ARTHRITIS & RHEUMATISM
Vol. 43, No. 9, September 2000, pp 1905–1915

Arthritis & Rheumatism

Official Journal of the American College of Rheumatology
www.arthritisrheum.org

SPECIAL ARTICLE

RECOMMENDATIONS FOR THE MEDICAL MANAGEMENT OF OSTEOARTHRITIS OF THE HIP AND KNEE

2000 Update

AMERICAN COLLEGE OF RHEUMATOLOGY SUBCOMMITTEE ON OSTEOARTHRITIS GUIDELINES

Osteoarthritis (OA) is the most common form of arthritis in the United States (1). Patients with OA have pain that typically worsens with weight bearing and activity and improves with rest, as well as morning stiffness and gelling of the involved joint after periods of inactivity. On physical examination, they often have tenderness on palpation, bony enlargement, crepitus on motion, and/or limitation of joint motion. Unlike the case with rheumatoid arthritis (RA) and other inflammatory arthritides, inflammation, if present, is usually mild and localized to the affected joint. Although the causes of OA are not completely understood, biomechanical stresses affecting the articular cartilage and subchondral bone, biochemical changes in the articular cartilage and synovial membrane, and genetic factors are all important in its pathogenesis (2–4).

Although there is no known cure for OA, treatment designed for the individual patient can reduce pain, maintain and/or improve joint mobility, and limit functional impairment. In 1995, the American College of Rheumatology (ACR) published recommendations for the medical management of OA of the hip and knee (5,6). Those guidelines outlined the use of nonpharmacologic modalities, including patient education and physical and occupational therapy—the foundation of treatment of individuals with OA—as well as the use of pharmacologic agents. Specific recommendations for surgical management of OA, however, were not included. Since that time, several systematic reviews of drug therapy for OA have been published (7–11), and many clinical trials have been conducted which have resulted in the approval, or pending review, by the Food and Drug Administration (FDA) of new devices and drug treatments for OA.

In 1998, the ACR established an ad hoc subcommittee, comprising several of the American authors of the 1995 recommendations, to review interim developments in the field and update the recommendations. As in the original review, the subcommittee followed the

Members of the Subcommittee on Osteoarthritis Guidelines are as follows. Roy D. Altman, MD: Department of Veterans Affairs Medical Center, and University of Miami School of Medicine, Miami, Florida; Marc C. Hochberg, MD, MPH: University of Maryland School of Medicine, Baltimore; Roland W. Moskowitz, MD: Case Western Reserve University School of Medicine, Cleveland, Ohio; Thomas J. Schnitzer, MD, PhD: Northwestern University Medical School, Chicago, Illinois.

Members of the Subcommittee have relationships with the following pharmaceutical or biotechnology companies. Roy D. Altman, MD: Abbott, Aventis Pharmaceutical Co., Boehringer-Ingelheim, Eutovita, Fidia Co., Johnson & Johnson, Ortho-McNeil, Merck Sharp and Dohme, Novartis, Pierre Farber, Procter and Gamble, Sanofi, Searle, United Therapeutics, Whitehall Robbins, Negma, and NeuColl Corp. Marc C. Hochberg, MD, MPH: Merck & Co., Aventis Pharmaceutical Co., NEGMA Laboratories, Procter and Gamble, Roche, Wyeth-Ayerst, Johnson & Johnson, Eli Lilly, and Schering Plough. Roland W. Moskowitz, MD: Searle (Pharmacia), Sanofi-Synthelab, Fidia Co., and NeuColl Corp. Thomas J. Schnitzer, MD, PhD: Abbott, Boehringer-Ingelheim, Johnson & Johnson, McNeil Consumer, Merck & Co., Novartis, Ortho-McNeil, Parke-Davis, Searle, Wyeth-Ayerst, and SmithKline Beecham.

The American College of Rheumatology is an independent professional, medical, and scientific society which does not guarantee, warrant, or endorse any commercial product or service.

Address reprint requests to American College of Rheumatology, 1800 Century Place, Suite 250, Atlanta, GA 30345.

Submitted for publication January 29, 2000; accepted in revised form May 12, 2000.

principles of evidence-based medicine as used in the process of making clinical decisions (12). As stated by Guyatt, "Physicians practicing [evidence-based medicine] will search for the highest evidence available, integrate this evidence with their clinical experience and judgment, and acknowledge the value judgments implicit in moving from evidence to action" (12).

The strongest weight was given to data from systematic reviews, meta-analyses, and published findings of randomized controlled trials; data from randomized controlled trials presented as abstracts at scientific meetings were also considered. Where such data were not available, however, the subcommittee followed the approach taken by the Agency for Health Care Policy and Research, as outlined in the ACR document "Guidelines for the Development of Practice Guidelines," which combines a detailed, evidence-based approach with a process that accommodates expert opinion. This was utilized particularly in reviewing the recommendations for nonpharmacologic modalities, especially the use of assistive devices, bracing, and footwear. Finally, recently published data on OA patients' preferences regarding treatment with analgesics and nonsteroidal antiinflammatory drugs (NSAIDs) were also reviewed (13,14).

The goals of the contemporary management of the patient with OA continue to include control of pain and improvement in function and health-related quality of life, with avoidance, if possible, of toxic effects of therapy. The recommended approach to the medical management of hip or knee OA includes nonpharmacologic modalities and drug therapy. The Subcommittee on OA Guidelines emphasizes that these recommendations are not fixed, rigid mandates, and recognizes that the final decision concerning the therapeutic regimen for an individual patient rests with the treating physician.

Table 1. Nonpharmacologic therapy for patients with osteoarthritis

Patient education
Self-management programs (e.g., Arthritis Foundation Self-Management Program)
Personalized social support through telephone contact
Weight loss (if overweight)
Aerobic exercise programs
Physical therapy
Range-of-motion exercises
Muscle-strengthening exercises
Assistive devices for ambulation
Patellar taping
Appropriate footwear
Lateral-wedged insoles (for genu varum)
Bracing
Occupational therapy
Joint protection and energy conservation
Assistive devices for activities of daily living

Nonpharmacologic modalities

The components of nonpharmacologic therapy are outlined in Table 1. Patient education and, where appropriate, education of the patient's family, friends, or other caregivers are integral parts of the treatment plan for patients with OA. Patients should be encouraged to participate in self-management programs, such as the Arthritis Foundation Self-Management Program. Individuals who participate in these programs report decreases in joint pain and frequency of arthritis-related physician visits, increases in physical activity, and overall improvement in quality of life (15). Additional educational materials, including videos, pamphlets, and newsletters, are available from the Arthritis Foundation and other national voluntary health organizations. Another cost-effective nonpharmacologic approach for patients with OA is provision of personalized social support, either directly or by periodic telephone contact. Studies of the results of monthly telephone calls by trained nonmedical personnel to discuss such issues as joint pain, medications and treatment compliance, drug toxicities, date of next scheduled visit, and barriers to keeping clinic appointments showed moderate-to-large degrees of improvement in pain and functional status without a significant increase in costs (16). These studies underscore the concept that improved communication and education are important factors in decreasing pain and improving function in patients with OA.

