Knee osteoarthritis

Management as a chronic disease

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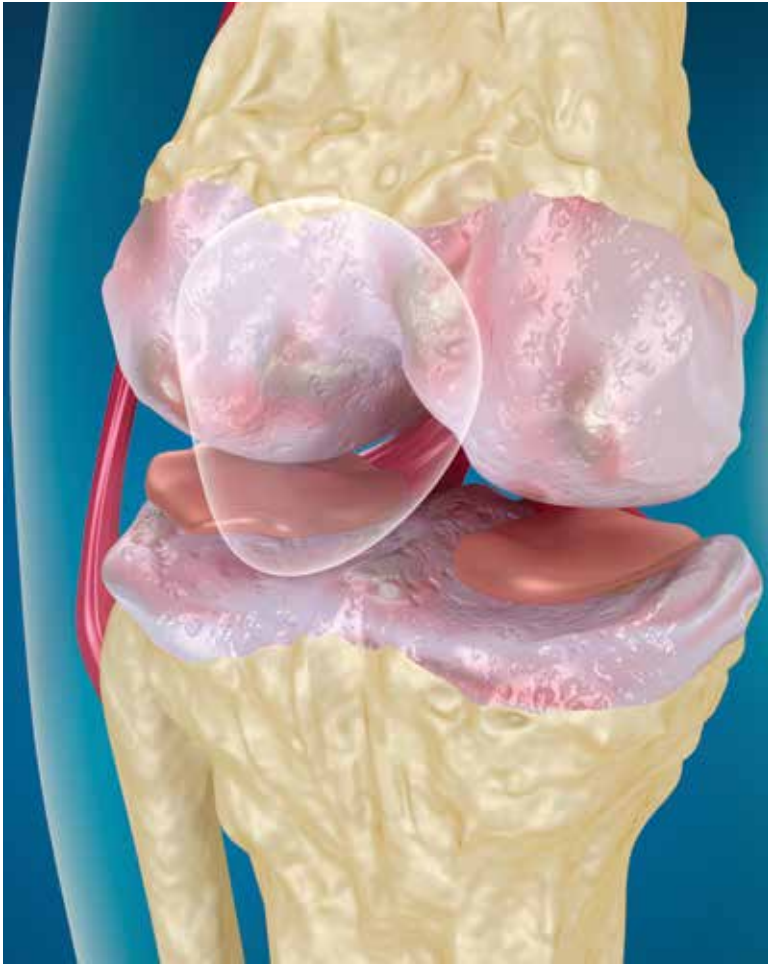

The mainstay of treatment of osteoarthritis should be an integrated chronic disease management plan rather than episodic/reactive care. Long-term disease prevention is receiving greater focus, particularly weight control and injury prevention.

Osteoarthritis (OA) is the most prevalent joint disease, with an estimated 250 million people affected worldwide in 2012.[1] The symptoms affect 10 to 12% of the adult population and this prevalence is estimated to increase by 50% over the next two decades.[2-4] Self-reported estimates from the Australian Bureau of Statistics 2011–12 National Health Survey suggest that about 1.8 million people in Australia have this condition.[5]

The financial burden of OA is escalating. In addition to the direct costs, the indirect cost related to OA stems from absenteeism, early retirement and premature death. In 2009, it was estimated that arthritis contributed to 17% of the total $2.1 billion of taxation revenue lost to the Australian Federal Government from illness-related early retirement, and 19% of the total $1.5 billion in government support payments to those in early retirement due to illness.[3]

MedicineToday 2016; 17(3): 39-47

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KEY POINTS

- Comprehensive and multidisciplinary osteoarthritis (OA) management involves a combined treatment approach of nonpharmacological and pharmacological treatment to improve pain and function.
- Regardless of symptom severity or radiographic change, all patients with OA should engage in exercise and neuromuscular training.
- Weight reduction in overweight or obese patients can improve physical function and pain by up to 50% in weight-bearing joints.
- Regular education/advice and monitoring are key to patients' long-term maintenance of physical activity and weight reduction.
- Choice of analgesia requires careful consideration of risk versus benefit and proven efficacy.
- Platelet-rich plasma treatment and stem cell injections are not advocated for the management of knee OA.
- Arthroscopic surgery is not indicated for treating pain associated with knee OA.
- Referral to an orthopaedic surgeon should be considered in patients with knee OA who have severe symptoms and functional decline and have failed conservative management.

