Research Review Speaker Series™

Pain Management in Osteoarthritis and Rheumatoid Arthritis

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Dr Petrie is a Consultant Rheumatologist at the Queen Elizabeth Hospital in Rotorua. He has more than 20 years clinical experience in the diagnosis and management of rheumatological conditions and other disorders impacting on the musculoskeletal system, such as chronic pain and neurological disability. His career has included positions in Cambridge, England as the Arthritis and Rheumatism Council (UK) Dorothy Eden Fellow, and as Consultant Physician in Peterborough England, and Waikato Hospital. Dr Petrie is actively involved in undergraduate medical training for the University of Auckland and in postgraduate medical training for the Royal Australasian College of Physicians Advanced Training Programme.

This publication is a summary of Dr John Petrie's presentation to general practitioners on 14 March, 2012 in Christchurch. The presentation focused on the impact of chronic pain for the individual and the role of patient self-management and specific pharmaceutical agents in assisting patients with osteoarthritis and rheumatoid arthritis to manage their pain and to maintain a healthy and active lifestyle.

Chronic pain is common and disabling

The impact of chronic pain on a person's life is significant. For doctors, pain is a symptom to aid diagnosis and to monitor treatment success. In Dr Petrie's view, chronic pain sometimes engenders a sense of 'failure' in doctors. For the patient, pain is both a physical and emotional experience.

International Association for the Study of Pain definition

*Pain is an unpleasant sensory **and** emotional experience arising from actual or potential tissue damage or described in terms of such damage*

Chronic pain is very prevalent in industrialised countries worldwide. Data from Australia and the UK suggest chronic pain affects between 19 -47% of the adult population[1,2] and that it is of moderate to severe intensity for the majority of patients. Most chronic pain is musculoskeletal, with arthritis a leading cause.[2]

Chronic pain: impact on activities of daily living

Areas of daily life affected:

- Participating in hobbies or activities
- General enjoyment of life
- Ability to perform their job
- Ability to care for children/family
- Ability to walk
- Ability to get up from a sitting position
- Ability to cope
- Socialising with friends and family

67% of respondents indicated that their daily lives had been affected by their chronic pain.[3]

Talking about iatrogenic pain in the context of osteoarthritis, Dr Petrie stressed that it is important that doctors do not inadvertently contribute to a patient's pain and disability. This can happen when a patient misinterprets 'degeneration of the joint due to wear and tear' as a cue to 'preserve' the joint through limiting physical activity. Similarly, advice to use pain relief as needed, can lead to a patient rationing use and pain further limiting activity. Rather than being a condition of 'wear and tear', Dr Petrie stated that in the last decade it has been recognised that osteoarthritis begins as an inflammatory condition and that radiological changes associated with osteoarthritis are late changes. The condition may be precipitated by injury but is initially an inflammatory process followed by an aggressive repair process, better characterised as 'flare, tear, and repair'.

Persistent pain leads to neural changes

Key aspects of chronic pain, are the development of hyperalgesia, a heightened sense of pain in response to noxious stimuli and allodynia, where pain can result from normally painless stimuli, such as touch or vibration (see Figure 1). These are a result of healing with plasticity, with persisting pain which leads to changes within the dorsal horn, the thalamus and the cerebral cortex resulting in increased neural sensitivity.[4]

Hyperalgesia and allodynia are features seen in the chronic pain of osteoarthritis and rheumatoid arthritis. In Dr Petrie's experience most patients tend to present with at least an element of central or neuropathic pain as well as peripheral (nociceptive) pain. Neuropathic pain gives rise to patient descriptions of burning, lancinating and electric shock-like pain, whereas nociceptive pain is described as tenderness or stiffness and achiness. Dr Petrie commented that reporting of neuropathic pain symptoms can sometimes lead to diagnostic confusion if the role of central neural plasticity in chronic pain is not appreciated.