Individuals with OA of the lower extremity may have limitations that impair their ability to perform activities of daily living (ADLs), such as walking, bathing, dressing, use of the toilet, and performing household chores. Physical therapy and occupational therapy play central roles in the management of patients with functional limitations. The physical therapist assesses muscle strength, joint stability, and mobility; recommends the use of modalities such as heat (especially useful just prior to exercise); instructs patients in an exercise program to maintain or improve joint range of motion and periarticular muscle strength; and provides assistive devices, such as canes, crutches, or walkers, to improve ambulation. Similarly, the occupational therapist can be instrumental in directing the patient in proper joint protection and energy conservation, use of splints and other assistive devices, and improving joint function. In addition, the input of a vocational guidance

counselor may be important to patients who are still actively employed.

Quadriceps weakness is common among patients with knee OA, in whom it had been believed to be a manifestation of disuse atrophy, which develops because of unloading of the painful extremity. Recent studies, however, have indicated that quadriceps weakness may be present in persons with radiographic changes of OA who have no history of knee pain, and in whom lower extremity muscle mass is increased, rather than decreased (17); and that quadriceps weakness may be a risk factor for the development of knee OA, presumably by decreasing stability of the knee joint and reducing the shock-attenuating capacity of the muscle (18). These data have recently been reviewed by Hurley (19).

The beneficial effects of both quadriceps-strengthening and aerobic exercise for patients with knee OA, noted in the original recommendations, were confirmed in the Fitness Arthritis and Seniors Trial (20), in which patients with mild disability due to symptomatic knee OA were randomly assigned to aerobic exercise, resistive (muscle-strengthening) exercise, or an education/attention control group. Patients in both exercise groups had modest but significant improvement compared with the control group; this improvement was sustained over an 18-month followup period. In post hoc analyses, the authors found that the degree of adherence to the exercise regimen was significantly associated with the magnitude of improvement in pain and functional limitation. The ability of elderly subjects to maintain conditioning levels of exercise is noteworthy, since many patients with advanced hip or knee OA are sedentary, deconditioned, and at increased risk for cardiovascular disease (21).

Another recent study demonstrated the efficacy of an exercise program in improving muscle strength, mobility, and coordination in patients with OA of either the knee or hip (22). In this study, patients randomly assigned to the exercise group not only had improvement in pain and observed disability, but also reported taking less acetaminophen and had made fewer physician visits by 12 weeks after entry. The effectiveness of exercise was similar in patients with hip or knee OA. These exercise programs, however, require a commitment of time and effort on the part of the patient.

In addition to quadriceps weakness, sensory dysfunction, reflected by a decrease in proprioception, has been documented in patients with knee OA (23,24). Hurley and Scott (25) showed that an easily performed exercise regimen improved knee joint position sense as well as quadriceps strength and performance of ADLs, and that these improvements were maintained for as long as 6 months.

The 1995 ACR guidelines also recommended that overweight patients with hip or knee OA lose weight. A randomized open trial of an appetite suppressant and low-calorie diet was completed in 40 overweight patients with knee OA; all patients received instruction in an exercise walking program (26). Patients randomly assigned to the appetite suppressant group lost a mean of 3.9 kg over the course of 6 weeks, and also had significant improvement in their knee OA, as measured by the Lequesne algofunctional index. Although this study had limitations, it provided the only data from a randomized trial demonstrating a relationship between loss of body fat (rather than loss of body weight) and improvement in symptoms of knee OA.

As noted in the 1995 ACR recommendations (5,6), proper use of a cane (in the hand contralateral to the affected knee) reduces loading forces on the joint and is associated with a decrease in pain and improvement of function. In addition, patients may benefit from wedged insoles to correct abnormal biomechanics due to varus deformity of the knee (27,28). Another useful maneuver for patients with OA of the knee who have symptomatic patellofemoral compartment involvement is medial taping of the patella (29).

Pharmacologic therapy

All of the pharmacologic agents discussed in this section should be considered additions to nonpharmacologic measures, such as those described above, which are the cornerstone of OA management and should be maintained throughout the treatment period. Drug therapy for pain management is most effective when combined with nonpharmacologic strategies (30).

For many patients with OA, the relief of mild-to-moderate joint pain afforded by the simple analgesic, acetaminophen, is comparable with that achievable with an NSAID (8,10,31–33). Furthermore, Bradley and colleagues failed to demonstrate differences in responses to acetaminophen and ibuprofen in knee OA patients with clinical features of joint inflammation (34). However, this finding was based on a post hoc analysis with limited statistical power that used a definition of inflammation which included joint-line and soft-tissue tenderness or soft-tissue swelling. Eccles and colleagues, in a meta-analysis of trials comparing simple analgesics with NSAIDs in patients with knee OA, did note that NSAID-treated patients had significantly greater improvement in both pain at rest and pain on motion (33).

Two recent trials, findings of which were presented at the ACR's 1999 annual meeting, also provide data on the relative efficacy of acetaminophen and NSAIDs in patients with OA. In one study, acetaminophen and ibuprofen were comparably effective in patients with mild-to-moderate pain, but ibuprofen was statistically superior to acetaminophen in patients with severe pain (35); in the other study, diclofenac was statistically superior to acetaminophen for both pain and function measured with several validated outcome measures (36). Furthermore, two recent studies of patients with OA demonstrated greater preference for NSAIDs than for acetaminophen, although many patients continue to take acetaminophen (13,14). Nevertheless, although a number of patients may fail to obtain adequate relief even with full doses of acetaminophen, this drug merits a trial as initial therapy, based on its overall cost, efficacy, and toxicity profile (33,37). In patients with knee OA with moderate-to-severe pain, and in whom signs of joint inflammation are present, joint aspiration accompanied by intraarticular injection of glucocorticoids or prescription of an NSAID merits consideration as an alternate initial therapeutic approach.

The daily dose of acetaminophen should not exceed 4 gm. Although it is one of the safest analgesics, acetaminophen can be associated with clinically important adverse events. Recent reports have highlighted long-recognized conditions in which increased awareness of potential toxicity is important. For example, because acetaminophen can prolong the half-life of warfarin sodium, careful monitoring of the prothrombin time is recommended in patients taking warfarin sodium who subsequently begin high-dose acetaminophen treatment (38,39). Hepatic toxicity with acetaminophen is rare with doses of ≤4 gm/day. Nonetheless, the drug should be used cautiously in patients with existing liver disease and avoided in patients with chronic alcohol abuse because of known increased risk in these settings (40–42). Even though acetaminophen was reported to be weakly associated with end-stage renal disease, the Scientific Advisory Committee of the National Kidney Foundation recommends it as the drug of choice for analgesia in patients with impaired renal function (43).

