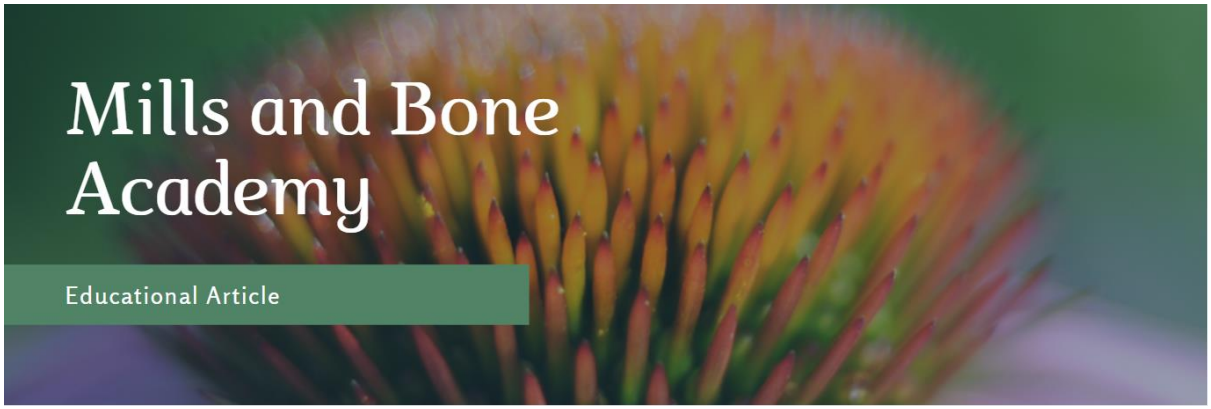

Herbal Alternatives to NSAIDs– Kerry Bone

The NSAID Crisis

NSAIDs (nonsteroidal anti-inflammatory drugs) are the mainstay of the conventional treatment for osteoarthritis and other inflammatory conditions. These drugs act by inhibiting the enzyme cyclo-oxygenase (COX) which produces pro-inflammatory prostaglandins. Because this activity often results in the undesirable side effects of gastric erosion and increased bleeding tendency, sometimes leading to death by gastrointestinal haemorrhage, a more selective class of COX inhibitors were developed. The goal with these selective COX-2 inhibitors was that the anti-inflammatory activity would be preserved, but the undesirable side effects would be minimised.

The risk of serious side effects from NSAIDs was indeed the main factor behind the development of selective COX-2 inhibitors. In fact, the safety statistics for the use of conventional non-selective NSAIDs is alarming. The landmark and often quoted study was published in the conservative *New England Journal of Medicine* in 1999.[i] In this study it was estimated that the number of hospitalisations in the United States for serious gastrointestinal complications was at least 103,000 patients per year. It was also estimated in the same study that 16,500 NSAID-related deaths occurred every year in the United States. This figure was similar to the number of deaths per year from AIDS.

Later studies have suggested that the real numbers are possibly lower, but the mortality rates remain unacceptably high. A recent editorial in the *American Journal of Gastroenterology* suggested the lower end of the estimated US mortality from gastrointestinal side effects of NSAIDs was 3200 deaths per year.[ii] Realistic estimates from the UK suggest that about 1000 patients per annum die from the gastrointestinal effects of NSAIDs or aspirin (including low-dose aspirin) in that country, implying 100,000 worldwide die every year.[iii] To put this in perspective, if naturopathic practice caused just one small fraction of these deaths, it is likely that there would be no naturopaths allowed to practise in Australia.

Not surprisingly physicians, especially rheumatologists and gastroenterologists, breathed a sigh of relief when the selective COX inhibitors were released on the market. Yes they were expensive, but they were seen as lifesavers. Unfortunately this euphoria was short-lived. In 2004 rofecoxib (Vioxx) was withdrawn from the US and Australian

markets, shortly followed by valdecoxib (Bextra) in 2005. This was because both drugs were linked to unacceptably high risks of heart attacks and strokes. But we now know that this problem is not just confined to selective NSAIDs.