The limitations, lack of understanding and underutilisation of current treatment strategies for OA mean that the number of total joint replacement procedures continues to rise. The 2015 Australian Orthopaedic Association National Joint Replacement Registry listed approximately 97,500 hip and knee joint replacement procedures in 2014, an increase of 5.4% compared with the previous year.[6]

The typical care received by most patients with osteoarthritis is characteristically inappropriate. From the CareTrack study, which attempted to determine the appropriateness of healthcare delivery in Australia, only 43% of encounters of patients presenting with OA received appropriate care;[7] other studies support this claim. The results of a recent survey performed following the release of the Royal Australian College of General Practitioners Guideline for the nonsurgical management of hip and knee OA were compared with a similar survey undertaken seven years earlier.[8] Although the use of simple analgesia such as paracetamol, paracetamol/codeine combination and oral NSAIDs were consistent with recommendations, there was a marked increase in tramadol and more potent opioid usage that raises concerns of associated increased risks of fractures from falls, cardiovascular risks and all-cause mortality.[9] There was recognition of a multidisciplinary approach to management but nonpharmacological modalities such as exercise, physiotherapy, hydrotherapy and weight loss remained underutilised despite guideline recommendations.[8] In general, there is discordance between what is recommended in the guidelines and what occurs in practice.

This review briefly covers the pathophysiology and aetiology of OA in general and focuses on the diagnosis and management of knee OA, encompassing the new treatment paradigm change with a target towards a holistic approach with an integrated patient management plan. Suggestions are made regarding conservative care management programs that can be used in addition to current management practice for OA in general practice.

Pathophysiology

OA is a complex disease involving the whole joint. It is characterised by structural changes that include loss of articular cartilage, meniscal damage, osteophyte formation, synovial inflammation, subchondral bone remodelling, bone marrow lesions, muscle weakness and laxity of ligaments. An interplay between genetic, biomechanical, metabolic and biochemical factors leads to the progression of disease.

The aetiology of pain in osteoarthritis involves a complex biopsychosocial model that includes a combination of catabolic and inflammatory cytokines and sensitisation of nociceptive pathways from the activation of primary afferent nerves in response to inflammation or tissue injury.[10,11]

Aetiology

Multiple risk factors contribute to the development of OA. Genetics and systemic factors of overweight/obesity, ethnicity, female sex and vitamin D deficiency increase an individual's susceptibility. Local risk factors, especially mechanical factors (namely joint injuries such as meniscal and anterior cruciate injuries, and joint malalignment), are the most important factors to target, with longitudinal evidence demonstrating that they increase the risk of structural disease progression in those with established disease.[12] Underlying anatomical abnormalities and, less commonly, metabolic conditions such as haemochromatosis and acromegaly and inflammatory conditions such as rheumatoid arthritis are also potential risk factors.

Presentation and diagnosis

The diagnosis of OA should be based on a combination of history and examination. For knee OA, the diagnosis is determined by symptoms of persistent knee pain, limited knee stiffness and reduced function and clinical features of restricted range of movement, crepitus and bony enlargement.[13]

