Medical Management of Osteoarthritis

Ng Swee Cheng, M.B.B.S., M.Med (Int Med), F.A.M.S. (Rheumatology)

Department of Medicine
Alexandra Hospital, Singapore

INTRODUCTION

Osteoarthritis is the most common joint disorder in the world and one of the leading causes of pain and disability in the elderly[1]. Epidemiological studies showed that there is a predilection for weight bearing joints like the knees and hips causing difficulty in walking. Other targeted joints include finger joints, lower cervical and lumbar spine. Fortunately despite structural changes, most patients with osteoarthritis are not symptomatic.

When managing such patients, the main objectives are to :

- Educate patient
- Relieve pain
- Reduce disability
- Maintain / improve function
- Modify the OA process to reduce further cartilage loss (hopefully)
- Avoid drug toxicity while trying to achieve the above

There had been many advances in the management of osteoarthritis and important guidelines have been published e.g. the American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Recommendations for the medical management of osteoarthritis of the hip or knee:2000 update[2], and the 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)[3]. Both these guidelines are in general agreement and this article follows the guidelines closely.

As in most rheumatic diseases, treatment should always start with non-pharmacologic modalities. These are generally helpful and safe. Then medication is added on judiciously. As in the treatment of rheumatoid arthritis, medication may be classified into two groups – symptoms modifying and disease modifying.

(I) Non-Pharmacological Treatment of Osteoarthritis

1. Patient education
2. Physical therapy
3. Occupational therapy
4. Diet
5. Others – e.g. acupuncture

Correspondence should be sent to :
Dr Ng Swee Cheng
Department of Medicine
Alexandra Hospital
378 Alexandra Road
Singapore 159964

*1. **Patient education***

Patient education is important because the patient is a vital partner in healthcare. Doctors should try to tell the patient about osteoarthritis, the natural history of the disease and treatment options. Patient educational material (often free from voluntary welfare organizations) and online resources are available. In addition, public lectures by health care professionals are also helpful. The patient who understands his/her illness is better able to manage pain and use medication. The educated patient will also be more motivated to do therapeutic exercises. It has been shown that a self-management programme with health education and exercise instruction for patients with knee or hip osteoarthritis led to improvement in mobility and pain versus a control group[4].

*2. **Physical therapy***

Physiotherapy will help patients with osteoarthritis do the correct exercises and use therapeutic modalities like heat or cold[5]. Specific exercises are important, e.g. quadriceps-strengthening exercises for knee osteoarthritis. Exercises may also improve the range of joint movement and improve balance. Application of heat to the affected joint prior to exercise makes it more comfortable for the patient. Patients with osteoarthritis should avoid unsupervised weight bearing exercises as such activities may aggravate cartilage damage. Gentle non-impact aerobic exercises and swimming are often recommended as they improve mobility, increase self confidence and improve cardiovascular stamina. A physically active lifestyle is indeed beneficial to older adults with osteoarthritis and guidelines for exercise for such patients have been published[6].

*3. **Occupational therapy***

Patients who have functional disability from osteoarthritis should be referred to the occupational therapist. Advice on energy conservation, care of joints, and use of splints, proper shoes and insoles are practical and useful. Women should minimize the wearing of high heel shoes as they lead to increases in forces along the medial and patello-femoral compartments of the knee[7]. Canes and walkers can help patients to move about fairly independently despite knee osteoarthritis.

*4. **Diet***

Obesity is associated with osteoarthritis. In the Framingham study, weight in subjects with median age of 37 years predicted knee osteoarthritis 36 years later[8]. In women, a decrease in body mass index of 2 units over the previous 10 years decreased the odds of knee osteoarthritis[9]. A low calorie diet for overweight patients with OA has been shown to improve the symptoms. Obese

patients with osteoarthritis going for joint surgery should also be reminded that they have increased operative morbidity and mortality.

*5. **Acupuncture***

Acupuncture is a popular form of traditional non-pharmacological therapy for osteoarthritis. Some patients with osteoarthritis go to the acupuncturist before seeing a Western trained doctor. A 2000 review of the evidence for acupuncture as treatment for rheumatic conditions concluded that they was no definitive evidence from large scale randomized controlled trials but "moderately strong evidence from controlled trials to support the use of acupuncture as an adjunctive therapy for osteoarthritis"[10]. A recent randomized placebo-controlled double blind trial showed no difference in pain, function, activities of daily living and satisfaction between subjects receiving acupuncture and those receiving sham treatment[11].