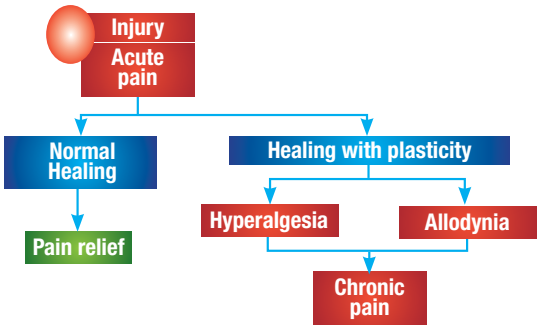


Figure 1: Chronic pain and plasticity

Non-pharmacological interventions

Effective self-management

This is best achieved by an interdisciplinary approach, as undertaken by Dr Petrie and his colleagues at Queen Elizabeth Hospital. It involves the use of cognitive behavioural strategies, relaxation training and arthritis education, using small group sessions with the same trained leaders.[5] This is a process of giving the patient knowledge and skills and changing their beliefs, the aim being to get them back to regular physical activity and to improve their health and quality of life.

Barriers to self-management that have been identified in the literature include:

- Negative beliefs concerning pain and damage
- Fear of progressive structural damage
- Pain-related distress, depression and anxiety
- Social factors, such as lack of external motivation or encouragement.

Dr Petrie reiterated that a key barrier for patients is the negative belief that if they reduce use of their joints through limiting physical activity, they are reducing the 'wear and tear' and therefore increasing the life of the joint. The reality is very different, and as illustrated in Figure 2 the impact of pain and lack of movement can compound rather than reduce the problem.

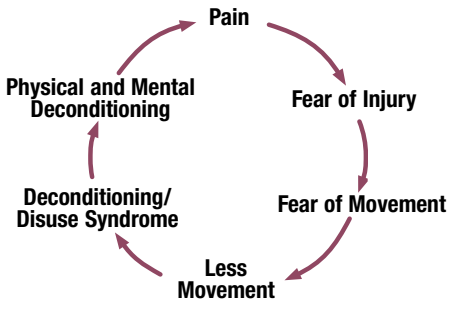


Figure 2: Fear factor: the interaction of pain and inactivity

Dr Petrie highlighted that the value of exercise for patients with osteoarthritis in terms of increased physical function and reduced pain is supported by Cochrane Review findings.[6,7] These and other studies including one showing a positive cartilage response to exercise, allow confidence in advising patients that active exercise is beneficial.

Dr Petrie also cited a large cohort study from Scandinavia which counters the often-held patient view that joint replacement surgery is inevitable. Follow-up of 2953 patients undergoing colon radiography found that of those identified with radiographic osteoarthritis of the hip more than 80% had not had a total hip joint replacement 11-28 years later.[8]

Other complementary interventions

A number of other complementary interventions can have a role for individual patients with arthritis including:

- Footwear and orthoses
- Knee braces (e.g., neoprene brace)
- Walking sticks
- Local heat application
- Massage

Therapeutic needling (acupuncture) is also found by some patients to be helpful.

In Dr Petrie's experience, knee braces are most often of benefit for those with early osteoarthritis, and a period of physiotherapy is essential to optimise use of a walking stick. This latter intervention includes ensuring best length and hand fit, as well as appropriate technique and though a modest intervention may result in both an increase in activity and in functional independence. Queen Elizabeth Hospital has spa facilities (balneotherapy) and these are often used by patients in preparation for physiotherapy sessions. Other aspects of the interdisciplinary rehabilitation include occupational therapy, psychology, and specialty clinics.

Pharmacological treatment

Identification and early management of rheumatoid arthritis

Dr Petrie briefly reviewed the new American College of Rheumatology/ European League Against Rheumatism (ACR/EULAR) classification criteria for rheumatoid arthritis and EULAR recommendations for initial management of this patient group.

Patients who should be tested for rheumatoid arthritis include those with at least one joint with definite clinical synovitis, where the synovitis is not better explained by another disease. A score-based algorithm: add score of categories A–D; a total score of ≥6 confers a definite diagnosis of rheumatoid arthritis.[9]

ACR/EULAR Classification criteria for rheumatoid arthritis[9]

Table 1. Four categories assessed	Score
Joint involvement Large, small, 1-10 or more	0-5
Serology Rheumatoid factor, anti-citrullinated peptide antibodies	0-3
Acute phase proteins C reactive protein/erythrocyte sedimentation rate normal/abnormal	0-1
Duration of symptoms <6 weeks/ ≥6 weeks	0-1

Definite diagnosis = score of 6 or greater out of a possible 10.