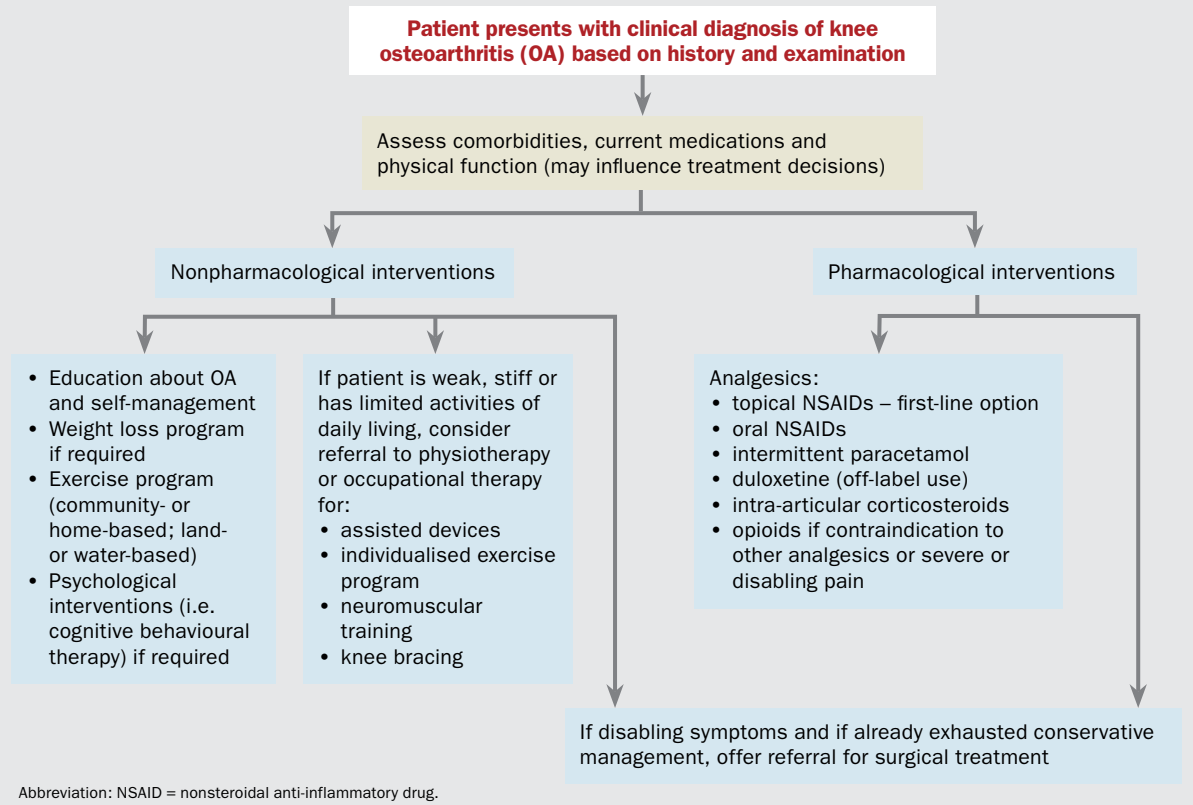
Radiography is used to confirm the clinical findings if the diagnosis is uncertain and to exclude other differential diagnosis. However, it is important to note that the correlation between structural OA change and an individual's symptoms is highly variable and often not in accord.

Magnetic resonance imaging (MRI) should not be performed for the diagnosis of OA, as it typically does not alter management decisions. It may, however, be useful in patients with persistent joint pain after a few months of conservative treatment, in whom the aetiology is not known.[14] This joint pain may be caused by rare conditions such as pigmented villonodular synovitis, avascular necrosis and osteochondritis dissecans, which can be diagnosed by MRI. Therefore, MRI should be reserved for cases with unusual clinical presentations or where treatment decisions will be altered based on the imaging findings. Incidental findings on MRI of meniscal tears are common in the older population without OA and uniformly present in those with knee OA, and can result in unnecessary arthroscopic knee surgery, which may potentially hasten OA progression.

Conservative treatment

To date, there is no cure available for OA. Current treatments encompass a combination of lifestyle and behavioural modification and traditional analgesic medication to achieve improvement in joint function and symptomatic relief. The present guidelines for nonsurgical management of knee OA (the Osteoarthritis Research Society International guidelines) incorporate a combination of land- and water-based exercises, weight management and strength training.[15] Compliance with these treatment models is often poor, however, thus the overuse of over-the-counter analgesia and subsequently prescription pain medications. It is therefore important to facilitate longer-term adherence by

AN APPROACH TO MANAGING PATIENTS WITH KNEE OSTEOARTHRITIS



Abbreviation: NSAID = nonsteroidal anti-inflammatory drug.

co-ordinating the patient's care and instilling self-management skills. The recommended management of patients with knee OA is shown in the flowchart.

