Continuing Professional Development

CPD

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60 Second Summary

Osteoarthritis (OA) is the most common form of arthritis, one of the leading causes of pain and disability in the world . It is a syndrome of joint pain affecting over 25% of people over 18. The major symptoms are chronic pain, joint instability, joint stiffness, and joint space narrowing.

OA is characterised by a progressive loss and destruction of cartilage locally in the joint, thickening of subchondral bone, osteophyte formation, synovial inflammation, degeneration of knee ligaments/menisci, hypertrophy of the joint capsule, and inflammation.

According to NICE guidance, OA can be diagnosed clinically if a person is over 45, presents with activity related joint pain, and has no morning joint related stiffness that lasts less than 30 minutes. Both NICE and Osteoarthritis Research Society International (OARSI) guidelines recommend specified "Core Treatments" for OA.

OA is best considered within the context of comorbidity: it is often present along with e.g. cancer, heart disease, hypertension, diabetes and depression. Between 59 and 87% of people with OA have at least one chronic comorbidity, and 30% have 5 or more. The pain and functional limitations associated with OA can result in a negative cycle that not only prevents people from managing their OA, but can also be detrimental to the progression of their other comorbidities.

Appropriate use of pharmacological interventions along with the core treatments is important. Paracetamol, long regarded as a mainstay of OA treatment, was not recommended in many recently updated OA treatment guidelines.

1. REFLECT - Before reading this module, consider the following: Will this clinical area be relevant to my practice?

2. IDENTIFY - If the answer is no, I may still be interested in the area but the article may not contribute towards my continuing professional development (CPD). If the answer is yes, I should identify any knowledge gaps in the clinical area.

3. PLAN - If I have identified a knowledge gap - will this article satisfy those needs - or will more reading be required?

4. EVALUATE - Did this article meet my learning needs - and how has my practise changed as a result? Have I identified further learning needs?

5. WHAT NEXT - At this time you may like to record your learning for future use or assessment. Follow the 4 previous steps, log and record your findings.

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Management of Osteoarthritis and Joint Pain

Introduction

Osteoarthritis (OA) is the most common form of arthritis, one of the leading causes of pain and disability in the world.[1] It is a syndrome of joint pain affecting over 25% of people over 18.[2] The major symptoms are chronic pain, joint instability, joint stiffness, and joint space narrowing. OA can affect how people are able to work, their relationships, mental wellbeing and leisure activities. It is most commonly reported in the knee, with hips and small hand joints also commonly affected, although it can occur in any joint (Figure 1). Up to 25% of people with OA report multiple joint involvement. With no preventative treatment or cure available, OA is a considerable financial cost to individuals, governments and economies.[3]

Pain associated with any disorder is a complex biopsychosocial issue that is influenced by the person's expectations and self-efficacy (which refers to a person's belief in their capacity to execute the behaviours necessary to produce the desired outcomes), and can significantly impact mood, sleep and the ability to cope. Although it is commonly believed that OA is caused by ageing and deteriorates with time, this is not necessarily true.

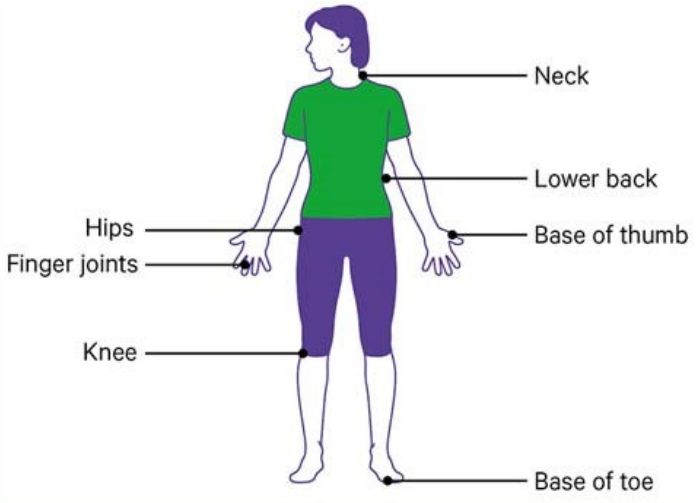
Figure 1. Joints most often affected by OA[4]

Clinical trials investigating treatments for OA have shown a substantial placebo effect, particularly for people with high pain levels. On a positive note, embracing this placebo effect may enhance the effects of therapies, providing even better patient outcomes with reduced costs and risks.

