

Medical management of knee, hand and hip osteoarthritis

To date there are still no 'cures' or modalities to reverse osteoarthritis, but numerous nonpharmacological and pharmacological interventions have been shown to improve affected patients' pain, function and quality of life.

DAVID MASSASSO

MB BS, BSc, BSc(Med)

LYN MARCH

MB BS, MSc, PhD, FRACP, FAFPHM

Dr Massasso is Rheumatology Advanced Trainee, Department of Rheumatology, Liverpool Hospital, Liverpool. Professor March is Associate Professor of Medicine, University of Sydney, Department of Rheumatology at Royal North Shore Hospital, Sydney, NSW.

Osteoarthritis (OA) is a common degenerative condition with changes seen in the articular cartilage, subchondral bone and, to a lesser extent, the synovial lining, with low grade inflammation. It can be classified as primary (or idiopathic) or secondary. Primary OA is the more common condition, predominantly affecting people over the age of 50 years. Certain joints are affected with increased frequency, including the spine, hand (Figure 1), hips and knees (Figure 2). OA is an important cause of morbidity affecting both mobility and activities of daily living. Although OA is the third most frequent reason for patients to present to GPs, it is highly likely that a history of OA will be forthcoming with directed questioning in most patients over 50 years of age.

The sequelae of OA are pain and reduced physical function with consequent effects on

psychological functioning and quality of life. Although loss of cartilage is a central pathological feature in OA, cartilage lacks a nerve supply. However, loss of normal articular cartilage causes stress on surrounding structures. Intra-articular structures that may generate pain include:

- periosteum
- subchondral bone
- ligaments
- synovium
- capsule.

Periarticular sources of pain include:

- tendons
- bursae
- adjacent connective tissue.

Most clinical OA trials have focused on OA of the knees, but the principles of management should apply to any joint site. To date there are

IN SUMMARY

- There are no 'cures' or modalities to reverse osteoarthritis (OA), but numerous nonpharmacological and pharmacological interventions have been shown to improve pain, function and quality of life.
- Nonpharmacological strategies that should be considered in all patients include educational techniques, individualised exercise programs and regular review.
- Some patients with OA may benefit from the use of appliances or mechanical aids, acupuncture and/or occupational therapy assessment.
- Pharmacological interventions for OA involve both systemic and localised therapies; a stepped approach to therapy is often appropriate and should be individualised depending on the patient's situation and comorbidities.
- A multifaceted approach is essential in the management of patients with OA.

still no 'cures' or modalities to reverse OA, but numerous nonpharmacological and pharmacological interventions have been shown to improve pain, function and quality of life. Treatment options range from simple to more complex, including joint replacement. In general practice, sessions dedicated to addressing the various management issues would seem worthwhile. Furthermore, there is evidence that patients benefit from ongoing follow up, such as periodic phone calls, from their health professional.

Given that a wide range of structures may be the source of pain and many different tissues are undergoing pathogenic changes, it is now well recognised that OA management should be multimodal and include nonpharmacological as well as pharmacological strategies. With the recent heightened awareness of increased risk of adverse cardiac events associated with perhaps all the anti-inflammatory medications, patients are increasingly looking to the medical profession to provide advice on nonpharmacological and alternative treatments. This review provides an update of the latest evidence for OA interventions.

Nonpharmacological interventions

Education

Several randomised controlled trials have shown benefits from different educational techniques for OA. These include self-management and group programs, as well as coping skills training for patients and their partners. Such interventions may improve both pain and quality of life.

The cost-effectiveness of these programs has come under some question recently because the sizes of the benefit effects, as measured by our traditional pain and function outcomes, are small. However, consumer support for these programs is strong, and recommendations for their use will be made in the upcoming National Health Plan for Arthritis. Further information for patients can be obtained from Arthritis Australia's website (www.arthritisaustralia.com.au), or patients can be referred to local self-management programs.

Weight loss

Obesity is a well-recognised risk factor for development of OA of the knee. Weight loss is a strategy recommended to most patients, although evidence from prospective intervention studies is

Managing osteoarthritis

This image is unavailable due to copyright restrictions

Given that a wide range of structures may be the source of pain and many different tissues are undergoing pathogenic changes, the management of patients with osteoarthritis should be multimodal, including nonpharmacological as well as pharmacological strategies.