The concept of holistic assessment of the patient is central to the development of a successful individualised management plan. The patient must take part in the decision-making of a plan, and the plan should incorporate pain control, physical therapy and modification of lifestyle factors. Providing accurate educational information about the OA disease process and self-management have been shown to have positive effects on long-term pain and disability and to improve adherence to nonpharmacological therapies.[16] Establishment of short- and long-term goals with regular follow up enhances compliance with and efficacy of the interventions instituted.

Patients with OA often have comorbid health concerns, including cardiovascular disease, hypertension, diabetes, obesity, back pain, gastrointestinal ulcerations, kidney disease and depression. Assessment of comorbidities and current medications may influence treatment decisions such as selection of analgesia – for example, cautious use of NSAIDs in individuals with hypertension or cardiovascular or renal disease.

Nonpharmacological management

Exercises

Many people with OA are concerned that continued physical activity may further aggravate their OA progression. However, as OA can result in weakness and wasting of all the muscles that act over the affected joint, people with OA should be encouraged to maintain activity and commence local neuromuscular training (Figure). There is good evidence that strengthening, flexibility and aerobic fitness exercises can reduce pain and disability from hip and knee OA.[15,17-20] The aim of neuromuscular training is to improve sensorimotor control and achieve compensatory functional stability through functional weight-bearing exercises in various positions, resembling conditions of daily life and more strenuous activities.[21] The exercises not only reduce pain but also improve muscle strength, balance and proprioception.[22]

All individuals with OA should be encouraged to engage in low-impact exercises based on their individual preference and physical ability. Water-based exercises are usually advised for patients with severe mobility and functional impairment, rather than land-based exercises. Tai chi

Figure. Low-impact strengthening, flexibility and aerobic fitness exercises can reduce pain and disability in patients with knee osteoarthritis.

has been shown to improve health-related quality of life and physical function.[23] Referral to a physiotherapist for neuromuscular training exercises is recommended to enhance the efficacy of the exercise programs. Often people engaged in high-impact activities such as running, tennis and basketball ask whether they can continue these activities in the context of symptomatic knee OA. Because of the risks for further symptomatic and structural decline of their joints, these patients should be encouraged to participate in low-impact activities and to minimise their high-impact activity involvement.

In conclusion, based on the comments above, all patients with OA should participate in an exercise program unless they have a valid reason for not exercising.[24]

Weight loss management

The maintenance of an ideal body weight is essential for the symptomatic improvement and preservation of joint structure. As the lower limb joints bear a considerable load during weight-bearing activities, obesity management is an important modifiable risk factor for knee OA. In several randomised studies in overweight or obese patients with hip or knee OA, up to a 50% reduction in pain scores has been shown with a 10% weight reduction.[25-27] Similar findings have been obtained in a community-based sample enrolled in a weight loss program readily available to GPs in Australia (the 'Osteoarthritis Health Weight for Life' program).[28]

It is challenging to help patients achieve and subsequently maintain weight reduction. Successful weight loss programs advocate individualised programs that involve diet, regular healthy eating with reduced portion size, improved nutritional awareness through education, and modification of eating triggers such as stress.[29]

Biomechanical interventions

Biomechanical interventions such as walking sticks, braces and lateral wedge insoles are potential adjuncts to knee OA treatment; an appropriate specialist, such as an orthotist or physiotherapist, should direct their use.

The use of a walking stick is supported by most OA guidelines to reduce the mechanical load on the knee joint. Walking stick use has been shown to improve function and some aspects of quality of life in patients with knee OA.[15]

Knee bracing for both tibiofemoral and patellofemoral knee OA has shown reasonable effect based on limited evidence.[15] The tibiofemoral brace aims to reduce load in the medial tibiofemoral compartment. The patellofemoral brace is similar to the concept of patellofemoral taping, altering the malalignment of the patella with flexion movements. Adherence to bracing is often limited by local complications, general aesthetics and cost.[30]

Lateral wedge insoles for medial tibiofemoral OA, a previous popular treatment modality, is now contraindicated, with a recent meta-analysis failing to demonstrate superiority to neutral insoles.[31]

Pharmacological management

Complementary medicines/ supplements

The efficacies of glucosamine, chondroitin and their combination in the treatment of knee OA are uncertain, with mixed conclusions from reviews and conflicting results from published trials.