For those patients who fail to obtain adequate symptomatic relief with the above measures, alternative or additional pharmacologic agents should be considered. The choice should be made after evaluation of risk factors for serious upper gastrointestinal (GI) and renal toxicity. Data from epidemiologic studies show that among persons of age ≥65 years, 20–30% of all hospitalizations and deaths due to peptic ulcer disease were attributable to therapy with NSAIDs (44–46). Furthermore, in the elderly, the risk of a catastrophic GI event in patients taking NSAIDs is dose dependent (44). Risk factors for upper GI bleeding in patients treated with NSAIDs include age ≥65 years, history of peptic ulcer disease or of upper GI bleeding, concomitant use of oral glucocorticoids or anticoagulants, presence of comorbid conditions, and, possibly, smoking and alcohol consumption (Table 2) (47–49). Risk factors for reversible renal failure in patients with intrinsic renal disease (usually defined as a serum creatinine concentration of ≥2.0 mg/dl) who are treated with NSAIDs include age ≥65 years, hypertension and/or congestive heart failure, and concomitant use of diuretics and angiotensin-converting enzyme inhibitors (50).

Table 2. Risk factors for upper gastrointestinal adverse events

Age ≥65
Comorbid medical conditions
Oral glucocorticoids
History of peptic ulcer disease
History of upper gastrointestinal bleeding
Anticoagulants

Additional considerations involved in a practitioner's decision to treat the individual OA patient include existing comorbidities and concomitant therapy, as well as the side effects and costs of specific treatments. In individuals with OA of the knee who have mild-to-moderate pain, do not respond to acetaminophen, and do not wish to take systemic therapy, the use of topical analgesics (e.g., methylsalicylate or capsaicin cream) is appropriate as either adjunctive treatment or monotherapy. Capsaicin cream should be applied to the symptomatic joint 4 times daily; a local burning sensation is common, but rarely leads to discontinuation of therapy. A systematic review of topical NSAIDs also demonstrated efficacy in patients with OA (51); there are no published findings of trials comparing the same NSAID administered orally versus topically.

Initiation of treatment in the patient at increased risk for an upper GI adverse event

The options for medical management of OA that has not responded to the above measures in patients who are at increased risk for a serious upper GI adverse event, such as bleeding, perforation, or obstruction, are summarized in Table 3; these include either oral agents or local intraarticular therapy. Two cyclooxygenase 2 (COX-2)–specific inhibitors, celecoxib and rofecoxib, have been studied in patients with OA (52,53). Cele-

Table 3. Pharmacologic therapy for patients with osteoarthritis*

Oral
Acetaminophen
COX-2–specific inhibitor
Nonselective NSAID plus misoprostol or a proton pump inhibitor†
Nonacetylated salicylate
Other pure analgesics
Tramadol
Opioids
Intraarticular
Glucocorticoids
Hyaluronan
Topical
Capsaicin
Methylsalicylate

* The choice of agent(s) should be individualized for each patient as noted in the text. COX-2 = cyclooxygenase 2; NSAID = nonsteroidal antiinflammatory drug.
† Misoprostol and proton pump inhibitors are recommended in patients who are at increased risk for upper gastrointestinal adverse events.

coxib has been found to be more effective than placebo and comparable in efficacy with naproxen in patients with hip or knee OA (54–56). Rofecoxib has also been found to be more effective than placebo and is comparable in efficacy with both ibuprofen and diclofenac in patients with hip or knee OA (57,58). Endoscopic studies have shown that celecoxib and rofecoxib are both associated with an incidence of gastroduodenal ulcers lower than that of the comparator NSAIDs and similar to that of placebo (52,59–61). These data suggest an advantageous safety profile compared with that of nonselective NSAIDs, especially for treatment of high-risk patients. However, the results of large, long-term studies that were designed to demonstrate differences between COX-2–specific inhibitors and nonselective NSAIDs with respect to major GI clinical outcomes have not yet been published. Such studies have been completed, and results are expected to be published some time in 2000.

Of further advantage with respect to upper GI bleeding, neither of the COX-2–specific inhibitors has a clinically significant effect on platelet aggregation or bleeding time. This is a consideration, especially in pre- and perioperative management of patients with OA (in whom nonselective NSAIDs have traditionally been discontinued as long as 2 weeks prior to surgery), as well as for patients taking warfarin sodium. Accordingly, these agents appear preferable to currently available nonselective NSAIDs for use in patients at risk for upper GI complications. Additionally, at doses recommended for treatment of OA, both celecoxib and rofecoxib appear to be better tolerated, with a lower incidence of dyspepsia and other GI side effects, than comparator nonselective NSAIDs (59,62). Like nonselective NSAIDs, however, COX-2–specific inhibitors can cause renal toxicity. Caution must be exercised, therefore, if they are used in patients with hypertension, congestive heart failure, or mild-to-moderate renal insufficiency; they should not be used in patients with severe renal insufficiency. In addition, the use of celecoxib is contraindicated in patients with a history of an allergic reaction to a sulfonamide.

An alternative to the use of COX-2–specific inhibitors is the use of nonselective NSAIDs with gastroprotective agents, as described in the 1995 ACR recommendations (5,6) and endorsed by the American College of Gastroenterology (49). As noted above, serious adverse upper GI events attributed to NSAIDs in the elderly are dose dependent. Therefore, if nonselective NSAIDs are used, they should be started in low, analgesic doses and increased to full antiinflammatory doses only if lower doses do not provide adequate symptomatic relief. In the patient who is at increased risk for a serious upper GI adverse event, gastroprotective agents should be used even if nonselective NSAIDs are given at low dosage.

In a study of 8,843 patients with RA, 200 μg misoprostol 4 times a day reduced the incidence of complicated ulcers, including those with perforation, bleeding, and obstruction, by 51% (63). In a 12-week, randomized, double-blind, placebo-controlled endoscopy study, 200 μg misoprostol 3 times a day had comparable efficacy in preventing both gastric and duodenal ulcers; however, 200 μg misoprostol twice a day conferred significantly less protection from gastric ulcers (64). Nonetheless, side effects, particularly diarrhea and flatulence, may occur with this agent, in a dose-dependent manner (64). Alternative approaches to prophylaxis with misoprostol include the use of high-dose famotidine or omeprazole, both of which have been shown to be effective in treating and preventing NSAID gastropathy in carefully conducted endoscopy studies (65–68). H_2 blockers in usual doses, however, have not been found to be as effective as misoprostol (67). Either 20 mg/day or 40 mg/day omeprazole was as effective as 200 μg misoprostol twice a day in the treatment of existing ulcers, and was better tolerated and associated with a lower rate of relapse (68). Proton pump inhibitors, however, have not been approved by the FDA for use in prophylaxis, although they are being widely used for that purpose.

In addition to their effects on the GI mucosa, nonselective NSAIDs inhibit platelet aggregation, fur-

ther increasing the risk of GI bleeding. Nonacetylated salicylates (e.g., choline magnesium trisalicylate, salsalate) are not accompanied by the antiplatelet effects or renal toxicity associated with nonselective NSAIDs (69), and can also be considered in management of the high-risk patient; however, ototoxicity and central nervous system toxicity at clinically efficacious doses may limit their use.