© CHRISTY KRAMES, 2003

lacking. Obesity is associated with radiological progression and disability in knee OA. Obesity is also associated with increased risk of developing hip OA. Modest weight loss is associated with reduced future development of symptoms and reduced short and long term symptoms with existing OA. A 5 to 10% reduction in body weight is associated with symptomatic improvement. Whether such weight reductions also prevent the progression of OA in existing disease is unclear.

continued

Both exercise and dietary factors are important for weight reduction. Most studies of weight loss have included exercise components. Dietician input can be invaluable in many situations, including when:

- there is poor patient insight
- there is lack of improvement despite exercise
- exercise components are difficult to perform because of pain or other factors.

Exercise

Exercise and physical therapy reduce pain and disability in both hip and knee OA. Benefits have been shown to be maintained both short and long term. The aim of exercise is to maximise muscle strength and thus joint stability and range of movement. Exercises can be joint specific (strength and range of movement) and general aerobic.

As mentioned, exercise combined with dietary therapy also has potential benefits for weight reduction. Evidence favours cardiovascular training for hip OA and quadriceps strengthening for knee OA. There is also evidence for the effectiveness of both formal and home-based programs, as well as those that are water- and land-based. Individualised programs are useful to tailor exercise to

the patient's symptoms and limitations. Patients should choose something they like to do and include a range of different actions. These should be incorporated into daily activities. Walking, cycling and water-based exercise are well tolerated by many patients. These programs are often best co-ordinated initially through a physiotherapist or fitness instructor. Tai Chi classes are also associated with improved mobility and quality of life, and both videos and instructions on this form of exercise are available.

Patients are more likely to take up the exercise advice if their doctor specifically prescribes this or they are given a referral letter to take to the physiotherapist.

Occupational therapy, appliances and mechanical aids

Evidence for the effectiveness of appliances and mechanical aids is not strong, but their use may improve both pain and function. Appropriate footwear, including insoles with adequate arch and heel supports, may improve pain. Lateral heel wedges reduce NSAID use in medial compartment knee OA, and elastic bandages or braces may reduce pain. The use of the latter may be limited by cost.

Patellofemoral taping has been shown in some small studies to improve quality

of life and symptoms in patients with anterior knee pain secondary to OA, although a recent larger study did not confirm this. However, it is a simple measure that the physiotherapist could try while patients are commencing their exercise program as it may benefit some people.

The use of TENS therapy for knee OA has been shown to alleviate pain, especially in high-intensity, repeated and longer duration (more than four week) courses.

Although often used, there are no specific trial data on the efficacy of walking sticks for reducing symptoms or progression of arthritis. Recent biomechanical studies found that, when used properly, walking sticks could reduce the weight-bearing pressure through the affected knee by more than 10% and thus have potential to offer symptom benefit and the possibility of joint protection. It is recommended that they should be prescribed on an individual basis after physiotherapist assessment.

Further evaluation is needed before knee braces and orthotic sleeves can be recommended; however, for osteoarthritis of the first carpometacarpal joint, thumb splints have been shown to help symptoms and may reduce the need for surgery.

Occupational therapy assessment may



Figure 1. Osteoarthritis of the hands showing Heberden's nodes at the distal interphalangeal joints and squaring of the base of the thumb indicating arthritis of the first carpometacarpal joints.



Figure 2. Osteoarthritis (OA) of the left knee showing a varus deformity produced by loss of the lateral joint space due to secondary OA after previous surgery for a lateral meniscus tear.

also be useful on an individual basis for both knee and hip OA patients to help with activities of daily living.

Acupuncture

A recent review encompassing five trials suggests that acupuncture is useful for pain relief for OA of the knee (Figure 3). Patients with the highest pain level seem to benefit most and pain relief is continued in the medium term. Adverse effects include nausea and bruising. A recent placebo-controlled randomised trial of patients with knee OA showed benefit of acupuncture plus diclofenac over diclofenac alone in terms of pain, physical and psychological function and reduced analgesic use.