Glucosamine has been shown to have a similar effect to placebo for pain, with independent investigator-initiated trials showing a smaller effect than commercially-funded trials.[32] In a US National Institutes of Health-funded study, glucosamine was not significantly better than placebo for knee pain reduction.[33]

Varying effects are also seen with chondroitin, with some reviews showing a reduction in the rate of decline in joint space and others not showing any statistically meaningful changes.[34-36]

There is no clear evidence with either of these agents that they have symptom reduction properties or reduce structural modification over time.[15,37]

Fish oil, another popular nutraceutical, has questionable efficacy in the management of OA. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), the long-chain omega-3 fatty acids found in fish oil, have been shown to reduce inflammatory cytokines in OA in vitro.[38,39] However, clinical studies have not been able to demonstrate retardation of progression of symptomatic knee OA at either low or high dosages of these fatty acids.[40]

Paracetamol

Paracetamol was once the recommended oral analgesic of first choice for many practitioners due to its perceived safety profile compared with other oral analgesics. However, there is growing evidence that it has similar side effects to oral NSAIDs, including gastrointestinal (GI) bleeding, hypertension and renal impairment.[41] The main concerns pertain to the inhibition of cyclooxygenase-2 (COX-2).[42] In addition, a meta-analysis of recent OA trials revealed limited effectiveness of paracetamol for pain management, with

only modest short-term benefits seen in patients with knee and hip OA.[43]

As a result, many OA guidelines are no longer recommending paracetamol as first-line analgesia.[15]

Nonsteroidal anti-inflammatory drugs

NSAIDs have demonstrable efficacy over paracetamol for OA pain management.[44] The potential side effects of routine NSAID use of GI toxicity and associated cardiovascular risks are well documented.[45,46] These risks pertain to both nonselective and COX-2-selective NSAIDs, although COX-2 inhibitors have a better GI safety profile, with a meta-analysis of 26 studies comparing the two in relation to dyspepsia demonstrating a 12% relative risk reduction and an absolute risk reduction of 3.7% for COX-2 inhibitors.[47]

The concomitant use of a proton pump inhibitor (PPI) is generally recommended with NSAIDs, especially in patients with associated comorbidity risks. Studies comparing dyspepsia between patients treated with an NSAID alone and those treated with an NSAID–PPI combination showed a 66% relative risk reduction and 9% absolute risk reduction for the combination therapy.[47,48] Although there is no efficacy superiority of any particular NSAIDs, their safety profiles differ. The risk of cardiovascular harm is lower with naproxen compared with other NSAIDs,[48] but the risks of GI and renal complications are increased (a relative risk of GI complications of 1.8 compared with non-usage).[49] Although celecoxib has a safer GI profile than nonselective NSAIDS, its cardiovascular risks are similar. From systematic reviews of arthritis trials, one additional cardiovascular event occurred for about every 270 patients treated for one year with celecoxib compared with placebo.[48]

If used and monitored appropriately in the right patients, NSAIDs are deemed clinically useful for managing pain in patients with OA. The balance of risk factors should be considered in the choice of the NSAID.

Topical NSAIDs

With growing concerns over paracetamol, topical NSAIDs offer an appropriate alternative for painful peripheral joint OA. The route of local drug delivery reduces GI adverse reactions and efficacy is demonstrated over placebo and is comparable with oral NSAIDs.[50,51]

To date, most studies of topical NSAIDs for pain management in patients with OA have focused on individuals with knee and hand OA, thus the effects of topical NSAIDs on individuals with multiple-joint OA remain uncertain. Regardless, topical NSAIDs are now increasingly considered as a first-line pharmacological option for patients with OA, especially in those with increased risk of adverse events. It is an attractive management option, associated with good adherence; the main potential side effect is local skin reactions.

Opioids

Due to the increased risk of adverse events and small-to-modest effects on pain, opioid use is generally discouraged in most OA management guidelines. Compared with nonselective NSAIDs, opioids have increased adverse events, including fractures (hazard ratio [HR], 4.47; 95% confidence interval [CI], 3.12 to 6.41), cardiovascular events (HR, 1.77; 95% CI, 1.39 to 2.24) and all-cause mortality (HR, 1.87; 95% CI, 1.39 to 2.53).[8]

Opioids such as oral oxycodone, tramadol and tapentadol and topical buprenorphine can be considered as alternatives to NSAIDs in patients who are unable to tolerate them or in whom they are contraindicated due to comorbidities. However, the opioid starting dose should be low and patients require regular monitoring of side effects, including constipation, dizziness and drowsiness.