Osteoarthritis Pathophysiology

OA is characterised by a progressive loss and destruction of cartilage locally in the joint, thickening of subchondral bone, osteophyte formation, synovial inflammation, degeneration of knee ligaments/menisci, hypertrophy of the joint capsule, and inflammation.[2,3] Joints are often required to repair and heal, which can result in a structurally altered, but symptom free joint. However, sometimes due to the overwhelming level of trauma or inadequate repair, OA symptoms present, which may be thought of as "joint failure". The visible pathology in joints from OA seen from x-rays does not necessarily correlate with the person's symptoms - even minimal joint changes can be associated with significant pain.

The molecular mechanisms behind OA are still not well understood, and as a result, there are no available interventions to restore



damaged cartilage or to slow disease progression. Animal studies suggest involvement of growth factors and signalling molecules. A transcription factor that regulates enzymes that cause degradation of articular chondrocytes is also involved.[2] Overall, at the cellular level of OA, the healthy homeostatic state is altered and becomes more so catabolic.

Risk Factors for Osteoarthritis

Age: Most individuals over the age of 65 display some radiographic changes in one or more joints. When damaged, ageing chondrocytes are less able to elicit a full repair response, and ageing cells show an increase in oxidative stress that promotes cell senescence.

Obesity: Patients with obesity develop OA earlier than those at a healthy weight. Symptoms are more severe, and there are more risks and difficulties for joint replacement surgery. Obesity leads to increased biomechanical loading on the joints and a general low-grade systemic inflammation (through secretion of cytokines derived from adipose tissue called adipokines). This inflammation may stimulate the catabolism of articular chondrocytes.

Sports Injury: Up to half of people with a history of previous knee injuries show radiographic evidence of knee OA in later years. Traumatic sports injuries can cause bone, cartilage, ligament and meniscus damage, as well inflammation.

Inflammation: The chronic, low-grade inflammation in OA perpetuates disease progression. A whole host of inflammatory factors - interleukins, TNF, damage associated molecular patterns (DAMPs) and alarmins - are abundant in OA-affected joints.

Genetics: As with many diseases, the genetic contribution to OA is highly significant, but highly complex. Recent genome-wide association studies (GWAS) have identified over 80 gene mutations or single-nucleotide polymorphisms (SNPs) involved in OA pathogenesis. These include mutations in genes for structural and signalling molecules.[2]

Diagnosis and Management

According to NICE guidance, OA can be diagnosed clinically if a person is over 45, presents with activity related joint pain, and has no morning joint related stiffness that lasts less than 30 minutes.[1]

Both NICE and Osteoarthritis Research Society International (OARSI) guidelines recommend specified “Core Treatments” for OA.[1,5] These are “treatments deemed appropriate for use by the majority of patients in nearly any scenario and deemed safe for use in conjunction with first line and second line treatments”. All Core Treatments are non-pharmacological: education, physical activity, weight management and support for self management, and widely considered to be the gold standard for the management of OA.[3]

Education: Many different types of educational OA programmes have been used successfully, with no current consensus on what the ideal programme looks like. Free online educational programmes are available, including from Arthritis Ireland. Providing consistent, accurate and understandable health information empowers people to become more active in health decisions and developing self-management skills.

Exercise: People with OA frequently think that exercise will cause additional joint damage and worsen pain, but this is not what evidence shows. All international guidelines for OA management recommend therapeutic exercise along with maintaining appropriate levels of everyday physical activity. Nearly all types of physical activity have positive effects on pain, function, quality of life, sleep and mood; regardless of age, disease severity, affected joint, or function. These improvements are thought to be attributable to increased muscle strength, or a possible anti-inflammatory effect of moderate mechanical loading of the joint. Land based exercise is thought to be superior to water for hip and knee OA because of the weight bearing nature, but water based exercise is a great alternative for those who have increased pain on weight bearing. Appropriate physical activity should be recommended for each person with OA to avoid the cycle of physical activity causing pain, resulting in avoidance of physical activity, which causes a decrease in muscle strength and increase in stiffness, resulting in more pain and avoidance of physical activity. Land based exercise programmes in particular were recommended for people with polyarticular OA, along with OA education.[5] Exercise also has benefits for many other comorbidities.

