Chronic Pain and Medication

Key Messages:

1. Chronic non-cancer pain research has found:
    a. Opioids (morphine like medications) become less effective over time.
    b. The risk of harm from opioids is higher than previously thought
    c. The long term value and safety of non-opioid pain medications is unclear.
    d. Active self-management skills are more effective than medication in retraining the nervous system and reducing pain.

2. Current treatment recommendations:
    a. In acute pain opioids can mostly be stopped within 1 week. In complex cases, opioids may be continued for up to 90 days.
    b. Opioids should no longer be started for chronic non-cancer pain.
    c. For people already taking long term opioids for chronic non-cancer pain the standard approach is to wean and cease. The time frame can vary from a few weeks up to a year.
    d. Time limited medication is used to help with the change to active self-management

Background

Recommendations for medication use in chronic or persistent pain have changed as a result of scientific research. Chronic pain research shows that the greatest pain reduction comes from using a whole person approach to management and that in many situations it is possible to use medication for a time limited phase and then wean and cease it as active self-management skills come into play.

Types of Medication

Several groups of medication are used to treat pain. These include opioids (morphine like drugs), anti-inflammatory drugs, paracetamol, antidepressants and anticonvulsants.

Opioids: Opioids act at specialised receptors which occur mainly in the brain and spinal cord. These receptors are also the site of action of endorphins, the body's own morphine-like substances. When endorphins are released naturally, for example in response to physical activity, they activate receptors in a balanced way that modifies pain without side effects. When an external drug such as morphine is used the receptor systems are overwhelmed. Pain can be reduced in the short term but at the cost of substantial side effects.

The effectiveness of opioids becomes less over time (tolerance) and pain may even become worse as opioids increase nervous system sensitisation (opioid induced hyperalgesia). Additional side effects include constipation, sedation, clouded thinking,

depression, addiction, sexual dysfunction, other hormonal problems, sleep interference, driving impairment, falls, dental problems and increased risk of death.

Opioid research shows clear evidence of benefit in treating acute and cancer pain but lack of benefit and substantial risk of harm with longer term use to treat chronic non-cancer pain. There is also evidence supporting the use of opioids in palliative care and opioid dependency or addiction. In palliative or 'comfort' care towards the end of life the main focus is on medication use to reduce distress and suffering rather than to improve physical and psychological function. In treating opioid dependency/addiction the focus is on reducing craving for a 'hit' of short acting opioid.

Thus recent research has led to a change in treatment approach and opioids are no longer recommended for chronic non-cancer pain.

Non-steroidal anti-inflammatory drugs (NSAIDs): These drugs work by modifying the inflammatory response which occurs after acute injury. Many chemical mediators are released at the site of injury causing redness, swelling and pain. This is necessary for repair of injured tissues. A group of inflammatory substances called prostaglandins are part of this process. Prostaglandin production is controlled by enzymes called COX-1 and COX-2. Anti-inflammatory drugs act by inhibiting the action of COX-1 and COX-2 and therefore reducing prostaglandin levels. This can reduce pain in the acute setting when there is a component of inflammation involved.

Unfortunately side effects are common and can at times lead to death. The inhibition of COX-1 plays a key role in side effects such as bleeding from the gut and kidney impairment. This is because the prostaglandins controlled by COX-1 are involved in maintaining healthy function of the gut and kidney. The selective COX-2 inhibitors have been developed in recent years in an attempt to reduce side effects. These newer agents have a lower risk of stomach irritation, bleeding from the gut, fluid retention and kidney problems but there are concerns about other complications such as the risk of heart attack.

Short term studies (typically over several weeks) have shown modest benefit from NSAIDs in various chronic pain conditions. Whether any benefit is sustained over the longer term is not known. However the high risk of harm outweighs any potential benefits. The current recommendation is to use NSAIDs in short bursts only except in conditions such as active rheumatoid arthritis where there may be ongoing inflammation.