Duloxetine

The role of central sensitisation in pain modulation in chronic knee OA is increasingly being recognised. Use of a centrally-acting agent such as the serotonin and noradrenaline reuptake inhibitor (SNRI) duloxetine has been shown to be efficacious in OA, with no significant differences in effect on pain when indirectly compared with NSAIDs and opioids.[52,53] Duloxetine is a potential adjunct to conventional OA treatment for pain modulation, as additional pain reduction and improvement in function is seen when it is added to oral NSAIDs in comparison with placebo.[54] Common side effects of duloxetine include nausea, constipation, fatigue, dry mouth and decreased appetite. Although it is recommended in international OA guidelines, duloxetine is not TGA-indicated for this purpose in Australia.

Other antidepressants that have been used in chronic pain syndromes, such as low-dose amitriptyline, have not been adequately studied for OA pain. The authors are unable to advocate this off-label use of amitriptyline despite this tricyclic antidepressant being a potential cheap and safe option.

Intra-articular injections – corticosteroids and hyaluronic acid

Based on a Cochrane review of their use for treatment of knee OA, intra-articular corticosteroids provide short-term relief (two or less weeks) in terms of pain and function.[55] Their use can be considered in patients who present with acute OA exacerbations with joint effusions and local inflammation. Although the evidence is not strong, it has been advised that regular intra-articular corticosteroid injections more frequently than once every four months can potentially result in knee cartilage and joint damage.[56,57] This concept was based on some very early nonprimate studies.[57]

The benefit of intra-articular hyaluronic acid injections is uncertain, with inconsistent findings seen in meta-analyses evaluating their efficacy compared with intra-articular saline; generally there is no difference or only small effect size for pain

CONSERVATIVE CARE PROGRAMS FOR PATIENTS WITH OA[1]

Victoria

- Osteoarthritis Hip and Knee Service (OAHKS)
  https://www2.health.vic.gov.au/hospitals-and-health-services/patient-care/specialist-clinics/osteoarthritis-hip-knee-service
- Rehabilitation at home
  http://www.remedyhealthcare.com.au/home-healthcare

Queensland

- The Queensland Orthopaedic Physiotherapy Screening Clinics (OPSC), available at Mater Adult Hospital, Brisbane and the Nambour General Hospital, Nambour
  http://brochures.mater.org.au/home/brochures/mater-adult-hospital/orthopaedic-physiotherapy-screening-clinic-and-mul

New South Wales

- Osteoarthritis Chronic Care Program
  http://www.aci.health.nsw.gov.au/resources/musculoskeletal/osteoarthritis_chronic_care_program/osteoarthritis-chronic-care-program
- Osteoarthritis Management Program
  http://www.huntershillprivate.com.au/Rehabilitation/Osteoarthritis%20Management%20Program
- nib Health Funds and Sigma Osteoarthritis Program
  https://www.nib.com.au/nib-news/health-cover/2015/07/be-good-to-yourself-and-improve-your-health

Western Australia

- Elective Joint Replacement Service Model of Care
  http://www.healthnetworks.health.wa.gov.au/modelsofcare/docs/Elective_Joint_Replacement.pdf
- Service model for community-based musculoskeletal health in Western Australia
  http://www.healthnetworks.health.wa.gov.au/network/musculoskeletal.cfm

National

- Osteoarthritis Healthy Weight for Life Program
  http://oa.hwfl.com.au
- Arthritis Australia – for a tailored osteoarthritis management plan
  http://www.arthritis.org.au/arthritis/my-joint-pain

compared with placebo.[58] Although there are data suggesting that high molecular weight viscosupplements may provide more benefit than low molecular weight products, meta-analysis has been unable to show meaningfully important differences.[59] Existing guidelines also show inconsistency. The American Academy of Orthopaedic Surgeons 2013 clinical practice guideline on the treatment of knee OA does not recommend the use of hyaluronic acid in patients with OA.[59] The American College of Rheumatology 2012 recommendations for use of therapies in OA of the hand, hip and knee do not advocate the use of intra-articular hyaluronate for the initial management of knee OA; however, its use is conditionally recommended if a patient does not have a satisfactory response to initial therapy.[18]

Platelet-rich plasma and stem cell injections

Commercial uses of platelet-rich plasma (PRP) and stem cell therapies have recently emerged for knee OA management.