An alternative approach to the use of oral agents in the palliation of joint pain is the use of intraarticular therapy such as hyaluronan (hyaluronic acid) or glucocorticoids. Two preparations of intraarticular hyaluronan have been approved by the FDA for the treatment of knee OA patients who have not responded to a program of nonpharmacologic therapy and acetaminophen. To date, differences in clinical efficacy between these preparations as a function of molecular weight have not been demonstrated (70). Because the duration of benefit reported for these agents exceeds their synovial half-life, their mechanisms of action are unclear; proposed mechanisms include inhibition of inflammatory mediators such as cytokines and prostaglandins, stimulation of cartilage matrix synthesis and inhibition of cartilage degradation, and a direct protective action on nociceptive nerve endings.

In clinical trials of intraarticular hyaluronan preparations, pain relief among those who completed the study was significantly greater than that seen after intraarticular injection of placebo, and comparable with that seen with oral NSAIDs (71–73). In addition, pain relief among those who completed the study was comparable with or greater than that with intraarticular glucocorticoids (73). Although pain relief is achieved more slowly with hyaluronan injections than with intraarticular glucocorticoid injections, the effect may last considerably longer with hyaluronan injections (73). Intraarticular hyaluronan therapy is indicated for use in patients who have not responded to a program of nonpharmacologic therapy and simple analgesics; intraarticular hyaluronan injections may be especially advantageous in patients in whom nonselective NSAIDs and COX-2–specific inhibitors are contraindicated, or in whom they have been associated either with a lack of efficacy or with adverse events. Limited data are available concerning the effectiveness of multiple courses of intraarticular hyaluronan therapy (74). Transient mild-to-moderate pain at the injection site may occur; occasionally, mild-to-marked increases in joint pain and swelling have been noted following hyaluronan injection.

Intraarticular glucocorticoid injections are of value in the treatment of acute knee pain in patients with OA, and may be particularly beneficial in patients who have signs of local inflammation with a joint effusion. When joints are painful and swollen, aspiration of fluid followed by intraarticular injection of a glucocorticoid preparation (e.g., up to 40 mg triamcinolone hexacetonide) is an effective short-term method of decreasing pain and increasing quadriceps strength (73,75). Injection can be used as monotherapy in selected patients or as an adjunct to systemic therapy with an analgesic, a nonselective NSAID, or a COX-2–specific inhibitor. Joints should be aspirated/injected using aseptic technique, and the fluid should be sent for a cell count. Gram stain and culture should be performed if infection is suspected. Some patients may experience a mild flare of synovitis due to a reaction to the crystalline steroid suspensions; however, these postinjection flares are temporary and can be treated with analgesics and cold compresses. The risk of introducing infection into an OA joint is exceedingly low if standard aseptic technique is used.

Tramadol, a centrally acting oral analgesic, is a synthetic opioid agonist that also inhibits reuptake of norepinephrine and serotonin. It has been approved by the FDA for the treatment of moderate-to-severe pain and can be considered for use in patients who have contraindications to COX-2–specific inhibitors and nonselective NSAIDs, including impaired renal function, or in patients who have not responded to previous oral therapy. Although there are numerous studies of the use of tramadol in general pain, few controlled studies have examined its use in OA. The efficacy of tramadol has been found to be comparable with that of ibuprofen in patients with hip and knee OA (76), and it has been found to be useful as adjunctive therapy in patients with OA whose symptoms are inadequately controlled with NSAIDs (77). Mean effective daily doses of tramadol have generally been in the range of 200–300 mg, given in 4 divided doses. Side effects are common and include nausea, constipation, and drowsiness. Despite its opioid pharmacology, a comprehensive surveillance program has failed to demonstrate significant abuse, and tramadol remains an unscheduled agent.

Patients who do not respond to or cannot tolerate tramadol and who continue to have severe pain may be considered candidates for more potent opioid therapy (30). In one study, the combination of codeine plus acetaminophen was shown to provide significantly better analgesia than acetaminophen alone in patients with hip OA, although one-third of patients receiving the combination discontinued therapy due to nausea, vomiting, dizziness, or constipation (78). In a short-term study of

acute pain in patients with hip or knee OA, no difference in analgesic efficacy was demonstrated between combinations of acetaminophen with either dextropropoxyphene or codeine; however, the combination with dextropropoxyphene was significantly better tolerated (79). The American Pain Society and American Academy of Pain Medicine recently published joint guidelines on the use of more potent opioids in the management of chronic, nonmalignant pain (80). Tolerance, dependence, and adverse effects, including respiratory depression and constipation, may occur with opioid usage.

Although the efficacy of therapy with combinations of the above pharmacologic agents has not been established in controlled clinical trials, in general, it is reasonable to use the recommended agents in combination in an individual patient. However, only a single NSAID should be used at any given time, the sole exception being the concomitant use of a cardioprotective dose of aspirin (81–325 mg/day) with other NSAIDs. Even these low doses of aspirin, however, will increase the risk of upper GI bleeding in patients taking NSAIDs. In this regard, it should be noted that the incidence of endoscopically identified ulcers in patients taking a COX-2–specific inhibitor and a cardioprotective dose of aspirin was lower than that in comparator groups taking nonselective NSAIDs with or without concomitant low-dose aspirin (52).

Initiation of treatment in the patient who is not at increased risk for an upper GI adverse event

The approach recommended for treatment of patients not at increased risk for an upper GI adverse event is similar to that described above (Table 3). As in the case of patients at increased risk for a serious upper GI adverse event, if a nonselective NSAID is used, it should be started at a low, analgesic dosage which should be increased only if it is ineffective in providing symptomatic relief. Use of concomitant gastroprotective therapy with misoprostol or a proton pump inhibitor, however, is not recommended in the low-risk patient.

Management of OA in the patient who is already taking an NSAID

The above sections address the management of OA in patients who have not had prior treatment of their disease. In OA patients who are already taking an NSAID, but who have not incorporated relevant nonpharmacologic measures (e.g., an exercise program, weight loss program, adherence to principles of joint protection) into their treatment program, such measures should be implemented. This may permit reduction of the dosage of NSAID or replacement of the NSAID with acetaminophen. In all patients whose symptoms are well controlled, attempts should be made periodically to reduce the dosage of NSAID and/or analgesic agents and to determine whether it is possible to use such agents on an as-needed basis, rather than in a fixed dosing regimen.

Tidal irrigation

While the 1995 ACR guidelines recommended that tidal irrigation (TI) should be considered for those patients with knee OA that did not respond satisfactorily to nonpharmacologic and pharmacologic measures (6), it was cautioned that information did not exist concerning the magnitude of the placebo response to this procedure. An ongoing, sham-controlled study of TI is currently in progress, but results are not available. The placebo response to an invasive procedure, such as TI, may be large, and results of properly controlled studies of TI, which would permit guidance in this area, are not yet available. Accordingly, although some data suggest that TI may be efficacious in some patients (6,81), the subcommittee believes that a statement concerning the role for this modality should await further study.

