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CORE TRAINING FOR DOCTORS

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Osteoarthritis

Introduction

Osteoarthritis is the most common condition to affect synovial joints and is characterized mainly by focal loss of articular hyaline cartilage and an accompanying bone response (*Figure 1*). The impact of osteoarthritis on the health of the population is vast – knee osteoarthritis alone is the single most common cause of lower limb disability after retirement age, and hip and knee osteoarthritis together affect over 20% of older people (Peat et al, 2001).

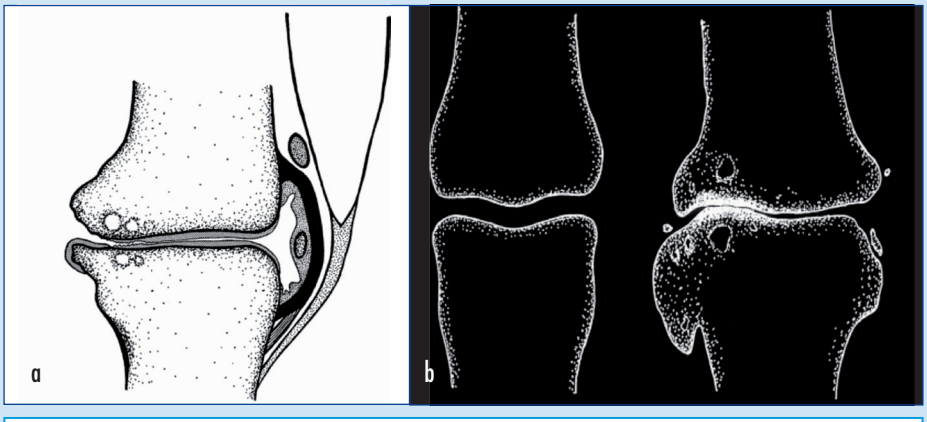
Osteoarthritis is commonly associated with other comorbidities such as cardiovascular disease and obesity which may influence the impact of osteoarthritis and also influence the selection of treatments in individual patients (Felson et al, 1987). Although the traditional view that osteoarthritis is an inevitable consequence of ageing for which little can be done remains widespread, it is now clear that osteoarthritis is a dynamic process involving both tissue damage and repair (Lohmander, 2000).

Clinical features

The characteristic symptom of osteoarthritis is use-related pain that is relieved by rest, usually in individuals over the age of 40 years. The pain follows a diurnal rhythm and is typically worst at the end of the day and best in the morning although brief morning stiffness ('gelling') may occur. Pain may arise from several sites in and around an osteoarthritic joint (subchondral bone, synovium/capsule, peri-articular tissues) and the severity of pain and functional impairment are greatly influenced by psychosocial factors (e.g. anxiety, depression) and daily activity.

Symptoms usually change only slowly and affect just one or a few joints at any one time, although examination may reveal signs of asymptomatic osteoarthritis at multiple other sites, especially in people with nodal hand osteoarthritis. Less common symptoms are more rapid progression and mechanical locking. Examination may reveal joint-line and/or peri-articular

Figure 1. a. Osteoarthritis is a metabolically active process showing both tissue attrition and new tissue production. Typical features include: focal hyaline cartilage loss, subchondral trabecular condensation, marginal new bone (osteophyte) arising by endochondral ossification of new fibrocartilage, subchondral 'cysts', synovial hypertrophy and capsular thickening, osteochondral bodies embedded in synovium, and muscle weakness or atrophy. Accompanying peri-articular lesions (bursitis, enthesopathy) may also result, especially in large joint osteoarthritis. b. Radiographic features of osteoarthritis: focal hyaline cartilage loss, subchondral bone sclerosis, marginal new bone (osteophyte), subchondral 'cysts', osteochondral bodies, bone remodelling and deformity.



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tenderness, limitation of movement, course crepitus, bony enlargement, deformity and occasionally instability. Effusion and synovial thickening are usually absent or only mild, but muscle weakness or wasting often accompanies chronic severe osteoarthritis. A full clinical assessment is necessary to diagnose osteoarthritis and to optimize management.

Risk factors for development of osteoarthritis and progression

Osteoarthritis is a common complex disorder with two main categories of risk factors:

- Generalized constitutional factors, such as age, obesity, genetic factors, low muscle strength and female sex
- Localized factors resulting in abnormal mechanical loading at specific sites with abnormalities of joint shape or alignment – such as non-spherical femoral head, varus knee alignment, local trauma (e.g. meniscectomy, ligament tears).