PRP is derived from autologous blood, and its main constituent is platelets. The exact mechanism of action is not well understood, but PRP is thought to have high concentrations of growth factors, which can potentiate the proliferation of mesenchymal stem cells and increase matrix synthesis and collagen formation.[60] Recent data from meta-analyses suggest that PRP may have a helpful effect on symptoms but the exact ideal preparation and its frequency of administration remain controversial.[61,62] No trials have examined the structural effects of PRP in the OA joint, and there is a lack of standardisation of the PRP preparations in existing trials and in current clinical practices.

Similarly with stem cell therapy, the concept is based on the precursor cells' potential capability to differentiate into cells of the chondrogenic lineage. Typically, stem cells are collected from fat and bone marrow but, like PRP, there is no standardisation in current preparations.[63] To date, there is no substantive robust supportive evidence to advocate for stem cell therapies, and large randomised controlled trials are required to determine their efficacy. Furthermore, both the International Society for Stem Cell Research and the Australian Rheumatology Association are against their current use for OA.

Surgery – when to refer?

Surgery should be reserved for those patients with knee OA in whom conservative measures fail. Up to one-third of patients who have a total knee replacement do not have a favourable outcome.[64]

A recent trial demonstrated the efficacy of surgery for pain relief and functional improvement in patients with knee OA.[65] However, it is essential to consider the associated risk factors (the risks of surgery, anaesthetics and recovery) and the use of an invasive procedure in an ageing population, the members of which are often burdened with concomitant health issues. When the joint replacement fails, there are limited treatment alternatives.

A sizeable discrepancy exists between the clinical presentation and radiographic changes seen. Thus the indication for surgery should be based on persistent

moderate-to-severe symptoms despite adequate conservative management, significant impact on quality of life and overall decline in physical function.

The types of surgical intervention should be limited to total joint replacement and, where suitable, osteotomy, which is a potential in younger patient populations. Referral for arthroscopic lavage and/or debridement is not recommended for the treatment of OA, multiple recent trials having failed to demonstrate benefit of these procedures over placebo/sham procedures or intensive physiotherapy.[66] In addition to the cost and adverse events associated with the procedure, there is an increased risk of accelerating OA progression, necessitating an earlier need for joint replacement. Arthroscopic surgery should be reserved for patients with clear histories of mechanical symptoms such as locking or catching.[67,68]

Suggestions for GPs

An integrated management plan for patients with OA needs to start from the patient's first presentation in general practice, with a focus towards prevention especially with younger patients. Apart from diagnosis, screening for the presence of comorbidities such as depression and treating them accordingly will improve pain and function levels.

Education and advice, and regular reinforcement of this, to the patient regarding the importance of general physical activity, regular strengthening and aerobic exercise and weight loss will assist long-term compliance.

Pain medications should be an adjunct to other conservative measures. Referral to an orthopaedic surgeon should be considered when patients have severe symptoms despite conservative management.

Many conservative care programs for OA are available in Australia and can assist GPs in managing patients with the condition (Box). Although most of these programs are run by public hospitals, some are covered fully by several private health insurers.

Conclusion

OA is a complex disease with the main physical presentation of pain. A wide range of pharmacological interventions is available for OA pain, but the efficacy and side effect profile of these often limit their use. Focus is shifting towards the development of targeted therapies for OA, with agents aiming at structural modification, and targeting cytokines and proinflammatory mediators.

Treatment needs to be multifaceted and the provision of health care should be within the context of a chronic disease management model as opposed to episodic/reactive healthcare delivery. From a public health perspective, a greater focus is being developed towards long-term disease prevention, with particular attention to weight control and injury prevention. MT

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A list of references is included in the website version (www.medicinetoday.com.au) of this article.

COMPETING INTERESTS: None.

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