Treatment of the patient with hip OA

It should be noted that therapy for OA of the hip is similar to treatment of OA of the knee, except for a few minor differences. Intraarticular hyaluronan therapy is not approved for hip OA, and there are no published studies regarding its efficacy in patients with hip OA. Topical agents have not been studied in hip OA, and their efficacy is questionable because of the depth of that joint. Intraarticular glucocorticoid injections have not been studied in patients with hip OA, but are used occasionally and may be efficacious. Injections performed without fluoroscopic guidance should be administered only by those experienced in this approach. Modalities of physical therapy for patients with hip OA differ from those used in patients with OA of the knee. Consultation with a physical therapist should be considered as part of the overall management.

Surgical treatment

Patients with severe symptomatic OA who have pain that has failed to respond to medical therapy and

who have progressive limitation in ADLs should be referred to an orthopedic surgeon for evaluation. No well-controlled trials of arthroscopic debridement with or without arthroplasty have been conducted, and the utility of this intervention for the treatment of knee OA is unproven. In appropriately selected patients who are not yet candidates for total joint arthroplasty, osteotomy may provide pain relief and prevent progression of disease. Total joint arthroplasty provides marked pain relief and functional improvement in the vast majority of patients with OA (82,83), and has been shown to be cost effective in selected patients (83,84). Indications for total hip replacement, developed at a National Institutes of Health (NIH) Consensus Conference, include "radiographic evidence of joint damage and moderate to severe persistent pain or disability, or both, that is not substantially relieved by an extended course of nonsurgical management" (85). While there are no published evidence-based indications for total knee replacement, Dieppe and colleagues have summarized the indications derived from 3 consensus groups of orthopedic surgeons (83). Outcomes depend upon the timing of the surgery, the experience of the surgeon and the hospital with the procedure, and the patient's preoperative medical status, peri- and postoperative management, and rehabilitation.

Agents under investigation

While a number of studies support the efficacy of both glucosamine and chondroitin sulfate for palliation of joint pain in patients with knee OA (86,87), the subcommittee believes that it is premature to make specific recommendations about their use at this time because of methodologic considerations, including lack of standardized case definitions and standardized outcome assessments, as well as insufficient information about study design in a number of these published reports. A pivotal clinical trial being planned by the NIH should help define the role of these agents, singly and in combination, in the treatment of patients with knee OA.

In addition, currently existing data are insufficient or inadequate to permit the subcommittee to make definitive recommendations about the use of devices, such as pulsed electromagnetic fields and lasers. Further research is needed on vitamin deficiencies, which have been suggested as possible causes of (or aggravating factors in) OA, before dietary supplementation can be recommended for prevention or treatment of this disease (88). Similarly, the value, if any, of other nutritional supplements, including supraphysiologic doses of antioxidant vitamins, remains to be determined. In addition, therapeutic approaches such as acupuncture are difficult to evaluate and recommend because of large placebo effects of invasive procedures and the lack of adequate sham-controlled studies. An ongoing, pivotal, randomized, sham-controlled trial of acupuncture, supported by the NIH, is under way; this trial should help define acupuncture's role in the treatment of patients with knee OA.

The 1995 ACR recommendations briefly mentioned preliminary studies of disease-modifying OA drugs (DMOADs), drugs whose action is not aimed principally at the control of symptoms, but instead at the prevention of structural damage in normal joints at risk for development of OA, or at the progression of structural damage in joints already affected by OA. For the most part, such approaches have been aimed at inhibiting the breakdown of articular cartilage by matrix metalloproteinases, or at stimulating repair activity by chondrocytes. Although a number of agents are under study, including matrix metalloproteinase inhibitors and growth factors, no agent has been shown to have a DMOAD effect in humans, and none are available for this indication.

In addition to therapeutic agents targeted toward prevention, retardation, or reversal of cartilage breakdown in OA, significant advances, such as autologous chondrocyte transplantation (89), cartilage repair using mesenchymal stem cells (90), and autologous osteochondral plugs (mosaicplasty) (91), are being investigated for repair of focal chondral defects. These procedures are not currently indicated in the treatment of patients with OA.

Given the advances in therapy which can be anticipated for patients with OA, the subcommittee expects that current recommendations will change as new knowledge of the disease unfolds and new therapies become available.

ACKNOWLEDGMENT

The members of the subcommittee wish to thank Mr. Jim Moody, Vice President for Socioeconomic Affairs, American College of Rheumatology, for his invaluable assistance in shepherding this project to its conclusion.

REFERENCES

1. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum 1998;41:778–99.
2. Mow VC, Setton LA, Fuilak F, Ratcliffe A. Mechanical factors in articular cartilage and their role in osteoarthritis. In: Kuettner KE,

