Update on OXYCODONE what can primary care do about the problem?
Approximately 70% of people dispensed oxycodone in New Zealand are initiated on this medicine outside of general practice, i.e. by a doctor in secondary care. This supports the claim that much of the use of oxycodone is driven by secondary care prescribing. However, 30% of all prescriptions for oxycodone are initiated by a General Practitioner. In addition 17% of patients initiated on oxycodone in secondary care have their prescriptions continued by a General Practitioner. Oxycodone is a strong opioid indicated for the treatment of moderate to severe pain, when morphine is not tolerated, and all other options have been considered. Clinicians are urged to assess whether oxycodone is appropriate whenever initiating or continuing a prescription for this medicine.

**Why is oxycodone a problem?**

Oxycodone is not a new medicine. It was first synthesised in 1916 in Germany and became available for clinical use in the United States by 1939. For many years it has been used overseas as a component in combination short-acting analgesics. A controlled release formulation of oxycodone alone was released in the United States in 1996 and was in New Zealand by 2005. Since then, use of this medicine has increased dramatically and many countries are now dealing with issues of misuse, addiction and illegal diversion of prescriptions.

In New Zealand, the use of oxycodone has increased by 249% over the last five years (Figure 2). This has not been accompanied by a corresponding decrease in prescriptions for morphine, and the total amount of strong opioids dispensed is climbing rapidly.

This raises several questions:

- Which patients are being prescribed oxycodone? And by whom?
- Has the marketing of oxycodone been so effective that a whole new group of patients now “require” strong opioids?
- Is oxycodone being inappropriately prescribed instead of analgesics that are lower on the WHO pain ladder? If so, why?

We encourage every clinician to look critically at their prescribing of oxycodone and, if necessary, make changes on how they prescribe this medicine.
Oxycodone misuse in New Zealand

The Illicit Drug Monitoring System (IDMS) provides surveillance on the misuse of drugs in New Zealand. Oxycodone was first noted as an emerging drug of misuse by the IDMS in 2008. The latest report (to the end of 2010) shows that oxycodone is continuing to feature prominently amongst people who misuse drugs. Oxycodone was the second most common new drug to be used in 2010 by methamphetamine users, behind synthetic cannabis (which is now unavailable for commercial sale). In 2010, 18% of injecting drug users had illicitly used oxycodone in the past six months, compared to 9% in 2008. Pharmaceutical morphine remains one of the principal opioids used by injecting drug users in New Zealand (along with “homebake” heroin/morphine and methadone). The available supply of diverted opioids is directly related to the total amount of opioids prescribed.

Although other controlled release opioids can also be tampered with, the controlled release form of oxycodone (OxyContin), is rapidly gaining popularity as a drug of misuse. There has been criticism that the information warning patients not to break, chew or crush the tablets to avoid rapid release and absorption of a potentially harmful dose of oxycodone, may have actually instructed people in how to misuse the medicine. In response to this problem in the United States and Canada, the controlled release formulation has been replaced by a newer extended release formulation (OxyNeo) aimed to be tamper-resistant. In Canada from 2013, a special application will be required for patients to access oxycodone, unless they are being treated for cancer pain or palliative care. No changes to prescribing regulations or medicine formulation have been announced for New Zealand or Australia.

What is the appropriate indication for oxycodone?

There is no dispute that oxycodone is an effective analgesic, however, prescribing figures suggest that it is being chosen as the first-line opioid in many situations when it should not be.

Morphine is the preferred first-line option for the treatment of acute and chronic moderate to severe pain, when a strong opioid is indicated. When compared to morphine, oxycodone:

- Has no better analgesic efficacy
- Has a similar adverse effect profile
- May have more addictive potential
- Is significantly more expensive

Oxycodone should only be prescribed for the treatment of moderate to severe pain in patients who are intolerant to morphine and when a strong opioid is the best option. Although oxycodone has been reported to be potentially safer than morphine in patients with renal impairment, active metabolites can still accumulate. Fentanyl or methadone are likely to be safer in patients with renal impairment, who require a strong opioid, because they have no clinically significant active metabolites. Discussion with a pain or renal physician is recommended when considering the use of any strong opioid in a patient with severe renal impairment (creatinine clearance < 30 mL/min).

For further information see:
“Fentanyl patches to be available without Special Authority in 2011”, BPJ 33 (Dec, 2010).
“Methadone – safe and effective use for chronic pain”, BPJ 18 (Dec, 2008).

What can General Practitioners do to reduce oxycodone use?

Data from the Pharmaceutical Warehouse show that 30% of prescriptions for oxycodone are initiated within general practice (Figure 1). When considering initiation of oxycodone, always ask yourself if you would use morphine for this patient. If the answer is no then do not prescribe oxycodone. Oxycodone should not be prescribed when a weaker opioid, e.g. codeine, dihydrocodeine or tramadol, would be more appropriate.

Remember that: 5 mg oxycodone is approximately equivalent to 10 mg morphine, 50 – 100 mg tramadol, 100 mg dihydrocodeine or 100 mg codeine.
Best Practice Tip: Make it a practice policy, whenever prescribing a strong opioid, to record why the patient has been prescribed this medicine, the usual dose, the expected time frame for treatment, any concerns regarding the patient (such as low mood, poor social support) and specific instructions regarding actions if an increased dose is requested, an early prescription is sought, or if medicines are reported as lost.