PAUL BIDDLE & TIM MALLYON, SCIENCE PHOTO LIBRARY

Figure 3. Acupuncture has been shown to be useful for pain relief in patients with knee osteoarthritis.

Pharmacological interventions

Pharmacological intervention should be used as an addition to nonpharmacological measures. Pharmacological interventions involve both systemic and localised therapies. A stepped approach to therapy is often appropriate and should be individualised depending on the patient's situation and comorbidities (see the flowchart on page 22). In some patients, multiple interventions may be appropriate from the outset.

Topical therapies

Topical treatments (NSAIDs and capsaicin [Zostrix]) have clinical efficacy and are safe. Topical NSAIDs reduce pain significantly in patients with knee OA versus placebo (65% *v.* 30%). The major side effect of topical NSAIDs relates to local skin reaction (in fewer than 1.5% of cases), and no association has been shown between their use and upper gastrointestinal events.

Topical capsaicin reversibly desensitises nociceptive C fibres. In a single randomised trial it has demonstrated moderate pain reduction. Local burning discomfort is common but usually diminishes over time, and care should be taken to avoid the eyes and mucous membranes.

Paracetamol

Paracetamol is useful for mild to moderate pain in both hip and knee OA. It has been considered the oral analgesic of first choice in various international guidelines because of its favourable cost, efficacy and side effect profile. Although a number of recent publications have suggested that overall quality of life is improved in patients taking NSAIDs compared with paracetamol, about 30 to 40% of patients will respond to paracetamol, and it can be taken safely in the long term. Thus, it should be recommended as a first line agent, to be taken regularly.

The maximum recommended dose of paracetamol is 4 g, and it can be taken to correlate with pain-specific situations. It should be taken with caution in patients also taking warfarin (especially high doses) and in patients with chronic liver disease or excessive alcohol consumption.