Goldberg VM, editors. Osteoarthritic disorders. Rosemont (IL): American Academy of Orthopaedic Surgeons; 1995. p. 147–72.
3. Poole AR. Imbalances of anabolism and catabolism of cartilage matrix components in osteoarthritis. In: Kuettner KE, Goldberg VM, editors. Osteoarthritic disorders. Rosemont (IL): American Academy of Orthopaedic Surgeons; 1995. p. 247–60.
4. Holderbaum D, Haqqi TM, Moskowitz RW. Genetics and osteoarthritis: exposing the iceberg. Arthritis Rheum 1999;42:397–405.
5. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, et al. Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthritis Rheum 1995;38:1535–40.
6. Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, et al. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthritis Rheum 1995;38:1541–6.
7. Towheed TE, Hochberg MC. A systematic review of randomized controlled trials of pharmacological therapy in patients with osteoarthritis of the hip. J Rheumatol 1997;24:349–57.
8. Towheed TE, Hochberg MC. A systematic review of randomized controlled trials of pharmacological therapy in patients with osteoarthritis of the knee. Semin Arthritis Rheum 1997;27:755–70.
9. Watson MC, Brookes ST, Kirwan JR, Faulkner A. Non-aspirin, non-steroidal anti-inflammatory drugs for osteoarthritis of the knee (Cochrane review). In: The Cochrane library, issue 1. Oxford: Update Software; 2000. Accessed April 11, 2000. URL: www.cochrane.org/cochrane/revabstr/ab000142.htm.
10. Towheed T, Shea B, Wells G, Hochberg M. Analgesia and non-aspirin, non-steroidal anti-inflammatory drugs for osteoarthritis of the hip (Cochrane review). In: The Cochrane library, issue 1. Oxford: Update Software; 2000. Accessed April 11, 2000. URL: www.cochrane.org/cochrane/revabstr/ab000517.htm.
11. Gotzsche PC. Non-steroidal anti-inflammatory drugs. BMJ 2000; 320:1058–61.
12. Guyatt GH. Evidence-based management of patients with osteoporosis. J Clin Densitometry 1998;1:395–402.
13. Wolfe F, Zhao S, Lane N. Preference for nonsteroidal antiinflammatory drugs over acetaminophen by rheumatic disease patients: a survey of 1,799 patients with osteoarthritis, rheumatoid arthritis, and fibromyalgia. Arthritis Rheum 2000;43:378–85.
14. Pincus T, Swearingen C, Cummins P, Callahan LF. Preference for nonsteroidal antiinflammatory drugs versus acetaminophen and concomitant use of both types of drugs in patients with osteoarthritis. J Rheumatol 2000;27:1020–7.
15. Superio-Cabuslay E, Ward MM, Lorig KR. Patient education interventions in osteoarthritis and rheumatoid arthritis: a meta-analytic comparison with nonsteroidal antiinflammatory drug treatment. Arthritis Care Res 1996;9:292–301.
16. Weinberger M, Tierney WM, Cowper PA, Katz BP, Booher PA. Cost-effectiveness of increased telephone contact for patients with osteoarthritis: a randomized, controlled trial. Arthritis Rheum 1993;36:243–6.
17. Slemenda C, Brandt KD, Heilman DK, Mazzuca S, Braunstein EM, Katz BP, et al. Quadriceps weakness and osteoarthritis of the knee. Ann Intern Med 1997;127:97–104.
18. Slemenda C, Heilman DK, Brandt KD, Katz BP, Mazzuca SA, Braunstein EM, et al. Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? Arthritis Rheum 1998;41:1951–9.
19. Hurley MV. The role of muscle weakness in the pathogenesis of osteoarthritis. Rheum Dis Clin North Am 1999;25:283–98.
20. Ettinger WH Jr, Burns R, Messier SP, Applegate W, Rejeski WJ, Morgan T, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis: the Fitness Arthritis and Seniors Trial (FAST). JAMA 1997;277:25–31.
21. Ries MD, Philbin EF, Groff GD. Relationship between severity of gonarthrosis and cardiovascular fitness. Clin Orthop 1995;313: 169–76.
22. Van Baar ME, Dekker J, Oostendorp RAB, Bijl D, Voorn TB, Lemmens JAM, et al. The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial. J Rheumatol 1998;25:2432–9.
23. Hurley MV, Scott DL, Rees J, Newham DJ. Sensorimotor changes and functional performance in patients with knee osteoarthritis. Ann Rheum Dis 1997;56:641–8.
24. Sharma L, Pai Y-C, Holtkamp K, Rymer WZ. Is knee joint proprioception worse in the arthritic knee versus the unaffected knee in unilateral knee osteoarthritis? Arthritis Rheum 1997;40: 1518–25.
25. Hurley MV, Scott DL. Improvements in quadriceps sensorimotor function and disability of patients with knee osteoarthritis following a clinically practicable exercise regime. Br J Rheumatol 1998;37:1181–7.
26. Toda Y, Toda T, Takemura S, Wada T, Morimoto T, Ogawa R. Change in body fat, but not body weight or metabolic correlates of obesity, is related to symptomatic relief of obese patients with knee osteoarthritis after a weight control program. J Rheumatol 1998;25:2181–6.
27. Sasaki T, Yasuda K. Clinical evaluation of the treatment of osteoarthritis knees using a newly designed wedged insole. Clin Orthop 1985;221:181–7.
28. Keating EM, Faris PM, Ritter MA, Kane J. Use of lateral heel and sole wedges in the treatment of medial osteoarthritis of the knee. Orthop Rev 1993;22:921–4.
29. Cushnaghan J, McCarthy C, Dieppe P. Taping the patella medially: a new treatment for osteoarthritis of the knee joint? BMJ 1994;308:753–5.
30. American Geriatrics Society Panel on Chronic Pain in Older Persons. The management of chronic pain in older persons. J Am Geriatric Soc 1998;46:635–51.
31. Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. Comparison of an anti-inflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee. N Engl J Med 1991;325: 87–91.
32. Williams HJ, Ward JR, Egger MJ, Neuner R, Brooks RH, Clegg DO, et al. Comparison of naproxen and acetaminophen in a two-year study of treatment of osteoarthritis of the knee. Arthritis Rheum 1993;36:1196–206.
33. Eccles M, Freemantle N, Mason J, for the North of England Non-Steroidal Anti-Inflammatory Drug Guideline Development Group. North of England Evidence Based Guideline Development Project: summary guideline for non-steroidal anti-inflammatory drugs versus basic analgesia in treating the pain of degenerative arthritis. BMJ 1998;317:526–30.
34. Bradley JD, Brandt KD, Katz BP, Kalasinski LA, Ryan SI. Treatment of knee osteoarthritis: relationship of clinical features of joint inflammation to the response to a nonsteroidal antiinflammatory drug or pure analgesic. J Rheumatol 1992;19:1950–4.
35. Altman RD, IAP Study Group. Ibuprofen, acetaminophen and placebo in osteoarthritis of the knee: a six-day double-blind study [abstract]. Arthritis Rheum 1999;42 Suppl 9:S403.
36. Pincus T, Callahan LF, Wolfe F, Cummins P, Weaver A, Caldwell J, et al. Arthrotec compared to acetaminophen: a clinical trial in patients with osteoarthritis of the hip or knee [abstract]. Arthritis Rheum 1999;42 Suppl 9:S404.
37. Holzer SS, Cuerdon T. Development of an economic model comparing acetaminophen to NSAIDs in the treatment of mild-to-moderate osteoarthritis. Am J Managed Care 1996;2 Suppl: S15–26.
38. Hyiek EM, Heiman H, Skates SJ, Sheehan MA, Singer DE. Acetaminophen and other risk factors for excessive warfarin anticoagulation. JAMA 1998;279:657–62.