Table 2. Joint involvement	Score
1 large joint	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
Greater than 10 joints (at least 1 small joint)	5

Initial management recommended by ACR/EULAR[10] for rheumatoid arthritis:

- A combination of methotrexate and low dose glucocorticoids (prednisone) as soon as the diagnosis is made
- The target is remission or low disease activity
- Use leflunomide, sulfasalazine or gold injections if methotrexate is contraindicated
- Initiate a TNF inhibitor if disease-modifying antirheumatic drug (DMARD)/glucocorticoid is ineffective
- Change to another 'biological' if TNF inhibitor is ineffective.

Opioids – are they being used inappropriately for chronic arthritic pain?

The use of opioids for arthritic pain appears to be increasing. However, Dr Petrie expressed some concern at this trend which is not supported by a strong evidence base. The comprehensive literature review recently published in *Pain Physician*[11] documents this and suggests that long-term opioid therapy should be provided with great restraint and caution for those with chronic non-cancer pain.

Dr Petrie highlighted the many known adverse effects seen with opioid use, including recent data on the increased risk of fractures in older adults with arthritis taking opioids[12] and the problems of opioid tolerance and hyperalgesia.

Adverse effects of opioids include:

- **Neuropsychiatric**
  Sedation, mental clouding, euphoria, sleep disorder, hyperalgesia
- **Cardiopulmonary**
  Respiratory depression, bronchoconstriction (high doses), orthostatic hypotension, bradycardia (high doses)
- **Gastrointestinal**
  Nausea, vomiting, constipation, gastrointestinal or biliary spasm
- **Urinary**
  Urinary retention
- **Endocrine**
  Reduced testosterone, menstrual irregularities
- **Allergic or Immunologic**
  Pruritus, immunosuppression

Opioid use can not only lead to the need for higher doses to get the same effect (tolerance) but can also lower the pain threshold (hyperalgesia).

For the patient, tolerance and hyperalgesia can mean that:

- Pain may persist or increase with an increased opioid dose
- Pain may increase with a constant opioid dose
- Duration of analgesia may decrease with duration of therapy
- Pain may become increasingly diffuse and less defined in character
- Pain may be worse on opioid treatment than before treatment with opioids.

In summary, Dr Petrie noted that opioids have a poor benefit to risk ratio in patients with chronic, non-malignant pain. Long-term opioid use should be avoided in patients with chronic musculoskeletal pain.

COX-2 inhibitors and other NSAIDs: benefits versus risks

There has been attention to possible risks associated with these agents in recent years and Dr Petrie noted that for the clinician there is always the need to weigh the potential risks of a treatment against the potential gains for the patient.

Dr Petrie reviewed the background to this topic, including the study reported in the New England Medical Journal in 2005 that showed an increase in cardiovascular events for patients at increased risk of colorectal adenomas taking rofecoxib.[13]

Reviewing risks associated with NSAIDs, Dr Petrie presented findings from a Bandolier review of key studies[13,14,15] and highlighted that an often overlooked finding that low dose aspirin use was also associated with an increase in risk of cardiovascular events in a trial looking at preventing colorectal cancer.

Dr Petrie also commented that the risk ratios that have been reported for cardiovascular events in large epidemiological studies undertaken in California[16] and the UK[17] have been in his view relatively low, with risk ratios less than 2 for all agents. The numbers needed to harm (NNH) generated from the UK study for people 65 years and older were as follows: [17]

	Rofecoxib	Ibuprofen	Diclofenac
>65 yrs	695	1005	521

Prof. Singh, lead author of the California study concluded that agents should be selected on the basis of their relative GI and cardiovascular safety profile in any given patient.[16] Dr Petrie made similar conclusions, stating that these studies indicate a small increment in the risk of cardiovascular events with COX-2 selective and other NSAIDs. For the individual patient, Dr Petrie sees the need to weigh this risk against the known cardiovascular risk associated with inactivity and walking disability.