(II) Pharmacological Therapy of Osteoarthritis

1. Symptom Modifying Drugs
   (a) Analgesics – simple and narcotic analgesics
   (b) Non-steroidal anti-inflammatory drugs (NSAIDs) and COX 2 inhibitors
   (c) Intra-articular therapy
   (d) Herbal medicine and supplements

Symptom Modifying Drugs

For many years now, the management of osteoarthritis was focused on symptom relief. For many patients, analgesics and anti-inflammatory drugs are sufficient to maintain reasonable function.

(a) Analgesics

The commonest "pain-killer" used in Singapore is paracetamol. Indeed, paracetamol or acetaminophen is the initial drug recommended by the American College of Rheumatology guidelines 2000[2] for the management of osteoarthritis. Not only is paracetamol shown to be as effective as a non-steroidal anti-inflammatory drug for short-term use in osteoarthritis[12], it has also been shown to be effective for long-term use[13]. This medication is safe enough to be available over the counter. Unlike NSAIDs it may be given to patients with impaired renal function. However this drug is so common that some patients have already taken this before consulting the doctor. There is also evidence that patients prefer to be given an NSAID rather than a simple analgesic[14]. Narcotic analgesics are best thought of as reserve drugs for painful osteoarthritis. These include Tramadol and codeine in combination with acetaminophen. Tramadol is a synthetic opiod agonist and have been shown to be as effective as NSAID for osteoarthritis[15] and can be added on to the NSAID[16]. Codeine in combination with paracetamol has been shown to be more effective than paracetamol alone but may cause nausea, vomiting, dizziness and constipation[17]. When using opiod analgesics to relieve the chronic pain of osteoarthritis, we must always be wary of dependence, tolerance, respiratory depression and constipation in the elderly.

(b) Non-steroidal Anti-inflammatory Drugs (NSAIDs) and COX II Inhibitors (COXIBs) even though osteoarthritis is cartilage failure often from mechanical abnormalities, an associated inflammatory synovitis is often seen. Hence NSAIDs are useful. Topical NSAIDs (gel or plasters) are safe and mildly effective and can be used for mild osteoarthritis. Oral NSAIDs can be used if the patient does not respond to simple analgesics. In patients with inflammatory knee osteoarthritis (effusion) or moderate to severe pain, the ACR guidelines favor the initial use of NSAIDs before use of analgesics, although the EULAR guidelines did not. Many studies have been done to document that all NSAIDs have analgesics as well as anti-inflammatory effects and are effective in the management of osteoarthritis.

However adverse effects of NSAIDs are also very well recognized. These include gastrointestinal toxicity (gastric ulcers, duodenal ulcers, obstruction, bleeding and perforation), renal toxicity (NSAID nephropathy, fluid retention, hypertension and hyperkalaemia), central nervous system effects, transaminitis, rashes, and even exacerbation of asthma. Before prescribing an NSAID, it is important to evaluate the patient's risk for serious NSAID gastropathy and NSAID nephropathy (see below). Other factors to consider include cost and dosing convenience.

NSAID gastropathy

The risk factors for serious NSAID associated upper gastrointestinal adverse events are well known. They include age > 65 years, history of peptic ulcer disease or of upper gastrointestinal bleeding, concomitant use of oral steroids or anti-coagulant and presence of co-morbid conditions[18,19,20]. Patients who are at high risk of NSAID gastropathy should avoid taking NSAIDs altogether. However if the medical decision is that the benefit of the NSAID outweighs the risk, then the patient should be offered a COX II inhibitor or COXIB. The COX II inhibitor should be able to relieve the inflammatory pain by inhibiting COX II, the enzyme associated with inflammation, while sparing COX I, the housekeeping enzyme which regulates normal cellular function like gastric cytoprotection. FDA has approved the use of 3 COX II specific inhibitors – Celecoxib, Rofecoxib and recently, Valdecoxib. Clinical trials have shown that Celecoxib is more effective than placebo and as effective as a standard NSAID in patients with knee or hip osteoarthritis[21]. Rofecoxib has been shown to be more effective than placebo and as effective as standard NSAIDs in patients with knee or hip osteoarthritis[22,23]. Besides confirming efficacy, clinical trials have demonstrated relative lack of gastroduodenal toxicity for both drugs[24,25]. For patients who find COX II specific inhibitors too expensive, a COX II selective inhibitor may be tried.

A COX II specific inhibitor Meloxicam has been shown to be effective and safe for the treatment of osteoarthritis[26]. The National Institute for Clinical Excellence (NICE) in the United Kingdom recommended that COX II selective drugs (Celecoxib, Rofecoxib and Meloxicam) be used for osteoarthritis patients who are at high risk for serious upper gastrointestinal toxicity[27].

Another strategy is to give the patient a standard NSAIDs together with a gastro-protective agent like misoprostol at 200 ug 4 times a day has been shown to reduce the incidence of complicated ulcers[28] and when given 3 times a day can decrease both gastric and duodenal ulcers[29]. High dose H2 blocker, famotidine and a proton pump inhibitor, omeprazole are also effective in the treatment and prevention of NSAID gastropathy[30,31].