Weight management: Anyone with a BMI≥25kg/m2 should aim to reduce their weight due to the link between being overweight and obese with OA.[3] Weight loss is also potentially very beneficial for additional comorbidities. A starting point of losing 5-10% of body weight is recommended, however, the closer the person gets to a BMI of 18.5 to 24.9kg/m2, the better. The mechanisms behind symptom improvement after weight loss are still not fully understood, but even a decrease in biomechanical load on the knees during weight bearing helps to conserve joint structures and reduce pain. Weight loss also reduces adipokine levels which contribute to OA and cartilage damage. OARSI guidelines do not recommend dietary weight management for hip OA because of lack of direct evidence of efficacy, except in those with a BMI ≥30 kg/m2.

OA is best considered within the context of comorbidity: it is often present along with e.g. cancer, heart disease, hypertension, diabetes and depression. Between 59 and 87% of people with OA have at least one chronic comorbidity, and 30% have 5 or more. The pain and functional limitations associated with OA can result in a negative cycle that not only prevents people from managing their OA, but can also be detrimental to the progression of their other comorbidities.

Pharmacological Management

Appropriate use of pharmacological interventions along with the core treatments is important.[3] Paracetamol, long regarded as a mainstay of OA treatment, was not recommended in many recently updated OA treatment guidelines.[5] Evidence from multiple studies has suggested little to no efficacy in OA, with possible hepatotoxicity.[6] Oral and transdermal opioids in individuals with OA are strongly recommended against in the majority of guidelines, mainly

due to concerns about long term dependency. NICE is currently reviewing evidence on the pharmacological management of OA, but until this is done, recommendations from 2008 remain the most current, i.e. paracetamol and topical NSAIDs are recommended for pain relief in addition to the core treatments, with opioid analgesics or oral NSAIDs only advised if these treatments are not working.

Regular reviews (annually if taking medication for the condition) for people with OA should be offered by GPs in order to monitor symptoms and their impact on QOL and the long term course. This also offers a chance to support the patient's own management of the condition, review efficacy and tolerability of their treatments as well as their own concerns, personal preferences and knowledge of osteoarthritis.[1]

Topical NSAIDs are recommended by the OARSI guidelines for use in patients with knee and polyarticular OA with no comorbidities.[5] Modest benefits over a course of 12 weeks treatment were shown, with minimal and mild adverse effects. According to NICE guidance, topical NSAIDs are preferred over oral for knee, feet and hand joints due to safety concerns.[3] When any person is using topical NSAIDs, the number of joints being treated and the possible concurrent use of oral NSAIDs should be taken into account to ensure that the total recommended NSAID dose is not exceeded.[5]

Oral NSAIDs NICE guidelines[1] recommend the use of an oral NSAID/COX-2 inhibitor (with a PPI) instead of or in addition to paracetamol. Oral NSAIDs/COX-2 inhibitors have comparable analgesic effects, but vary in their risk of gastrointestinal, liver, cardiovascular and renal toxicity. Keeping this in mind, an appropriate choice should be made for the individual patient.

OARSI guidelines[5] recommend oral NSAIDs for knee, hip or polyarticular OA in those without additional comorbid conditions. Non-selective NSAIDs with a PPI, or selective COX-2 inhibitors are the treatments of choice, although these are not considered appropriate for any people with cardiovascular comorbidities due to the association between NSAIDs and an increase in cardiovascular risk. If NSAIDs are chosen to treat any at-risk patients, those with more favourable safety profiles are preferred, and ideally should be used at the lowest dose and shortest duration possible.

Topical capsaicin is also a potential adjunct for knee or hand arthritis.[1]

For moderate to severe OA, intra-articular corticosteroid injections (IACS) may be beneficial.[1] In particular, OARSI guidelines state that IACS can provide short term pain relief for knee OA.[5] There is mixed evidence however: one RCT looking at IACS vs placebo in knee OA before starting an exercise programme showed comparable rates of pain reduction and functional improvement.[3] Furthermore, repeated administration can cause concerns about disease progression.