Arthritis and cardiovascular risk

Dr Petrie drew attention to the findings of studies such as that reported by Haara in a representative sample (n=8000) of the Finnish population, which showed an association between osteoarthritis and cardiovascular deaths.[18]

GI advantage of celecoxib

Dr Petrie presented findings of a recent randomised controlled trial: CONDOR – Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis. The trial comparing celecoxib with diclofenac plus omeprazole enrolled a total of 4484 patients. Patient assessment was conducted at 1, 2, 4 and 6 months after first patient evaluation, with further investigation signalled by the presence of haematemesis, melena, a drop in haemoglobin or haematocrit or other significant signs or symptoms. The primary endpoint - presence of clinically significant upper or lower GI events - was adjudicated by an independent committee.

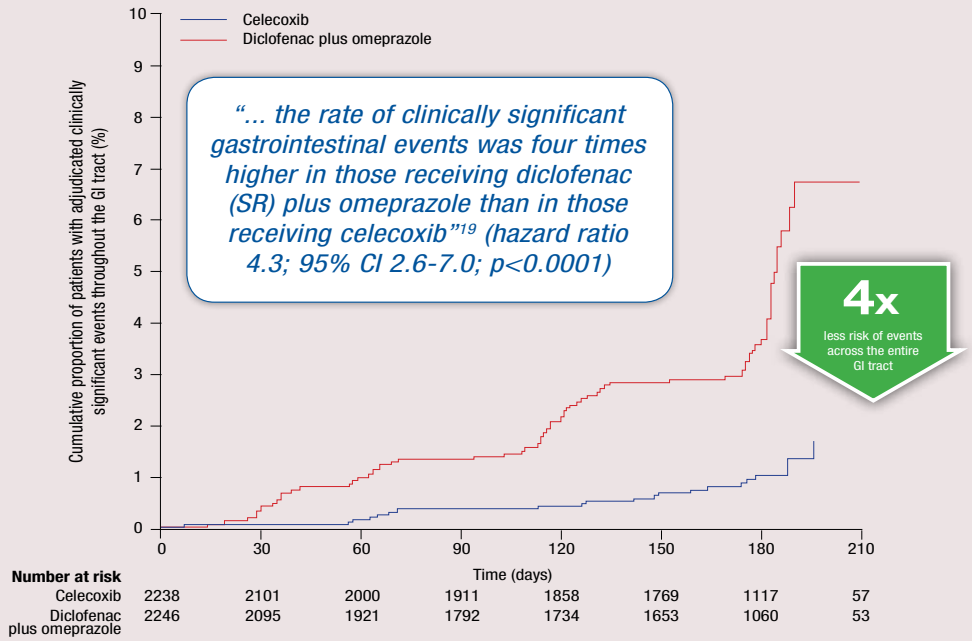
CONDOR trial[19]: New data shows celecoxib better for GI tract

- Conducted in 32 countries at 196 centres
- Study population: patients with osteoarthritis or rheumatoid arthritis expected to require regular NSAID treatment for ≥6 months (patients requiring aspirin were excluded)
- Celecoxib 200 mg bd *or* diclofenac SR 75 mg bd + omeprazole 20 mg OD
- Primary endpoint: a composite of clinically significant upper or lower GI events

Conclusion: The risk of clinical outcomes throughout the GI tract was lower in patients treated with a COX-2-selective NSAID than in those receiving a non-selective NSAID plus a proton pump inhibitor (hazard ratio 4.3; 95% CI 2.6-7.0; p<0.0001).

Significantly less GI events with celecoxib versus diclofenac SR plus omeprazole

Figure 3: CONDOR trial findings



The Queen Elizabeth Hospital Experience

Dr Petrie concluded the presentation by sharing data on patient outcomes at Queen Elizabeth Hospital. The data indicated that almost 40% of patients treated by the service have either osteoarthritis or rheumatoid arthritis, with osteoarthritis accounting for slightly more patients.

In terms of outcomes, 96.9% of patients reported improvement in at least one health outcome and 82.9% reported improvement across a battery of tests, such as the McGill Pain Score and the 6 Minute Walk test. Further analysis on a subgroup of patients, including rheumatology patients, indicated that improved patient outcomes continued for up to 12 months post-discharge.

Take home messages:

- It is important to manage the pain and disability associated with arthritis.
- Inactivity impacts on pain, quality of life and risk for cardiovascular and other diseases.
- Appropriate use of medication can promote mobility and reduce disability.
- Celecoxib has a GI advantage compared to diclofenac + omeprazole.

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