NSAID nephropathy

NSAID nephropathy is more commonly seen in those with pre-existing renal disease (serum creatinine >2mg/dl), age > 65 years, hypertension, congestive heart failure or are taking medications like diuretics and angiotensin-converting enzyme inhibitors[32]. Great care must be taken when patients with these risk factors are given NSAIDs. Some NSAIDs may have a lower nephrotoxic potential than others. Low-dose aspirin, low-dose ibuprofen and perhaps Sulindac appear to be safer because of their relative sparing of renal prostaglandin synthesis. COX II selective and specific inhibitors are not renal sparing.

(c) Intra-articular Therapy

Besides using oral therapy to relieve osteoarthritic pain, intra-articular injection of corticosteroids or hyaluronan can be given. Intra-articular corticosteroids are very useful particularly if the joint is inflamed with associated joint effusion. Aspiration of such an inflamed joint, followed by intra-articular injection of corticosteroids is rapidly effective in reducing joint pain[33]. Aseptic technique should be used, as there is a small risk of introducing infection during the procedure.

Intra-articular hyaluronan has been tested in clinical trials and shown to be effective in relieving pain[34,35]. The pain relief is as good if not better than steroids, and though onset of action is generally slower, the duration of symptom relief is often longer than intra-articular steroids.

(d) Herbal Medicine and Supplements

Herbal medicine and supplements have always been extremely popular because of the belief and hope that such therapies are naturally effective and safe. Some recent publications are mentioned here. None of them are officially recommended for the treatment of osteoarthritis.

Ginger (Zingiberis officinale)

A clinical trial was conducted to compare the effect of a ginger extract to ibuprofen and placebo in 75 patients with knee or hip osteoarthritis. Results showed that the pain (as assessed by the Visual analogue Scale) was decreased in ibuprofen > ginger > placebo. However there was no significant difference between placebo and ginger[36].

Ayurvedic Herbal Mixture

A standardized Ayurvedic herbal mixture *(Withani somnifera, Boswellia serata, Zingiberis officinale, and Circuma longa)* was tested in patients with rheumatoid arthritis and found to be effective and safe[37]. Hence some doctors give it to patients with osteoarthritis as well.

Chondroitin Sulphate

Some studies have been conducted to evaluate the efficacy of chondroitin sulphate for osteoarthritis. A meta analysis of 7 trials involving 372 patients with osteoarthritis showed that it was superior to placebo in treating pain (VAS) and function (Lequesne Index)[38].

Glucosamine

The Cochrane review of searches reported 16 randomized, controlled studies showing that Glucosamine was effective and safe in osteoarthritis. All but 1 of the 13 studies in which Glucosamine was compared with placebo showed Glucosamine superior in pain relief[39].

2. *Disease Modifying Osteoarthritis Drugs*

Disease modifying osteoarthritis drugs have long been on the wish list of rheumatologists. They should not just relieve the symptoms but should prevent the structural damage of joints at risk or at least retard the progression of structural damage. Such drugs often inhibit breakdown of cartilage (by targeting matrix metalloproteinase) or stimulate the repair of cartilage. No such drugs are currently available although some interesting positive findings have been reported.

Diacerein

Studies have shown that Diacerein inhibits the production and activity of interleukins and metalloproteinases. A 3-year randomized, blinded, placebo controlled trial was done to look at radiographic progression (joint space loss of at least 0.5 mm). At the end of the trial, 47% of the treated group versus 62% of the placebo group had radiographic progression (p=0.007)[40].

Glucosamine

Glucosamine may have the ability to stop the loss of cartilage in patients with knee osteoarthritis[41]. This was the finding of a study which looked at 212 patients with knee osteoarthritis, randomized to receive 1500 mg Glucosamine sulphate or placebo daily for 3 years. Those who were on placebo had progressive joint space narrowing of 0.31 mm over 3 years as compared to those on Glucosamine who had a non-significant mean joint space loss of 0.06 mm. This benefit was in addition to improvement in WOMAC pain and function scale.

Intra-articular Hyaluronan

A study was conducted to see the effect of intra-articular hyaluronan versus methyl-prednisolone on the histology of the synovium and cartilage before and after injection. In the hyaluronan group, the histology of the cartilage was associated with an increase in chondrocyte density and improvement in the territorial matrix in the cartilage[42].

CONCLUSION

The past few years has seen important progress in the management of osteoarthritis. Safer medications (COXIBs) are now available and guidelines have been published to help doctors in the management of this common rheumatic disease. The elusive disease modifying osteoarthritis drug may soon be found.

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