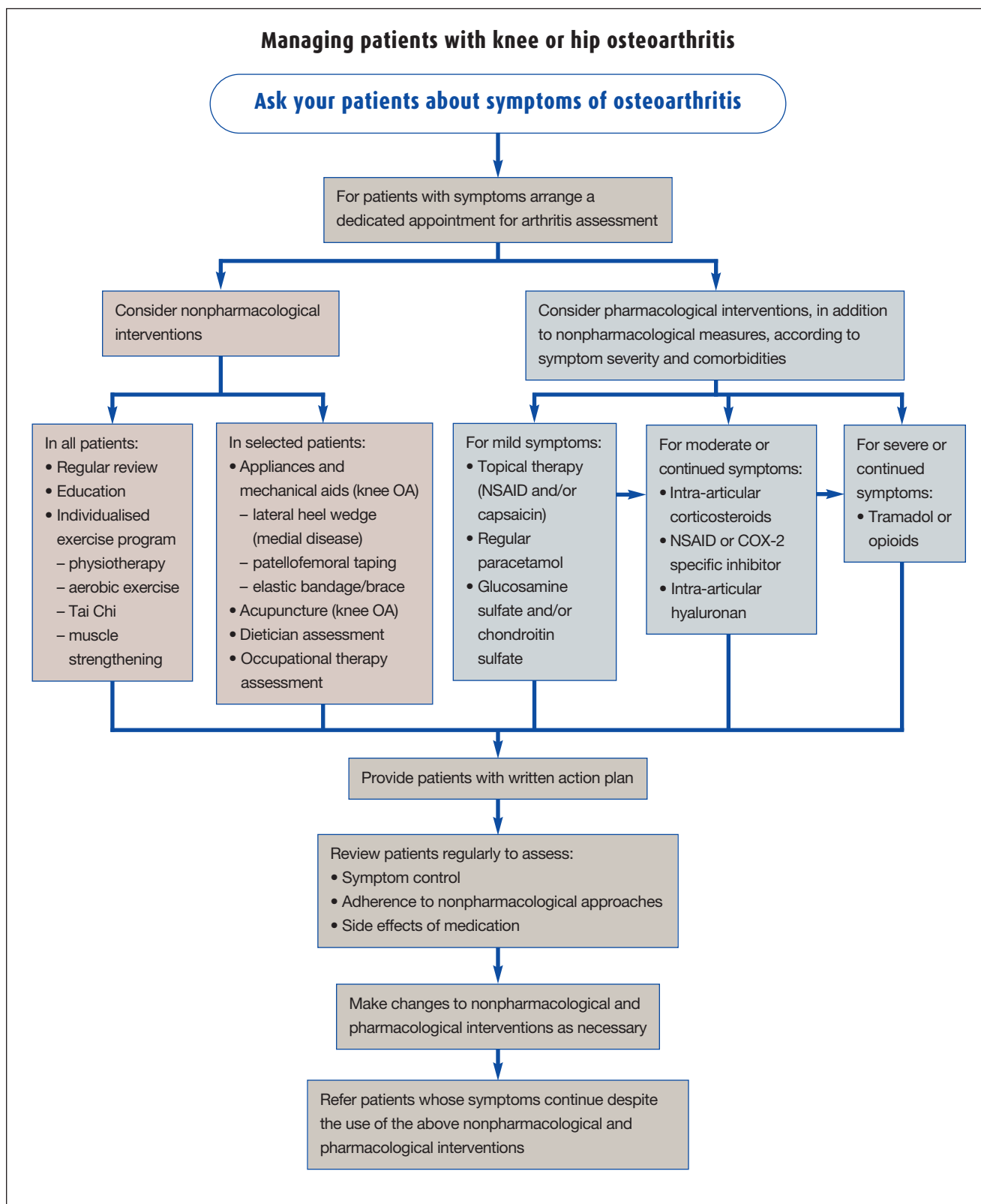
Traditional NSAIDs

Oral NSAIDs have been recommended in patients unresponsive to, or with inadequate relief from, paracetamol. The popularity of NSAID use has waxed and waned in recent decades. Their widespread uptake was a sign of the high prevalence of arthritis in the community, as well a

testament to their ability to relieve the associated pain and stiffness.

Systematic reviews show reduced short term pain due to hip and knee OA with NSAIDs versus placebo. In subjects with moderate to severe pain from hip or knee OA, short term studies favour NSAIDs over paracetamol. However, NSAIDs have not been shown to be superior in terms of function. There is little evidence to distinguish different NSAIDs on the basis of efficacy, although head-to-head trials of these agents are rarely undertaken. Considerable patient variability exists in the response to NSAIDs, and several different types may need to be tried to find the most appropriate one for the individual patient.

The 1980s saw a growing awareness of the gastrointestinal risks of peptic ulceration associated with NSAIDs and an appropriate drop in prescribing. Subsequent analyses of trials were able to show a variability in risk of serious peptic ulcer problems (bleeding, perforation, death) between different NSAIDs. Notably, the risk for peptic ulceration is lowest with ibuprofen (e.g. Advil, Brufen, Nurofen) and diclofenac (e.g. Voltaren, Fenac) and highest with longer acting NSAIDs such as piroxicam (Feldene, Mobilis, Pirohexal-D)



and ketoprofen (Orudis, Oruvail). Peptic ulcer risk can be reduced by concomitant use of misoprostol (Cytotec) or the better tolerated proton pump inhibitors, and these should be coprescribed if traditional NSAIDs are to be used in patients at risk of ulcers.

The 1990s saw an awareness of other significant side effects, especially in older people, including renal impairment, hypertension, fluid retention and heart failure exacerbation. However, the use of traditional NSAIDs declined dramatically during this time as the COX-2 specific NSAIDs were launched and cardiovascular effects tended to be overlooked.

With the recent reports of increased risk of myocardial infarction and stroke attributed to the COX-2 specific NSAIDs, some 'guidelines' and government recommendations are suggesting the return to traditional NSAIDs. Diclofenac, with or without proton pump inhibitors, would appear to be one of the best tolerated options. However, despite the millions of dollars invested in the development and marketing of these drugs, the definitive trials comparing all the relevant drugs, and of sufficient duration and sample size to confidently identify long term cardiovascular endpoints, have not been done. Recent analyses are suggesting that current use of all the anti-inflammatories – traditional and COX-2 specific – may be associated with increased cardiovascular risk. In addition, as many patients with OA are elderly with numerous comorbidities and taking multiple medications, interactions with other medications also need to be considered. Thus the jury is still out as to the real risk of these drugs. To the individual patient, the absolute risk is likely to be low, but the widespread use of these medications in the community leads to the alarming statements that hundreds and thousands of patients are being killed by these drugs.