39. Fitzmaurice DA, Murray JA. Potentiation of anticoagulant effect of warfarin. Postgrad Med J 1997;73:439–40.
40. Schiodt FV, Rochling FA, Casey DL, Lee WM. Acetaminophen toxicity in an urban country hospital. N Engl J Med 1997;337: 1112–7.
41. Whitcomb DC, Block GD. Association of acetaminophen hepatotoxicity with fasting and ethanol use. JAMA 1994;273: 1845–50.
42. Seifert CF, Lucas DS, Vondracek TG, Kastens DJ, McCarty DL, Bui B. Patterns of acetaminophen use in alcoholic patients. Pharmacotherapy 1993;13:391–5.
43. Henrich WL, Agodaoa LE, Barret B, Bennett WM, Blantz RC, Buckalew VM, et al. Analgesics and the kidney: summary and recommendations to the Scientific Advisory Board of the National Kidney Foundation from an Ad Hoc Committee of the National Kidney Foundation. Am J Kidney Dis 1996;27:162–5.
44. Griffin MR, Ray WA, Schaffner W. Nonsteroidal anti-inflammatory drug use and death from peptic ulcer in elderly persons. Ann Intern Med 1988;109:359–63.
45. Griffin MR, Piper JM, Daugherty JR, Snowden M, Ray WA. Nonsteroidal anti-inflammatory drug use and increased risk for peptic ulcer disease in elderly persons. Ann Intern Med 1991;114: 257–63.
46. Smalley WE, Griffin MR. The risks and costs of upper gastrointestinal disease attributable to NSAIDs. Gastroenterol Clin North Am 1996;25:373–96.
47. Gabriel SE, Jaakkimainen L, Bombardier C. Risk for serious gastrointestinal complications related to use of nonsteroidal anti-inflammatory drugs: a meta-analysis. Ann Intern Med 1991;115: 787–96.
48. Simon LS, Hatoum HT, Bittman RM, Archambault WT, Polisson RP. Risk factors for serious nonsteroidal-induced gastrointestinal complications: regression analysis of the MUCOSA Trial. Fam Med 1996;28:204–10.
49. Lanza FL, and the Members of the Ad Hoc Committee on Practice Parameters of the American College of Gastroenterology. A guideline for the treatment and prevention of NSAID-induced ulcers. Am J Gastroenterol 1998;93:2037–46.
50. Garell S, Matarese RA. Renal effects of prostaglandins and clinical adverse effects of nonsteroidal anti-inflammatory agents. Medicine (Baltimore) 1984;63:165–81.
51. Moore RA, Tramer MR, Carroll D, Wiffen PJ, McQuay HJ. Quantitative systematic review of topically applied non-steroidal anti-inflammatory drugs. BMJ 1998;316:333–8.
52. Hawkey CJ. COX-2 inhibitors. Lancet 1999;353:307–14.
53. Crofford LJ, Lipsky PE, Brooks P, Abramson SB, Simon LS, van de Putte LBA. Basic biology and clinical application of specific cyclooxygenase-2 inhibitors. Arthritis Rheum 2000;43:4–13.
54. Simon LS, Lanza FL, Lipsky PE, Hubbard RC, Talwalker S, Schwartz BD, et al. Preliminary study of the safety and efficacy of SC-58365, a novel cyclooxygenase 2 inhibitor: efficacy and safety in two placebo-controlled trials in osteoarthritis and rheumatoid arthritis, and studies of gastrointestinal and platelet effects. Arthritis Rheum 1998;41:1591–602.
55. Bensen WG, Fiechtner JJ, McMillen JI, Zhao WW, Yu SS, Woods EM, et al. Treatment of osteoarthritis with celecoxib, a cyclooxygenase-2 inhibitor: a randomized controlled trial. Mayo Clin Proc 1999;74:1095–1105.
56. Clemett D, Goa KL. Celecoxib: a review of its use in osteoarthritis, rheumatoid arthritis, and acute pain. Drugs 2000;59:957–80.
57. Cannon GW, Caldwell JR, Holt P, McLean B, Seidenberg B, Bolognese J, et al. Rofecoxib, a specific inhibitor of cyclooxygenase 2, with clinical efficacy comparable with that of diclofenac sodium: results of a one-year, randomized, clinical trial in patients with osteoarthritis of the knee and hip. Arthritis Rheum 2000;43: 978–87.
58. Day R, Morrison B, Luza A, Castaneda O, Strusberg A, Nahir M, et al. A randomized trial of the efficacy and tolerability of the COX-2 inhibitor rofecoxib vs ibuprofen in patients with osteoarthritis. Arch Intern Med 2000;160:1781–7.
59. Simon LS, Weaver AL, Graham DY, Kivitz AJ, Lipsky PE, Hubbard RC, et al. Anti-inflammatory and upper gastrointestinal effects of celecoxib in rheumatoid arthritis: a randomized controlled trial. JAMA 1999;282:1921–8.
60. Laine L, Harper S, Simon T, Bath R, Johanson J, Schwartz H, et al. A randomized trial comparing the effect of rofecoxib, a cyclooxygenase 2-specific inhibitor, with that of ibuprofen on the gastroduodenal mucosa of patients with osteoarthritis. Gastroenterology 1999;117:776–83.
61. Hawkey C, Laine L, Simon T, Beaulieu A, Maldonado-Cocco J, Acevedo E, et al. Comparison of the effect of rofecoxib (a cyclooxygenase 2 inhibitor), ibuprofen, and placebo on the gastroduodenal mucosa of patients with osteoarthritis: a randomized, double-blind, placebo-controlled trial. Arthritis Rheum 2000;43: 370–7.
62. Langman MJ, Jensen DM, Watson WJ, Harper SE, Zhao P-L, Quan H, et al. Adverse upper gastrointestinal effects of rofecoxib compared with NSAIDs. JAMA 1999;282:1929–33.
63. Silverstein FE, Graham DY, Senior JR, Davies HW, Struthers BJ, Bittman RM, et al. Misoprostol reduces serious gastrointestinal complications in patients with rheumatoid arthritis receiving nonsteroidal anti-inflammatory drugs: a randomized, double-blind, placebo-controlled trial. Ann Intern Med 1995;123:241–9.
64. Raskin JB, White RH, Jackson JE, Weaver AL, Tindall EA, Lies RB, et al. Misoprostol dosage in the prevention of nonsteroidal anti-inflammatory drug-induced gastric and duodenal ulcers: a comparison of three regimens. Ann Intern Med 1995;123:344–50.
65. Taha AS, Hudson N, Hawkey CJ, Swannell AJ, Trye PN, Cottrell J, et al. Famotidine for the prevention of gastric and duodenal ulcers caused by nonsteroidal antiinflammatory drugs. N Engl J Med 1996;334:1435–9.
66. Ekstrom P, Carling L, Wetterhus S, Wingren PE, Anker-Hansen O, Lundegardh G, et al. Prevention of peptic ulcer and dyspeptic symptoms with omeprazole in patients receiving continuous nonsteroidal anti-inflammatory drug therapy: a Nordic multicentre study. Scand J Gastroenterol 1996;31:753–8.
67. Yeomans NE, Tulassay Z, Juhasz L, Racz I, Hoard JM, van Rensburg CJ, et al. A comparison of omeprazole with ranitidine for ulcers associated with nonsteroidal antiinflammatory drugs. N Engl J Med 1998;338:719–26.
68. Hawkey CJ, Karrasch JA, Szczepanski L, Walker DG, Barkun A, Swannell AJ, et al. Omepraxole compared with misoprostol for ulcers associated with nonsteroidal antiinflammatory drugs. N Engl J Med 1998;338:727–34.
69. Furst DE. Are there differences among nonsteroidal antiinflammatory drugs? Comparing acetylated salicylates, nonacetylated salicylates, and nonacetylated nonsteroidal antiinflammatory drugs. Arthritis Rheum 1994;37:1–9.
70. Aviad AD, Houpt JB. The molecular weight of therapeutic hyaluronan (sodium hyaluronate): how significant is it? J Rheumatol 1994;21:297–301.
71. Altman RD, Moskowitz RW, and the Hyalgan Study Group. Intra-articular sodium hyaluronate (Hyalgan) in the treatment of patients with osteoarthritis of the knee: a randomized clinical trial. J Rheumatol 1998;25:2203–12.
72. Adams ME, Atkinson MH, Lussier AJ, Schulz JI, Siminovitch KA, Wade JP, et al. The role of viscosupplementation with hylan G-F 20 (Synvisc) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing hylan G-F 20 alone, hylan G-F 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone. Osteoarthritis Cartilage 1995;3:213–25.
73. Kirwan JR, Rankin E. Intra-articular therapy in osteoarthritis. Baillieres Clin Rheumatol 1997;11:769–94.
74. Kotz R, Kolarz G. Intra-articular hyaluronic acid: duration of