Most osteoarthritis is asymptomatic. This, together with the increased activity of all joint tissues in osteoarthritis, and the evolutionary conservation of osteoarthritis in man and other animals, suggests that osteoarthritis is the inherent repair process of synovial joints that can be triggered by a variety of joint insults. This slow repair process is often successful resulting in an anatomically altered but painless functioning joint. However, in some people overwhelming insult(s) or inherently poor repair results in 'joint failure' with pain and functional limitation and presentation as a patient with osteoarthritis.

Symptomatic hip osteoarthritis commonly progresses and superior pole involvement, which is the usual pattern in men, progresses more rapidly than other patterns such as medial or concentric hip involvement.

Knee osteoarthritis progression is variable but is usually only slowly progressive and any transition from mild to severe typically takes many years. Established knee osteoarthritis can remain relatively stable, both clinically and on radiographs for many years. The correlation between clinical outcome of knee osteoarthritis and its radiographic course is not strong but although radiographic improvement is unusual overall clinical improvement is common. Nodal hand osteoarthritis typically improves once fully developed, with the exception of the thumb base.

Principles of management of osteoarthritis

All guidelines concur in recommending that non-pharmacological measures should be central to the management plan of every person with osteoarthritis and that pharmacological agents are adjunctive options primarily for pain control (National Institute for Health and Clinical Excellence, 2008; National Institute for Health and Care Excellence, 2014) (*Figure 2*). These core non-pharmacological measures include:

- Full patient information and education (*Figure 3*) – this is a professional obligation, but also improves pain and function long term
- Weight loss if overweight or obese
- Exercise (*Figure 4*) – both local strengthening exercise (this improves the reduced muscle strength and proprioception associated with osteoarthritis, reduces pain and improves function), and aerobic fitness training (the latter reduces pain, increases delta sleep, increases wellbeing, assists a sensible weight loss programme, and benefits common comorbidities)
- Reducing adverse biomechanical factors – such as pacing of activities and appropriate footwear (thick, soft soles, no raised heel) – to avoid excessive loading of the osteoarthritis joint.

There is good evidence to support these lifestyle changes, all of which are safe, increase self-efficacy and may avoid, or reduce, the requirement for drug therapy. Examples of additional non-pharmacological approaches to reduce adverse biomechanical factors include wearing a knee brace (to reduce lateral patellar subluxation associated with patello-femoral osteoarthritis or varus mal-alignment with medial tibio-femoral osteoarthritis), use of a walking stick, and modification of the person's home or work environment (e.g. raised seats, walk-in shower).

Key factors to be take into account when treating individual patients include:

- The patient's perceptions and knowledge of osteoarthritis and its treatment
- The balance of efficacy and side effects of appropriate evidence-based interventions
- The costs, availability and logistics of treatment delivery

Figure 2. Diagram emphasizing the central role of key non-pharmacological measures. From National Institute for Health and Clinical Excellence (2008); National Institute for Health and Care Excellence (2014).