Despite maximal use of simple analgesics and nonpharmacological therapies, many patients still need relief of symptoms,

and NSAIDs can provide this in most cases. The one clear point that emerges from all the debates is that one can no longer prescribe these drugs without a detailed discussion of the benefits and potential harms for the individual patient. The recommendation to use the lowest dose possible for the shortest duration possible is sound. Regular follow up for monitoring of side effects and reassessment of the need for the drugs should be undertaken.

COX-2 specific inhibitors

COX-2 specific inhibitors show equivalent efficacy for pain reduction to conventional NSAIDs. Their initial widespread usage was in part related to their relative gastrointestinal protection over conventional NSAIDs. Rofecoxib was associated with a 50% reduction in serious upper gastrointestinal tract events: perforation, ulcers and bleeding. The benefit of celecoxib (Celebrex) in this regard has not been as clear from randomised trials, although it appears to be so in large postmarketing surveys and data linkage studies. In patients with previous peptic ulcer disease or taking aspirin, use of COX-2 specific inhibitors carries similar risk to the use of a combination of a traditional NSAID and proton pump inhibitor. Thus, COX-2 specific inhibitors are useful for analgesia in patients with increased upper gastrointestinal tract risk factors. However, they appear to have similar cardiorenal adverse effects to conventional NSAIDs.

Recent controversy surrounds the cardiovascular risk and increased thrombotic events associated with COX-2 specific inhibitors. The recently terminated Adenomatous Polyp Prevention on Vioxx (APPROVe) study, which looked at the rate of new colonic polyps in patients taking 25 mg/day of rofecoxib, showed an increased rate of myocardial infarction after 18 months and led to the worldwide withdrawal of this medication. Recent concerns have also been raised for the cardiovascular safety of high doses of

celecoxib. *In vitro*, rofecoxib has more COX-2 selectivity than celecoxib, which in turn shows increased selectivity over meloxicam (Mobic, Movalis). The risk of thrombosis associated with celecoxib and the newer COX-2 specific inhibitors (e.g. lumiracoxib, etoricoxib; both not yet available in Australia) is unclear, and large and long duration studies are needed to answer this.

In the interim, patients with increased cardiovascular risk should use COX-2 specific inhibitors only if there are clear indications when simple analgesics and nonpharmacological interventions are not providing adequate symptom relief, and then in low doses and for short periods of time. They should continue their anti-thrombotic treatments, including aspirin.

Other analgesics

Other forms of analgesia, with or without paracetamol, may be useful in patients who are intolerant of NSAIDs or COX-2 inhibitors. There is little direct evidence for this strategy, although it is used often in daily practice. There are attendant risks associated with this approach, particularly in the elderly, and there is potential for drug dependence.

One randomised controlled trial showed that tramadol (Tramal, Zydol) combined with paracetamol was effective for acute flares of OA pain. Tramadol may also allow reduction of NSAID use. Potential drug interactions need to be heeded – e.g. with tricyclic antidepressants and SSRIs.

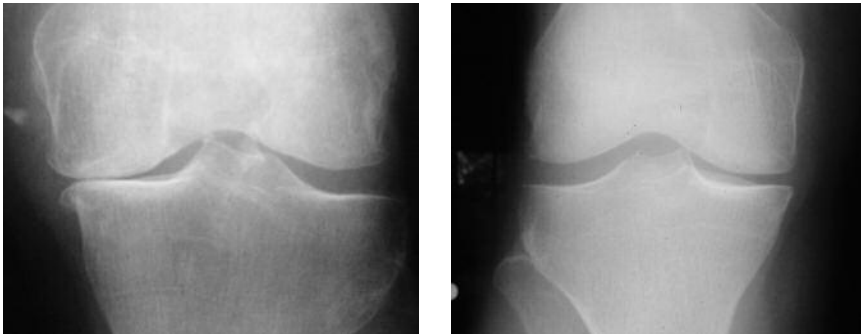
Long acting opioid analgesics may be appropriate in late stage OA (Figure 4a), when other forms of treatment have failed or are contraindicated.

