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Arthritis disease

The use of complementary therapies

Background

While effective drugs are available to deal with the symptoms and modify the progress of osteoarthritis and rheumatoid arthritis, these may cause serious adverse events and not all patients will obtain relief. Many people with these diseases use complementary medicines.

Objective

This article presents an overview of the evidence for the most promising complementary therapies for osteoarthritis and rheumatoid arthritis, with other information that general practitioners need to know.

Discussion

There is reasonable evidence to support the use of glucosamine, avocado/soybean unsaponifiables and chondroitin in osteoarthritis, and omega-3 fatty acids and gammalinolenic acid in rheumatoid arthritis. However, no current evidence does not equate to lack of effectiveness. Rigorous research into the use of complementary medicines in arthritis is evolving and many of the systematic reviews used in preparation of this article are being updated every few years to incorporate new trial evidence as it becomes available.

Keywords: complementary therapies; arthritis/rheumatic diseases; osteoarthritis; rheumatoid arthritis; musculoskeletal diseases; pain, therapy; pain, chronic disease

CPD

Osteoarthritis (OA) and rheumatoid arthritis (RA) are common causes of morbidity in Australia. In a South Australian Health Omnibus survey, 26% of participants aged 18 years and over reported having doctor-diagnosed arthritis; of these, two-thirds reported health related quality of life below that of Australian population norms.[1]

While Western medicine offers effective treatments for arthritis, both symptom and disease modifying, these drugs can have serious adverse events. For example, nonsteroidal anti-inflammatory drugs (NSAIDs) can cause gastrointestinal bleeding or perforation (one in 50–100 patient years)[2] and disease modifying drugs used in RA may cause severe anaemia and even death.[3] In addition, these drugs may not achieve good control of arthritis symptoms for all patients.

Therefore, it is understandable that patients with arthritis often turn to complementary medicines (CM): approximately 40% of Australians with OA use CM.[4] Complementary medicines can be purchased over-the-counter with no professional advice. People mistakenly consider CM to be 'natural' and therefore 'safe', or that they have been 'tested by the government'.[5] However, while generally safer than pharmaceuticals, CM can have side effects and interact with other medicines. In Australia, CM is regulated by the Therapeutic Goods Administration for quality and safety, although not necessarily for efficacy, so quality issues often detected internationally should not be an issue in products purchased in Australia.

A recent study found 260 CM offered for purchase through the internet for arthritis, yet only 41 had been subjected to any clinical testing.[6] Rigorous research into CM effectiveness is relatively recent, and many trials to date are substandard, due to poor methods or little funding: there is no equivalent of 'big pharma' pouring dollars into CM trials in the hope of recouping investment through lucrative patents.

Despite these issues, trial evidence regarding CM use in OA and RA is accumulating.

Osteoarthritis

Nutritional supplements

Several nutritional supplements, namely glucosamine, avocado/soybean unsaponifiables and diacerein, have some evidence for use in OA. They show a slow onset of action over 6–8 weeks, and a carryover of effect for up to 2 months after withdrawal.[7]

Glucosamine is naturally produced in humans and is a substrate used to make articular cartilage. Overall, several systematic reviews

found that glucosamine sulphate in dosages of 1500 mg/day is effective and safe in reducing pain and improving function, in particular, in mild to moderate OA of the knee.[6,8–11]

However, some uncertainty exists, as the size of effect of glucosamine is becoming smaller as more high quality trials are undertaken and incorporated into meta-analyses.[11] One proviso of these systematic reviews is that nearly all positive trials used one European company's glucosamine product, and it is not known whether other preparations are equally effective. The Royal Australian College of General Practitioners (RACGP) *Guidelines for the non-surgical management of hip and knee osteoarthritis* state that the evidence is uncertain, and recommend only that general practitioners may inform patients about its availability and safety.[2]

Glucosamine is well tolerated for at least 3 years and early concerns about its negative impact on glucose control do not appear to be justified by later research. However, there have been Australian reports of interactions with warfarin, usually causing an increase in International Normalised Ratio (INR). In fact, the Adverse Drug Reactions Advisory Committee recommends patients taking warfarin should have their INR assessed within a few days and no later than 2 weeks after commencing or changing the dose of any CM.[12]

Adverse effects include mild gastrointestinal symptoms and skin reactions.[13] Glucosamine is derived from shellfish and should not be taken by people with shellfish allergy. There is a lack of safety data to support its use by pregnant and lactating women, and by children under the age of 2 years.[9]

Glucosamine may work synergistically with chondroitin sulphate, fish oil, vitamin C and manganese, and there does not seem to be other clinically important interactions.[9]

Several reviews, including a Cochrane review, found that avocado/soybean unsaponifiables in dosages around 300 mg/day are superior to placebo in improving function, reducing pain and the use of NSAIDs in patients with OA of the hip and knee. The Cochrane review calls for more trials to confirm these results.[14] Adverse events were few and mainly involved the GIT.[6,11,14,15] In in-vitro studies, avocado/soybean unsaponifiables stimulated collagen synthesis and may promote cartilage repair mechanisms.[15]

Diacerein's active derivative is an anthraquinone found in plants of the generus Cassia and has moderate anti-inflammatory and analgesic activity and weak laxative effects.[16] Two meta-analyses of the trials to date found that diacerein (2 x 50 mg/day) seems to have a small effect on pain in patients with OA of the hip and knee, although studies with follow up of more than 6 months show no effect on pain or function. Unfortunately diacerein often (42%) causes diarrhoea.[16,17]