Intra-articular hyaluronic acid injections (IAHA) should not be offered according to the NICE guidelines, whereas the OARSI guidelines suggest that IAHA may have beneficial effects even beyond 12 weeks after administration and a better long-term safety profile than repeated IACS administration.

Glucosamine and chondroitin products are not recommended in the NICE guidelines for osteoarthritis treatment. A Cochrane Review[7] looked at the efficacy of chondroitin in treatment of OA symptoms. Findings (based on 43 RCTs) indicate that there may be a slight improvement in pain, but only in the short-term (<6 months). There was no improvement in cases of supplementation for longer than this. Chondroitin probably improves quality of life slightly (as measured by an index of pain, function, and disability) with very few or no adverse events (3% chondroitin vs 6% with placebo); and it slightly slows down the narrowing of joint space on x-rays. The authors concluded that improvement in joint pain with chondroitin (alone or with glucosamine) in participants with OA was clinically and statistically significantly better than with placebo, but this was based on trials of mostly low quality.

For patients with widespread pain and/or depression, the OARSI guidelines recommend oral NSAIDs of any type, duloxetine, IACS, IAHA and topical NSAIDs.

Where possible, medication should be used at the lowest dose and for the shortest duration. In people with chronic refractory symptoms with persistent pain despite physical activity and weight management, long term medication may be necessary.[3] These people need to be aware of the possible adverse effects from this, and/or be considered for joint replacement.

Adjunctive Treatments for Osteoarthritis

These therapies are often more passive, have a more local effect, or may have a lower level of clinical benefit than the core treatments. For end stage hip or knee OA, joint replacement surgery is an effective treatment, although there are associated risks and financial costs. A review of OA treatments in Nature[3] observes that over-reliance on surgery and inappropriate medication prescribing are prevalent, along with a lack of support for lifestyle interventions.

Cognitive Behavioural Therapy: CBT is a psychological intervention that aims to help people understand how their thinking and emotions can affect behaviours. CBT provides some benefits in coping ability, pain, depression and anxiety for people with OA in the knee, and for other medical conditions associated with pain. Some people may respond better to CBT than others, but CBT overall has a good safety profile.

Heat and Cold Therapy: Hot packs and hot water bottles can reduce OA associated pain. This may be due to an increase in the

circulation to the local area that relaxes the muscle around the joint. The evidence for use of heat in OA is minimal, but because it is easily accessible, inexpensive, often pleasant and has a low risk of harm, some clinical guidelines (e.g. OARSI) recommend it. Application of cold, e.g. an ice pack, aims to reduce swelling, muscle spasm and pain. A systematic review found, however, that there were still insufficient studies to definitively draw conclusions about its effectiveness in OA.

Walking aids, splints and orthoses: Data on the use of walking aids like canes, sticks or walkers are limited, although use of these devices is often recommended to improve stability and reduce risk of falls. There is some evidence that long term use of splints can be beneficial for pain and function in people with thumb OA, but evidence is not as clear for use of splints in knee OA. The benefits of shoe orthotics such as wedge insoles, shock-absorbing insoles and arch supports are still being investigated, though NICE guidelines[1] say that appropriate (shock-absorbing) footwear for lower limb arthritis, and assistive devices like walking sticks and tap turners, may be useful.

Transcutaneous electrical nerve stimulation: TENS machines work by applying an electrical current through electrodes on the skin to modify peripheral nerve activity. The theory behind this is that stimulation of the Aβ nerve fibres blocks nociceptive signal transmission in the spinal cord, altering the nociceptive stimulus to the brain. This is considered to be a short lived effect (limited to a few hours after use). RCTs have identified a positive effect on knee OA pain and function, an effect that is potentially generalisable to hip OA.[3]

Massage and Manual Therapies: These aim is to reduce pain and inflammation by improving range of motion, joint flexibility, blood circulation and increasing relaxation of the muscles and mind. Massage therapies are for muscles and soft tissues whereas manual therapies offer a variety of techniques including joint mobilisation and manipulation, manual traction, stretching and myofascial techniques. These therapies have not widely been investigated in OA in clinical trials. Most clinical guidelines support the short term use of these treatments as they have a low risk of harm, and may have other benefits for people with OA.