Intra-articular injections

Corticosteroids

Intra-articular corticosteroids are moderately effective for some patients with knee OA over short periods of time. The benefit occurs quickly, and the duration of pain relief is variable but may be up to

continued



Figures 4a and 4b. Osteoarthritis of the knee. (a left). Severe disease. b (right). Mild to moderate disease.

two to three weeks. No clinical features clearly predict response – e.g. patients with effusions may or may not respond. The evidence of benefit of intra-articular steroid injection for hip OA is less extensive. A recent randomised study demonstrated improvements in pain, functional ability and range of joint motion for three

to 12 weeks' duration after injection.

Current practice suggests that the same joint should not be injected more than three times a year. Response may diminish with repeated injections; however, over two years no deleterious radiological effect is observed.

Common adverse effects include post-

injection flare of pain, facial flushing, mood and sleep alteration, and hyperglycaemia. Transient increase in blood sugar levels may be seen up to 48 hours after injection.

Viscosupplementation

Hyaluronan is a component of the extracellular matrix of articular cartilage. Its molecular weight has a major role in the properties of synovial fluid for joint nutrition and shock absorption. It has a major role in absorbing loading forces in normal synovial fluid. In OA, both the molecular weight and concentration of hyaluronan is reduced.

Most trials of viscosupplementation with hyaluronan have shown a mild to moderate reduction in pain and improved function for OA of the knee. Efficacy may be comparable to that of NSAIDs, but a recent meta-analysis suggests the treatment effect is small. The period of

benefit can be prolonged from one to six months, and even up to a year. Structural improvements may be seen at arthroscopy. The onset of action is slow, and most studies have assessed either mild or moderate OA (Figure 4b).

The latest Cochrane review suggests that intra-articular corticosteroids are associated with greater symptom relief in the short term (one to four weeks) but that intra-articular hyaluronan is associated with greater improvement in pain and function at 12 and 26 weeks. A few patients (10%) will have an articular flare following the first injection of hyaluronan, and this may increase with subsequent courses. The expense of the injections (Synvisc, \$440 per course of three injections; Fermathron, \$106 per injection, administered weekly for a maximum of five weeks) is limiting for many patients. A few Australian health

funds will reimburse these products on a case-by-case basis.

Complementary and alternative therapies

Complementary and alternative therapies for OA have been recently reviewed in a previous issue of *Medicine Today* (September 2004, pages 63-66).

Glucosamine and chondroitin

Glucosamine and chondroitin are derivatives of glycosaminoglycans, found in both articular cartilage and synovial fluid. They are available in both oral (as tablet or powder) and topical forms. The recommended oral daily doses are glucosamine 1500 mg and chondroitin 1100 mg. Glucosamine is contraindicated in patients with seafood allergy.

These compounds, especially glucosamine, show mild to moderate analgesic

effects on knee OA compared with placebo. They seem to be more efficacious in patients with milder disease. Additionally, glucosamine may slow progression of OA. The onset of action is slow (up to two to three months), and the compounds are generally well tolerated, the most common side effects being gastrointestinal.

A recent randomised trial showed no reduction in disease flares versus placebo for up to six months in patients already on established treatment with glucosamine, thus bringing efficacy into question. The latest Cochrane review, which includes the recent studies, suggests a small symptomatic benefit. It is worthwhile recommending a two to three month trial of glucosamine with or without chondroitin for knee OA given that:

- other studies in knee OA show that the use of glucosamine may slow

Managing osteoarthritis: practice points

- Ask your patients about arthritis – more of them will have symptoms than you think.
- Talking to your patients about their arthritis can make a difference to symptoms.
- Organise a dedicated appointment for arthritis assessment and review.
- Give each patient a written management plan.
- Weight loss is an important contributor to symptomatic improvement in OA of the knee and hip – it requires both dietary modification and increased physical activity.
- Exercise strategies should include aerobic and strengthening components and, where possible, should be able to be incorporated into daily activities.
- Pharmacological strategies should start with simple analgesics and involve a stepped incremental approach.
- Individual patient benefits and risk need to be discussed before prescribing NSAIDs.
- Patients should be reviewed regularly for assessment of symptom control, adherence to exercise and weight-loss plans, and for monitoring for adverse medication effects.
- Use a multifaceted approach to arthritis management.