In preliminary studies, vitamin D may possibly have a direct effect on the chondrocytes of osteoarthritic cartilage and vitamin C supplementation may reduce the degree of joint damage. In the Framingham Osteoarthritis cohort, incidence of OA was not associated with low vitamin C or D levels, but progression of OA was significantly related to the lowest levels of vitamin D and limited by vitamin C supplementation.[18] A more recent Dutch prospective cohort study of elderly people found an association between low vitamin D levels and progression of OA of the knee, especially if the baseline bone mineral density was low.[19]

Chondroitin

Chondroitin, usually obtained from bovine trachea or shark cartilage,[10] may be both a symptom modifying and a disease modifying agent in OA. Recent systematic reviews show it is effective and safe to reduce pain in doses of 800–1200 mg/day; however, no benefit is found if only the highest quality trials are reviewed.[6,10,11] Four company sponsored trials found benefit in reducing cartilage loss.[11] Adverse events are similar to those of placebo in trials.[13]

Herbal medicines

A plethora of herbs have a history of use in OA. While the possible mechanisms of action for some herbs in OA have been discovered, such as for green tea, turmeric and ginger,[20] overall more research is needed, and at present no herbal medicines have clear evidence to support their use in OA.[14,21] Herbal products are widely used, so their excellent safety record is reassuring, as most herbs tested for OA have no, minor or rare severe adverse effects.[15,21] Details of rare severe adverse effects are beyond the scope of this article but may be found in the reference list. However, the benefit-harm ratio of the herbs mentioned here is clearly better than that for NSAIDs.[21]

No meta-analyses of herbal medicines for OA were found due to variations in doses used, assessment methods and observation periods in the studies. A Cochrane review found only single trials with positive results for a willow bark preparation and topical capsaicin;[14] the RACGP guidelines report weak evidence to support GP recommendation for topical capsaicin in the short term of hip and knee OA.[2] Other systematic reviews found, in addition to these two herbs, limited evidence for Articulin-F (an Ayuvedic herbomineral formulation of *Withrania somnifera*, *Boswellia serrata*, tumeric and zinc), cat's claw, celadrin, devil's claw, Duhuo Jisheng Wan, ginger, Phytodolor, SAM-e, stinging nettle, white willow and wobenzyme.[6,14,15,22]

Rheumatoid arthritis

Rheumatoid arthritis is a chronic painful disabling condition that affects about 1% of people worldwide and may have a significant impact on quality of life. One estimate of the cost of RA in Australia in 2004 was $400 million.[3] Rheumatoid arthritis is an inflammatory disease and many of the CM used have been shown to have anti-inflammatory mechanisms of action.[23]

The RACGP *Guidelines for management of early rheumatoid arthritis* recommend that GPs should recommend omega-3 supplementation as an adjunct for management of pain and stiffness in patients with RA, as there is excellent evidence to support use of up to 12 g omega-3 daily.[3] While there are theoretical concerns that fish oils may cause bleeding, a 2010 review in *Australian Prescriber* found only three case reports to support this. For safety, it is recommended to monitor patients using fish oils and warfarin concurrently, and consider ceasing fish oils 4–7 days

before elective surgery or during an acute bleeding event.[24]

The guidelines also recommend that GPs might recommend gammalinolenic acid for potential relief of pain, morning stiffness and joint tenderness in RA patients.[3] Three systematic reviews pooled trials of plant derived gammalinolenic acid from seed oils from evening primrose, blackcurrant and borage.[22,25,26] At higher doses of between 1400–2800 mg there were significant improvements in pain, duration of morning stiffness and joint tenderness in patients with RA.

Fatty acid interventions may also provide supplementary or alternative treatment to NSAIDs and enable a lower dose to be used for some patients.

Oral *Tripterygium wilfordii* Hook F extract was also found to have evidence of effectiveness in RA. One serious adverse event, fever and aplastic anaemia, was reported in one trial, and frequent reports of other adverse events, including headache, diarrhoea and hair loss, may limit its usefulness.[25]

Currently there is no evidence to support the use of other herbs in the treatment of RA.[25,26]

The literature regarding vitamin D and RA seems limited to advice to monitor its levels due to the risk of falls and osteoporosis.[27] As vitamin D has been shown in experiments to play a role in immunopathogenesis of, and low doses are associated with, other autoimmune diseases, it is reasonable to supplement low blood levels.[28]

Conclusion

There is reasonable evidence to support use of glucosamine, avocado/soybean unsaponifiables and chondroitin in OA and omega-3 fatty acids and gammalinolenic acid in RA. However, lack of current evidence does not equate to lack of effectiveness. Rigorous research into CM use in arthritis is evolving and many of the systematic reviews used in preparation of this article are being updated every few years to incorporate new trial evidence as it becomes available.

General practitioners should enquire about and record any CM that their patients with OA/RA may be using. While generally safe, many CM can cause minor side effects, interactions with other medicines, or occasionally more severe adverse events. Many unbiased and reliable websites now exist to access more information about specific CM, such as the United Kingdom National Health Service (www.evidence.nhs.uk) or the United States of America National Institute of Health (http://nccam.nih.gov/health/herbsataglance.htm).

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