Paracetamol: Paracetamol, like the anti-inflammatory drugs, reduces acute pain and fever. However, it does not affect COX-1 or COX-2. This explains its lack of inhibition of inflammation at the site of injury and also its lack of gut and kidney side effects. Its precise mechanism of action remains unclear but it does have an effect on reducing prostaglandin levels in pain related pathways of the brain and spinal cord. Although

paracetamol is safer than the anti-inflammatory group at usual doses, it is toxic to the liver in overdose. There is clear evidence of benefit from paracetamol in acute and cancer pain but not with sustained use in chronic non-cancer pain.

Antidepressants: Antidepressant drugs act by altering the levels of specific chemicals in the brain such as noradrenalin and serotonin. This can be helpful for mood and also for nerve injury (neuropathic) pain. While both noradrenalin and serotonin have an effect on mood, noradrenalin appears to be more important in damping down transmission of pain related messages. When brain levels of noradrenalin and serotonin increase naturally in response to positive life events side effects do not occur. However, like the opioid situation, when external drugs are used side effects common result.

There are a number of antidepressant groups each with different mechanisms of action. Tricyclic antidepressants (TCA) and other combined serotonin and noradrenalin reuptake inhibitors (SNRIs) act by blocking reuptake of both noradrenalin and serotonin once they have been released at their site of action. This increases the effective levels of both substances in the brain. In contrast selective serotonin reuptake inhibitors (SSRIs) act primarily to increase serotonin levels with minimal effect on noradrenalin. Interesting new research shows that antidepressants may also have a role in reducing inflammation in the brain and that this may be another mechanism contributing to pain reduction.

Common TCA side effects include dry mouth, blurry vision, constipation, difficulty passing urine, weight gain and drowsiness. The SSRI's are generally better tolerated but side effects can include nausea, loss of libido, tremor, hyper-arousal and drowsiness.

TCA's and other SNRIs are effective specifically in the treatment of nerve injury (neuropathic) pain. Only short term studies have been undertaken in chronic pain and therefore the long term benefit is unclear. SSRI's are generally effective in treating depressed mood but of less help in reducing pain.

Anticonvulsants: Anticonvulsants are a family of drugs that reduce excessive electrical activity in the brain and thereby stop seizures or epilepsy. Neuropathic pain also involves increased electrical activity. Therefore some of the drugs used to treat epilepsy can also be effective in neuropathic pain.

Anticonvulsants act by a number of different mechanisms. They can block the sodium or calcium channels in nerves that are part of the electrical transmission system. Some agents increase brain levels of inhibitory messengers such as GABA. Other mechanisms are yet to be completely understood.

Side effects are common and include sedation, loss of balance and weight gain. Some anticonvulsants can irritate the liver. Drug interactions can be a problem when combining anticonvulsants with other drugs. As with antidepressants only short term

studies have been undertaken in chronic pain and therefore the long term benefit is unclear.

Additional medication warnings

Marijuana: There have been many research trials investigating marijuana use in treating pain. These studies have shown a consistent lack of significant benefit. In addition side effects are common including dependency and demotivation. Even short term use can cause schizophrenia in vulnerable individuals. Prolonged use can cause serious brain toxicity. Marijuana is not recommended for treatment of pain.

Benzodiazepines: This group of drugs includes diazepam (Valium) and alprazolam (Xanax). Benzodiazepines can be useful for muscle relaxation in the first few days after acute injury if muscle spasm is involved. Beyond that time frame they are harmful. Benzodiazepines commonly cause dependency and often lead to depression and sleep interference (staying at lighter levels of non-refreshing sleep). When combined with opioids, the sleep problems worsen and the risk of sleep apnoea (stopping breathing during sleep) increases. With the combination of benzodiazepines and opioids driving is consistently impaired and the risk of death increases. If benzodiazepines are used at all in treating pain they should be stopped after several days.

Reference:
Reconsidering opioid therapy. Hunter Integrated Pain Service. Accessed 24/02/2014
http://www.hnehealth.nsw.gov.au/__data/assets/pdf_file/0007/76039/Reconsidering_opioid_therapy_Jan_2014.pdf