Some of the most commonly used nonselective NSAIDs (excluding aspirin) are in fact more likely to cause heart attacks than rofecoxib.[iv] A case-control study of more than 9000 people aged 25 to 100 who had suffered their first ever heart attack was published last year in the prestigious *British Medical Journal* (BMJ). After adjusting for all confounding variables, a significantly increased risk of heart attack was observed for diclofenac (55% increase), ibuprofen (24% increase), rofecoxib (32% increase) and naproxen (27% increase). Also for other nonselective NSAIDs (viewed as a whole) there was a significant 21% higher risk of heart attack. The authors concluded that their study suggested that enough concerns might exist to warrant a reconsideration of the cardiovascular safety of all NSAIDs.

NSAIDs have also taken a hammering concerning their clinical efficacy. A recent meta-analysis and systematic review of 23 clinical trials including more than 10,000 patients found that NSAIDs as a whole (including selective COX-2 inhibitors) were ineffective for long-term pain relief in osteoarthritis of the knee.[v] The authors of this BMJ study concluded that while NSAIDs can reduce short-term pain in osteoarthritis of the knee slightly better than placebo, the long-term use of NSAIDs for this condition is not supported on the current evidence. They added that as serious adverse events are associated with NSAIDs, only their limited use can be recommended.

Clearly the message from all the research is that NSAIDs should not be the first option for the treatment of arthritic pain. Unfortunately, they still are in many cases. If you can advise your patients about the use of alternatives to NSAIDs, you could be saving their lives (especially if they are over 60).

Herbal Alternatives

There are a number of credible herbal alternatives to NSAIDs that are supported by clinical research. Two important treatment options are willow bark (*Salix species*) and Boswellia (*Boswellia serrata*). The clinical efficacy of willow bark in pain management has already been demonstrated in several randomised controlled clinical trials.[vi] For example, in a randomised, double-blind, parallel group trial, the therapeutic efficacy and tolerance of standardised willow bark extract was compared with diclofenac sodium (a conventional NSAID) on patients with knee or hip arthritis.[vii] From the 79 patients enrolled, 59 completed the study. The patients were allocated randomly to one of three groups, receiving either 150 mg/day of diclofenac sodium or willow bark extract in two different doses (corresponding to 90 or 180 mg/day salicin, respectively). During the study period lasting over 3 weeks, no additional analgesic NSAID medication was allowed. The results indicated a good tolerance of the willow bark extract and demonstrated, statistically supported, its therapeutically relevant analgesic activity. In terms of pain intensity an effect comparable to diclofenac sodium was demonstrated. The willow bark extract used in all the clinical studies is standardised to contain 45 or 60 mg of salicin per tablet. It is important to note that only preparations and doses of willow bark capable of providing this activity will be

likely to reproduce the impressive results of these trials.

Boswellia or Indian frankincense is a herb that has been used for thousands of years in the Ayurvedic medical system. An extract of *Boswellia serrata* standardised to 40% boswellic acids yielded dramatic results in the treatment of osteoarthritis.[viii] A randomised, double blind, placebo-controlled, crossover study was conducted to assess the efficacy, safety and tolerability of Boswellia extract in 30 patients with osteoarthritis of the knee, 15 each receiving active treatment or placebo for 8 weeks. After the first intervention, washout was given and then the groups were crossed over to receive the opposite intervention for 8 weeks. All patients receiving herbal treatment reported a significant decrease in knee pain, increased knee flexion and increased walking distance. The frequency of swelling in the knee joint was substantially decreased, but radiologically there was no change. The dose used was 1000 mg of extract per day containing 400 mg of boswellic acids. Boswellia was well tolerated by the patients, except for minor gastrointestinal adverse reactions. What is striking about the trial is the substantial clinical benefit observed. Results were highly statistically significant ($p<0.001$) and changes in the treatment parameters were quite large. For example, in the first 8 week treatment period before crossover, the pain index in the Boswellia group fell from 2.7± 0.45 to 0.26 ± 0.45, the loss of movement index was reduced from 2.8 ± 0.41 to 0.30 ± 0.48 and the swelling index went from 1.1 ± 0.91 to zero.

Conclusions

There are also many other effective herbs that are used in the management of arthritic inflammation and pain. These include turmeric, ginger, celery seed, devil's claw, cat's claw and stinging nettle leaf. However, high dose therapy with willow bark and/or Boswellia is the frontline alternative to NSAIDs.

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