Acupuncture is not recommended in the NICE guidelines for OA treatment. Mind-body exercise (e.g. yoga, tai chi) is recommended by OARSI for both hip and knee OA. For people with polyarticular OA, gait aids, mind-body exercise, and self management programmes (except for those with frailty) were among the OARSI guideline recommendations.

NSAID Efficacy

A network meta-analysis[8] investigated pain relief and functional outcome in OA as the two primary outcomes of interest. The authors concluded that diclofenac (150mg per day) and etoricoxib (60mg/day) appear to be the most effective for hip and knee OA. The risk of adverse events from either of these did not significantly differ from placebo, although etoricoxib presents a lower risk for GIT events. Topical diclofenac 70-81 mg/day could be effective and safer due to reduced systemic exposure and lower dose, and should be considered as a first line pharmacological treatment for knee osteoarthritis. Of note, the only topical NSAIDs included in the analysis were diclofenac and flurbiprofen.

NSAID Safety Concerns

The two major COX isoenzymes are COX-1 (also known as prostaglandin G/H synthase 1) and COX-2 (also known as prostaglandin G/H synthase 2), both of which form prostaglandin H2 from arachidonic acid (9). Prostaglandin H2 is further catalysed to produce bioactive lipids (prostanoids) such as thromboxane A2, prostaglandin (D2, E2, F2) and prostacyclin which influence immune, cardiovascular, gastrointestinal, renovascular, pulmonary, central nervous system and reproductive functions. COX-1 in platelets and in myocardial, parietal and kidney cells regulates platelet aggregation, thrombosis, gastric protection and kidney function. COX-1 is upregulated in response to inflammation in e.g. atherogenesis, rheumatoid arthritis, ischaemia and neoplasms. COX-2 inhibition leads to suppression of the production of protective prostacyclin. Selective COX-2 inhibitors were intended to lower the rates of gastrointestinal adverse events (bleeding) but are associated with excess cardiovascular risk. The simplified hypothesis was that the more COX-2 inhibition compared to COX-1 inhibition, the higher the risk of cardiovascular events. However, this is debated because even non-selective NSAIDs have also been associated with increased cardiovascular risk. Other mechanisms might explain the harmful effects of NSAIDs; for example, prostacyclin has been found to act as a restraint on many prothrombotic stimuli.

- Sodium retention can occur in up to 25% of NSAID-treated patients. This can cause weight gain and peripheral oedema, potentially exacerbating any congestive heart failure.[10]
- Acute renal failure is an uncommon result of NSAID treatment that can occur due to the vasoconstrictive effects of NSAIDs, and is reversible. This usually happens in patients who have a depleted intravascular volume.
- NSAIDs may cause increases in mean arterial blood pressure of between 5 and 10 mmHg. As a result, the effects of antihypertensive agents including diuretics, angiotensin-converting enzyme inhibitors, and β-blockers, can be reduced.
- NSAIDs are linked with an increased risk of myocardial infarction. Drugs that inhibit less than 90% of the COX-2 enzyme at therapeutic concentrations have an estimated relative risk of 1.18, drugs that inhibit COX-2 to a greater degree present a relative risk of 1.60.

In a network meta-analysis[11] of cardiovascular safety data of seven non-steroidal anti-inflammatory drugs (etoricoxib, rofecoxib, lumiracoxib, celecoxib, ibuprofen, diclofenac, naproxen) and placebo, naproxen seemed least harmful, but this should be weighed against other side effects like gastrointestinal toxicity and the need for a PPI in many people. Other NSAIDs (ibuprofen, diclofenac and etoricoxib)

Despite well-documented risks, the lack of new, effective and safer alternatives has contributed to their continued widespread use because they provide effective analgesia. Care is needed to manage the cardiovascular and bleeding risks of NSAIDs for individual patients with the balance clearly being in favour of patient benefit. This should be appraised regularly by both patient and prescriber.

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