
| Oral NSAIDs and COX-2 inhibitors<br>Naproxen<br>Salsalate<br>Ibuprofen | 375–500 mg bid<br>1500 mg bid<br>600–800 mg 3–4 times a day | Take with food. Increased risk of myocardial infarction and stroke for some NSAIDs and especially COX-2 inhibitors. High rates of gastrointestinal side effects, including ulcers and bleeding, occur. Patients at high risk for gastrointestinal side effects should also take either a proton pump inhibitor or misoprostol.[a] There is an increase in gastrointestinal side effects or bleeding when taken with acetylsalicylic acid. Can also cause edema and renal insufficiency. |
| Topical NSAIDs<br>Diclofenac Na 1% gel | <br>4 g qid (for knees, hands) | Rub onto joint. Few systemic side effects. Skin irritation common. |
| Opiates | Various | Common side effects include dizziness, sedation, nausea or vomiting, dry mouth, constipation, urinary retention, and pruritus. Respiratory and central nervous system depression can occur. |
| Capsaicin | 0.025–0.075% cream 3–4 times a day | Can irritate mucous membranes. |
| Intraarticular injections<br>Steroids<br>Hyaluronans | <br><br>Varies from 3–5 weekly injections depending on preparation | <br><br>Mild to moderate pain at injection site. Controversy exists regarding efficacy. |

[a]Patients at high risk include those with previous gastrointestinal events, persons ≥60 years, and persons taking glucocorticoids. Trials have shown the efficacy of proton pump inhibitors and misoprostol in the prevention of ulcers and bleeding. Misoprostol is associated with a high rate of diarrhea and cramping; therefore, proton pump inhibitors are more widely used to reduce NSAID-related gastrointestinal symptoms.

***Abbreviations:*** COX-2, cyclooxygenase-2; NSAIDs, nonsteroidal anti-inflammatory drugs.

***Source:*** Adapted from DT Felson: N Engl J Med 354:841, 2006.



an anti-inflammatory dose selected (Table 394-1). Patients should be reminded to take low-dose aspirin and ibuprofen at different times to eliminate a drug interaction.

NSAIDs taken orally have substantial and frequent side effects, the most common of which is upper gastrointestinal toxicity, including dyspepsia, nausea, bloating, gastrointestinal bleeding, and ulcer disease. Some 30–40% of patients experience upper gastrointestinal (GI) side effects so severe as to require discontinuation of medication. To minimize the risk of nonsteroidal-related GI side effects, patients should not take two NSAIDs and should take medications after food; if risk is high, patients should take a gastroprotective agent, such as a proton pump inhibitor. Certain oral agents are safer to the stomach than others, including nonacetylated salicylates and nabumetone. Major NSAID-related GI side effects can occur in patients who do not complain of upper GI symptoms. In one study of patients hospitalized for GI bleeding, 81% had no premonitory symptoms.

Because of the increased rates of cardiovascular events associated with COX-2 inhibitors and with some conventional NSAIDs such as diclofenac, many of these drugs are not appropriate long-term treatment choices for older persons with OA, especially those at high risk of heart disease or stroke. The American Heart Association has identified rofecoxib and all other COX-2 inhibitors as putting patients at high risk, although low doses of celecoxib (≤200 mg/d) may not be associated with an elevation of risk. The only conventional NSAID that appears safe from a cardiovascular perspective is naproxen, but it does have GI toxicity.

There are other common side effects of NSAIDs, including the tendency to develop edema because of prostaglandin inhibition of afferent blood supply to glomeruli in the kidneys and, for similar reasons, a predilection toward reversible renal insufficiency. Blood pressure may increase modestly in some NSAID-treated patients. Oral NSAIDs should not be used in patients with stage IV or V renal disease and should be used with caution in those with stage III disease.

NSAIDs can be placed into a gel or topical solution with another chemical modality that enhances penetration of the skin barrier creating a topical NSAID. When absorbed through the skin, plasma concentrations are an order of magnitude lower than with the same amount of drug administered orally or parenterally. However, when these drugs are administered topically in proximity to a superficial joint (knees, hands, but not hips), the drug can be found in joint tissues such as the synovium and cartilage. Trial results have varied but generally have found that topical NSAIDs are slightly less efficacious than oral agents, but have far fewer GI and systemic side effects. Unfortunately, topical NSAIDs often cause local skin irritation where the medication is applied, inducing redness, burning, or itching in up to 40% of patients (see Table 394-1).

**Intraarticular Injections: Glucocorticoids and Hyaluronic Acid** Because synovial inflammation is likely to be a major cause of pain in patients with OA, local anti-inflammatory treatments administered intraarticularly may be effective in ameliorating pain, at least temporarily. Glucocorticoid injections provide such efficacy, but response is variable, with some patients having little relief of pain whereas others experience pain relief lasting several months. Glucocorticoid injections are useful to get patients over acute flares of pain and may be especially indicated if the patient has coexistent OA and crystal deposition disease, especially from calcium pyrophosphate dihydrate crystals (Chap. 395). There is no evidence that repeated glucocorticoid injections into the joint are dangerous.

Hyaluronic acid injections can be given for treatment of symptoms in knee and hip OA, but there is controversy as to whether they have efficacy versus placebo (Table 394-1).

**Other Classes of Drugs and Nutraceuticals** For patients with symptomatic knee or hip OA who have not had an adequate response to the treatments above and are either unwilling to undergo or are not candidates for total joint arthroplasty, opioid analgesics have shown modest efficacy and can be tried. Opioid management plans and patient selection are critical. Another option is the use of duloxetine, which has demonstrated modest efficacy in OA.

Recent guidelines recommend against the use of glucosamine or chondroitin for OA. Large publicly supported trials have failed to show that, compared with placebo, these compounds relieve pain in persons with disease.

Optimal nonsurgical therapy for OA is often achieved by trial and error, with each patient having idiosyncratic responses to specific treatments. When medical therapies have failed and the patient has an unacceptable reduction in their quality of life and ongoing pain