progression of articular cartilage thinning (joint space narrowing on x-ray)

- more than 50% of OA patients take some form of complementary or nonprescription preparation for the condition
- it is reasonable to try a treatment for which there is *in vitro* data suggesting how it might work in addition to the suggestive *in vivo* studies.

Most published studies were conducted using the purified sulfated forms of these compounds; however, it remains unclear whether this form should be recommended over the hydrochloride form that is used widely in Australia. A number of large studies are underway that may answer this question.

Fish oils

Evidence is emerging that long-chain omega-3 oils in high doses have COX-2 selectivity and provide anti-inflammatory and analgesic properties. Several randomised trials confirm their ability to reduce pain and swelling in rheumatoid arthritis, but, to date, no randomised controlled trials with these products in OA have been published. However, they are worth con-

sidering if the patient is showing signs of inflammation. Patients should be aware that they need to take high doses, and that there may be a delay of at least three to six weeks in the onset of benefit.

Conclusion

Although there are no cures or modalities to reverse OA, numerous nonpharmacological and pharmacological interventions have been shown to improve pain, function and quality of life in patients with this condition. Nonpharmacological approaches should be considered in all patients with OA, and pharmacological therapy should be individualised depending on patients' symptoms and comorbidities; a stepped approach to therapy is often appropriate (see the box on this page). Symptom control, adherence to nonpharmacological intervention, and any side effects of medication should be assessed at regular patient reviews. **MT**

Selected reading

1. Fitzgerald GK, Oatis C. Role of physical therapy in management of knee osteoarthritis. *Curr Opin Rheumatol* 2004; 16: 143-147.

2. Berman BM, Lao L, Langenberg P, Lee WL, Gilpin AM, Hochberg MC. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 2004; 141: 901-910. Comment in: *Acupuncture effective for osteoarthritis of the knee*. *J Family Practice* 2005; 54(3): 200.
3. Vas J, Méndez C, Perea-Milla E, et al. Acupuncture as a complementary therapy to the pharmacological treatment of osteoarthritis of the knee: randomised controlled trial. *BMJ* 2004; 329: 1216.
4. Deal CL, Schnitzer TJ, Lipstein E, et al. Treatment of arthritis with topical capsaicin: a double blind trial. *Clin Ther* 1991; 13: 383-395.
5. Day RO, Graham GG. The vascular effects of COX-2 selective inhibitors. *Aust Prescr* 2004; 27: 142-145.
6. Lo G, Lavalley M, McAlindon T, Felson DT. Intra-articular hyaluronic acid in treatment of knee osteoarthritis. *JAMA* 2003; 290: 3115-3121.
7. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Intraarticular corticosteroid for treatment of osteoarthritis of the knee. *The Cochrane Database of Systematic Reviews* 2005; Issue 2.
8. Kullenberg B, Runesson R, Tuvhay R, Olsson C, Resch S. Intraarticular corticosteroid injection: pain relief in osteoarthritis of the hip? *J Rheumatol* 2004; 31: 2265-2268.
9. Towheed TE, Maxwell L, Anastassiades TP, et al. Glucosamine therapy for treating osteoarthritis. *The Cochrane Database of Systematic Reviews*; 2005, Issue 2.
10. Grainger R, Cicuttini FM. Medical management of osteoarthritis of the knee and hip joints. *Med J Aust* 2004; 180(5): 232-236.
11. Jordan KM, Arden NK, Doherty M, et al. EULAR Recommendations 2003: an evidence based approach to 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* 2003; 62: 1145-1155.

DECLARATION OF INTEREST: Associate Professor Lyn March's department has received a research grant from Bayer Australia to study the effect of Synvisc on synovial fluid and she has received speaking honoraria from Bayer, Merck Sharp and Dohme, Pharmacia and Pfizer.