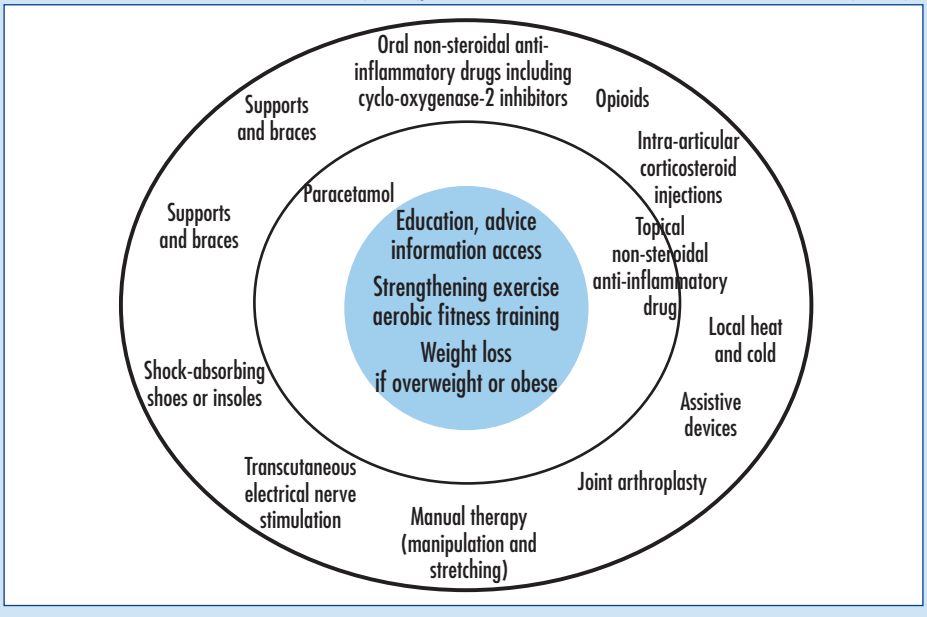

Figure 3. Quadriceps strengthening exercises are beneficial and appropriate footwear avoids excessive loading of the osteoarthritis joint.

- The presence of comorbid disease and its treatment
- The treatments and coping strategies already tried by the patient
- The individual's daily activity requirements, and work and recreational aspirations.

The National Institute for Health and Clinical Excellence (2008) and National Institute for Health and Care Excellence (2014) guidelines reinforce the principle that management of a person with osteoarthritis should be individualized and patient-centred. There is no algorithm that is applicable to all patients and a holistic approach is essential. Furthermore, although research evidence often relates to treatments given as monotherapy, a package of combined therapies is used successfully in clinical practice. Although the individual effect of each component may be small, the combined effects of the whole programme may be clinically significant. Addressing negative patient perceptions through full information and discussion is crucial in motivating adherence to lifestyle change, particularly with respect to exercise, weight loss and maintenance of reduced weight.

Contextual effects of treatment

The magnitude of non-specific beneficial effects of treatment in osteoarthritis, and indeed in other chronic painful conditions, merits attention (Miller and Kaptchuk, 2008). A meta-analysis of placebo response in 198 osteoarthritis randomized controlled trials by Zhang et al (2008) confirms the appreciable benefits of 'placebo'. For pain relief the overall effect size (the standardized mean difference between baseline and end point) was 0.51 (95% confidence interval 0.46–0.55) for placebo, but almost zero for untreated 'observation' controls (effect size 0.03, 95% confidence interval 0.13–0.18) (an effect size of 0.2 is small, 0.5 is moderate and 0.8 is high). This effect size was even higher (0.77, 95% confidence interval 0.65–0.89) in trials with head-to-head comparison between placebo and no treatment. Placebo was also effective for other subjective outcomes such as stiffness (effect size 0.43, 95% confidence interval 0.38–0.49) and self-reported function (effect size 0.49, 95% confidence interval 0.44–0.54). The following factors showed significant independent effects in determining the magnitude of placebo benefit:

- The higher the treatment effect size the higher the placebo effect, perhaps explained by higher expectation of benefit by participants
- The higher the baseline pain the greater the placebo effect size
- The route of delivery – randomized controlled trials involving needling (acupuncture, intra-articular injections) had the highest placebo effects, followed by topical and then oral routes.

It is noteworthy that the mean effect size of placebo for pain relief (0.51) is larger than the additional benefit achieved with conventional therapies, such as non-steroidal anti-inflammatory drugs (0.2–0.3). Such observations within randomized controlled trials are relevant to clinical care (Doherty and Dieppe, 2009). Patients can derive significant benefit from contextual effects especially if they are given a thorough assessment from an interested practitioner, if positive messages are reinforced, and if they are reassessed to determine the outcome. In audits of care of chronic conditions including osteoarthritis, common patient complaints are:

- The doctor was 'too busy' to listen
- The doctor did not undertake a thorough, or even any, examination
- The doctor did not address key concerns
- The doctor did not offer a follow-up appointment.

If clinicians were more aware of the power of contextual effects in relieving pain and suffering, and learnt how to optimize such effects in their clinical practice, the benefits of such 'contextual healing' to the population of people with osteoarthritis is likely to be considerable.

Figure 4. Patient education empowers osteoarthritis patients to manage their symptoms.