effect and results of repeated treatment cycles. Am J Orthop 1999;29 Suppl 1:5–7.
75. Creamer P. Intra-articular corticosteroid injections in osteoarthritis: do they work and if so, how? Ann Rheum Dis 1997;56:634–6.
76. Dalgin P, and the TPS-OA Study Group. Comparison of tramadol and ibuprofen for the chronic pain of osteoarthritis [abstract]. Arthritis Rheum 1997;40 Suppl 9:S86.
77. Roth SH. Efficacy and safety of tramadol HCl in breakthrough musculoskeletal pain attributed to osteoarthritis. J Rheumatol 1998;25:1358–63.
78. Kjaersgaard-Andersen P, Nafei A, Skov O, Madsen F, Andersen HM, Kroner K, et al. Codeine plus paracetamol versus paracetamol in longer-term treatment of chronic pain due to osteoarthritis of the hip: a randomised, double-blind, multi-centre study. Pain 1990;43:309–18.
79. Boissier C, Perpoint B, Laporte-Simitsidis S, Mismetti P, Hocquart J, Gayet JL, et al. Acceptability and efficacy of two associations of paracetamol with a central analgesic (dextropropoxyphene or codeine): comparison in osteoarthritis. J Clin Pharmacol 1992;32:990–5.
80. American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain. Glenview (IL): American Academy of Pain Medicine and American Pain Society; 1997.
81. Ravaud P, Moulinier L, Giraudeau B, Ayral X, Guerin C, Noel E, et al. Effects of joint lavage and steroid injection in patients with osteoarthritis of the knee: results of a multicenter, randomized, controlled trial. Arthritis Rheum 1999;42:475–82.
82. Towheed TE, Hochberg MC. Health related quality of life following total hip replacement. Semin Arthritis Rheum 1996;26:483–91.
83. Dieppe P, Basler HD, Chard J, Croft P, Dixon J, Hurley M, et al. Knee replacement surgery for osteoarthritis: effectiveness, practice variations, indications and possible determinants of utilization. Rheumatology 1999;38:73–83.
84. Chang RW, Pellisier JM, Hazen GB. A cost-effectiveness analysis of total hip arthroplasty for osteoarthritis of the hip. JAMA 1996;275:858–65.
85. NIH. Total hip replacement. NIH Consensus Statement 1994;12: 1–31.
86. McAlindon TF, LaValley MP, Gulin JP, Felson DT. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. JAMA 2000; 283:1469–75.
87. Deal CL, Moskowitz RW. Nutraceuticals as therapeutic agents in osteoarthritis. Rheum Dis Clin North Am 1999;25:379–95.
88. McAlindon T, Felson DT. Nutrition: risk factors for osteoarthritis. Ann Rheum Dis 1997;56:397–402.
89. Brittberg M, Nilsson A, Lindahl A, Ohlsson C, Peterson L. Rabbit articular cartilage defects treated with autologous cultured chondrocytes. Clin Orthop 1996;326:270–83.
90. Wakitani S, Goto T, Pineda SJ, Young RG, Mansour JM, Caplan AI, et al. Mesenchymal cell-based repair of large, full-thickness defects of articular cartilage. J Bone Joint Surg Am 1994;76A:579–92.
91. Hangody L, Kish G, Karpati Z, Eberhart R. Osteochondral plugs: autogenous osteochondral mosaicplasty for the treatment of focal chondral and osteochondral articular defects. Operative Tech Orthop 1997;7:312–22.

The Arthritis Self-Management Program is a community-oriented, peer-led program in which patients receive education and gain skills for self-managing the consequences of arthritis. The Arthritis Foundation of Australia coordinates the running of these courses, which are led by trained volunteers and held in community halls.Â Recommendations for the medical management of osteoarthritis of the hip and knee. Arthritis Rheum 2000; 43: 1905-1915. 3. Pendelton A, Arden N, Dougados M, et al. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis 2000; 59: 936-944. 4. Lorig KR, Manzonson PD, Holman HR. Osteoarthritis Cartilage. 2008 Feb;16(2):137-62. doi: 10.1016/j.joca.2007.12.013.Â Results: Twenty-three treatment guidelines for the management of hip and knee OA were identified from the literature search, including six opinion-based, five evidence-based and 12 based on both expert opinion and research evidence. Twenty out of 51 treatment modalities addressed by these guidelines were universally recommended. ES for pain relief varied from treatment to treatment. Overall there was no statistically significant difference between non-pharmacological therapies [0.25, 95% confidence interval (CI) 0.16, 0.34] and pharmacological therapies (ES=0.39, 95% CI 0.31, 0.47). ALGORITHMS Hip/knee osteoarthritis diagnosis and assessment algorithm Hip/knee osteoarthritis care planning and management algorithm Hip/knee osteoarthritis management flow chart. Summary of recommendations.Â The focus of this guideline is on OA of the hip and knee. Although many of the recommendations are relevant to OA in other sites, research relating to other forms of OA was not included in the literature review. The following process model identifies the stages in chronic disease management (CDM) and the focus of the guideline. 7. Guideline for the non-surgical management of hip and knee osteoarthritis July 2009. Reducing the risk of osteoarthritis Reduce joint injury Health promotion. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum. 2000 Sep;43(9):1905-15. doi: 10.1002/1529-0131(200009)43:9<1905::AID-ANR1>3.0.CO;2-P. Pmid: 11014340. Doi: 10.1002/1529-0131(200009)43:9<1905::AID-ANR1>3.0.co;2-P. No abstract available. Publication types.Â Osteoarthritis, Knee / therapy*. Substances. Anti-Inflammatory Agents, Non-Steroidal. Figure 1. Recommended therapies for the management of osteoarthritis (OA). Strongly and conditionally recommended approaches to management of hand, knee, and/or hip OA are shown. No hierarchy within categories is implied in the figure, with the recognition that the various options may be used (and reused) at various times during the course of a particular patientâ€™s disease. * = Exercise for knee and hip OA could include walking, strengthening, neuromuscular training, and aquatic exercise, with no hierarchy of one over another. Exercise is associated with better outcomes when supervised. *Â The Voting Panel made conditional recommendations when the quality of the evidence proved low or very low and/. 4. | kolasinski et al.