Treatments

Topical non-steroidal anti-inflammatory drugs are effective and safe

Topical non-steroidal anti-inflammatory drugs are popular with patients and account for a significant proportion of global analgesic sales. They achieve only low blood levels and are very safe compared with oral non-steroidal anti-inflammatory drugs. Despite some scepticism about their efficacy, a systematic review by Moore et al (1998) calculated a relative benefit of topical non-steroidal anti-inflammatory drug over placebo of 2.0 (95% confidence interval 1.5–2.7). Significant superiority was demonstrated in seven of the 12 studies in this review but in all 12 studies the results favoured topical non-steroidal anti-inflammatory drugs (*Figure 2*). A later meta-analysis by Lin et al (2004) also concluded that topical non-steroidal anti-inflammatory drugs are effective and have similar efficacy when compared to the parent or alternative oral non-steroidal anti-inflammatory drug. National Institute for Health and Clinical Excellence (2008) and National Institute for Health and Care Excellence (2014) guidelines recommend topical non-steroidal anti-inflammatory drugs as one of the first analgesics to consider for osteoarthritis of the knee, hand and other suitable sites.

Paracetamol is still recommended as first-line oral analgesic but has gastrointestinal toxicity

National Institute for Health and Clinical Excellence (2008) and National Institute for Health and Care Excellence (2014) guidelines recommended paracetamol as the first-line oral analgesic for symptomatic osteoarthritis, largely based on its perceived safety. The authors' review article (Courtney and Doherty, 2002) made the case strongly for paracetamol use based on safety and other comparisons with non-steroidal anti-inflammatory drugs. However, the accepted safety of paracetamol has been challenged by reports of gastrointestinal toxicity and other adverse effects.

Hinz and Brune (2012) argue convincingly that paracetamol is probably best considered as a weak non-steroidal anti-inflammatory drug by demonstrating evidence for peripheral cyclo-oxygenase inhibition. One study they cited was a randomized controlled trial involving 892 community-derived participants with chronic knee pain, predominantly as a result of knee osteoarthritis. On the basis of observed drops in haemoglobin levels the authors (Doherty et al, 2011) state that paracetamol 3 g/day may cause similar degrees of blood loss as ibuprofen 1.2 mg/day, and that the combination of the two appears to be additive, or even synergistic. These investigational results concur with observational evidence from a large Canadian database (Rahme et al, 2008) and challenge the belief that paracetamol is the oral treatment of choice based on an absent or lower risk of gastrointestinal complications compared with non-steroidal anti-inflammatory drug.

There are also concerns that paracetamol may have similar cardiovascular effects to traditional non-steroidal anti-inflammatory drugs and may exacerbate asthma in some patients (Hinz and Brune, 2012). Paracetamol is still recommended as first line but other strategies should be considered if inefficacy or side effects occur.

Traditional non-steroidal anti-inflammatory drugs and coxibs cause significant mortality and morbidity

Traditional non-steroidal anti-inflammatory drugs cause significant mortality and morbidity from gastrointestinal perforation, ulceration and bleeding. Rahme et al (2008) reported that this is a particular concern in the elderly. Other serious adverse effects include renal insufficiency, exacerbation of congestive heart failure, hypertension, possible increased risk of cardiovascular and cerebrovascular events (myocardial infarction, stroke) and exacerbation of asthma. Many patients with osteoarthritis are elderly and have common comorbidities that make them particularly at risk from side effects and drug interactions from non-steroidal anti-inflammatory drugs, and indeed most people with osteoarthritis are contraindicated for oral non-steroidal anti-inflammatory drugs.

Highly selective inhibitors of COX-2 (coxibs) were developed to reduce the serious gastrointestinal toxicity associated with standard non-steroidal anti-inflammatory drugs which results predominantly from COX-1 inhibition. Another effective strategy to reduce serious non-steroidal anti-inflammatory drug-associated gastrointestinal toxicity is co-prescription of a proton pump inhibitor with standard non-steroidal anti-inflammatory drug (Hooper et al, 2004). Prospective outcome studies have demonstrated varying levels of reduced gastrointestinal toxicity with coxibs and the National Institute for Health and Clinical Excellence recommends co-prescription of a proton pump inhibitor with both non-steroidal anti-inflammatory drug and coxibs.

Unfortunately, although coxibs may have better gastrointestinal safety than standard non-steroidal anti-inflammatory drugs, there is concern over the cardiovascular safety of coxibs as well as standard non-steroidal anti-inflammatory drug (Vonkeman et al, 2006). Current advice from the European Agency for the Evaluation of Medicinal Products is that COX-2 selective non-steroidal anti-inflammatory drugs are contraindicated in patients with ischaemic heart disease or stroke and that prescribers should exercise caution when prescribing COX-2 inhibitors for patients with risk factors for heart disease. This again includes a high proportion of the elderly, making this class of medication unsuitable for many osteoarthritis patients.

Other oral analgesics

Unfortunately at present there is no safe and generally well-tolerated oral analgesic with a moderate to good effect size for osteoarthritis. Weak opioids such as codeine have a low effect size and poor tolerability, especially in older patients, largely as a result of constipation, reduced concentration and sleep disturbance. Although relatively safe, oral glucosamine and chondroitin sulphate are not recommended in National Institute for Health and Clinical Excellence guidelines because of the marked heterogeneity of trial data and cost effectiveness considerations (National Institute for Health and Clinical Excellence, 2008; National Institute for Health and Care Excellence, 2014).

Intra-articular corticosteroid

Evidence for efficacy of intra-articular corticosteroid in osteoarthritis is mostly confined to the knee. This intervention (*Figure 5*) is quick and simple to do (Courtney and

Figure 5. Knee aspiration and corticosteroid injection has a relatively large effect size and is indicated for significant pain that is insufficiently helped by alternative measures.

Doherty, 2013) and has a large effect size for pain relief (1.27 at 7 days post-injection above placebo for knee osteoarthritis). It can relieve pain rapidly within just a few hours to a few days. Although benefit above placebo is relatively short-lasting in randomized controlled trials (1–4 weeks), many patients may derive benefit for several months which may largely be the result of the positive contextual response of an injection treatment.

The National Institute for Health and Clinical Excellence recommend their use as an adjunct to core treatment for the relief of moderate to severe pain in osteoarthritis patients. Although intra-articular knee injections are effective and can be considered for patients without effusion, most guidelines suggest that patients with a knee effusion, or having a 'flare', may particularly benefit. However, there are few research data to support better effects in 'inflamed' osteoarthritis joints, although Jones et al (1996) showed that the presence of an effusion improves injection accuracy, which itself is a predictor of good response.

There is no human evidence for any detrimental effect on cartilage or bone from infrequent steroid injections for osteoarthritis, although there are some theoretical concerns from animal experiments. Nevertheless it is generally agreed that injection frequency in any one joint should not exceed one injection every 3 months. Patients should be warned of possible facial flushing (c.12%) and temporary post-injection pain exacerbation (<10%). Using standard techniques, the risk of sepsis is almost negligible (estimated at <1:78 000) (Courtney and Doherty, 2013). In contrast to steroid injections, intra-articular injection of hyaluronan is not recommended by National Institute for Health and Clinical Excellence because of the marked heterogeneity of randomized controlled trials and the high cost.

Erosive osteoarthritis

Erosive osteoarthritis is an uncommon subset of hand osteoarthritis associated with more inflammatory clinical features and worse clinical outcome than common hand osteoarthritis, occasional interphalangeal joint instability or ankylosis, and radiographically by subchondral erosive change early in its course. These patients are sometimes treated with hydroxychloroquine and other disease-modifying anti-rheumatic drugs and studies are in progress to assess efficacy. At present, however, traditional disease-modifying anti-rheumatic drugs (and biologic agents) are not recommended in osteoarthritis guidelines.

When to refer for surgery

Patients with persistent symptoms and participation restriction that are refractory to conservative management and which impact significantly on their quality of life should be referred for consideration of surgical intervention. Patient-specific factors such as age, smoking, obesity and other comorbidity should not be barriers to referral, and it is best to refer before the patient has progressed to a state of severe pain and functional limitation, in part because this reduces the likelihood of a successful surgical outcome. BJHM

KEY POINTS

- Osteoarthritis often co-exists with other comorbid conditions, and good history and musculoskeletal examination skills and a holistic patient assessment are essential to diagnose osteoarthritis and optimize management.
- National Institute for Health and Clinical Excellence guidelines recommend that non-pharmacological management (education, exercise, weight loss if obese) should be offered to all osteoarthritis patients.
- Osteoarthritis patients should be given a thorough assessment from an interested practitioner with reinforcement of positive messages and follow-up care to determine outcome.
- Topical non-steroidal anti-inflammatory drugs are safe and effective pharmacological management, but oral non-steroidal anti-inflammatory drugs have significant toxicity and evidence suggests paracetamol also has gastrointestinal toxicity.
- The National Institute for Health and Clinical Excellence recommends corticosteroid injection as an adjunct to core treatment for the relief of moderate to severe pain in osteoarthritis patients. Corticosteroid injections are safe, simple to administer and effective.

Conflict of interest: none.

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