Patients on oxycodone initiated in secondary care
Approximately 70% of oxycodone is initiated within secondary care. Prescribing data show that when oxycodone is initiated from outside general practice, 17% of patients have their prescription continued by a General Practitioner (Figure 1).

Knowledge of a patient’s clinical and medicines history and psychosocial background puts General Practitioners in a strong position to not simply “go with the flow”, but instead re-evaluate the indication for oxycodone, even if it has been initiated within secondary care.

Summary: management strategies for patients discharged on oxycodone
When a patient is discharged from secondary care on oxycodone, a suggested management strategy is as follows:

- When the patient presents for a renewal of a prescription of oxycodone, assess their level of pain and consider whether a strong opioid is still required.
- If a strong opioid is no longer required, step down to a weaker opioid or to paracetamol. Depending on the length of time the patient has been on oxycodone, a gradual tapering of the dose may be necessary.
- If a strong opioid is still required, consider changing the patient to morphine. Explain to the patient that morphine is equally effective, will not usually result in any other adverse effects and that it is the preferred option when strong opioids are used in general practice. Regularly reassess the patient and step-down treatment as appropriate.

Make sure the patient knows that oxycodone is a strong opioid
Many patients are unaware (and shocked to be told) that oxycodone is a strong opioid similar to morphine, but milligram for milligram, twice as potent. Both patients and clinicians have been known to mistakenly associate oxycodone with the weak opioid codeine, rather than with morphine, because of the similarity in the names of the medicines.

Reassess why oxycodone was initially prescribed
Establish the precise clinical problem for which oxycodone was initially prescribed, e.g. post-surgical pain or an acute injury. Does this same problem exist now? Most patients can gradually reduce analgesia in the days to weeks after surgery or acute injury.

What level of pain is the patient experiencing?
If there is an ongoing medical condition that requires analgesia, check that the level of pain being experienced warrants the use of a strong opioid.

Consider if oxycodone can be stopped
If the pain has reduced and oxycodone is no longer required, stop or taper the dose (Page 12). Weaker analgesia, such as codeine and paracetamol, may still be required. Tramadol and dihydrocodeine can also be used as alternatives. Check the patient’s understanding of any analgesic medicines that are used - are they being taken at the right time and in the right dose to gain effective pain relief and to minimise adverse effects?

Consider switching the patient to morphine
If a strong opioid analgesic is still indicated, consider switching the patient to morphine. Morphine should be the strong opioid of choice for the majority of patients unless they are allergic to morphine or intolerant to its adverse effects. A dose of 5 mg of controlled release oxycodone is approximately equivalent to 10 mg of long-acting morphine. This conversion rate is, however, only approximate and there is varying guidance on the dose of morphine that should be used when switching.9, 10 If the aim is to eventually discontinue opioids and the degree of pain allows, calculate the equivalent dose of morphine and then start the patient on half of this dose.2 The response of the patient to the change in medicine should be reviewed regularly and the dose adjusted as required to prevent any withdrawal symptoms. The “ABC” of opioid pain medicine use should be remembered:

- Anti-emetic prescription if nausea present
- Breakthrough dose of morphine may be required
- Constipation is likely, prescribe a laxative
If an opioid is continued, establish a pattern of regular review
Every patient prescribed a strong opioid analgesic on an ongoing basis requires regular review. The requirement for monthly prescriptions for opioids provides an ideal opportunity to review the need for the medicine, however, in some situations review will need to be more frequent, such as early in the course of treatment. Discuss the dose, the goals of treatment, adverse effects, the time frame for the use of opioid and if appropriate develop a clear plan for stopping the medicine. Check with the patient how they are managing day to day. The Australian and New Zealand College of Anaesthetists recommends a “5A assessment” when prescribing a strong opioid: assess the patient’s analgesia, activity, adverse effects, affect and aberrant drug taking behaviour (see “Detecting aberrant drug-taking behaviour”). Referral to a specialist pain clinic may be required if the patient’s pain is unable to be effectively controlled or if there are other concerns with aspects of the “5A” assessment.

How to discontinue oxycodone
Abrupt cessation
Patients who have been taking oxycodone at low doses (e.g. 10 – 20 mg daily) for less than one to two weeks can generally stop the medicine without experiencing withdrawal symptoms. Gradual tapering of oxycodone to avoid withdrawal symptoms is recommended in most other situations.

Gradual dose reduction
Patients who have been taking oxycodone for more than one to two weeks, or at high doses, should have the dose gradually tapered to avoid symptoms of opioid withdrawal.

How quickly and by how much the oxycodone can be reduced will depend on the current dose, the length of time the medicine has been taken for and individual patient factors, such as anxiety, co-morbidities (e.g. depression or other psychiatric conditions) and the likelihood that the patient is dependent on oxycodone, in which case the dose should be reduced more slowly.

Advice about tapering of opioids varies widely in the literature, however, in general:

- Reduce the dose in 20–25% increments or, if required, more slowly by 5–10%
- Reductions can be made every two or three days
Once the patient has been reduced to one-third of the initial dose, the rate of taper should be slowed.

Consider holding the dose at the same level if the patient develops withdrawal symptoms, an increase in pain or lowered mood.

Most patients can be withdrawn from oxycodone within one month, depending on how high the dose was prior to initiating tapering.

Referral to addiction services
In some situations it may be more appropriate to refer patients to a community based drug and alcohol programme, to withdraw from oxycodone. Patients who may benefit from referral include those who:

- Are unable to be slowly tapered off oxycodone in general practice due to factors such as a lack of success with tapering, non-compliance with tapering, accessing opioids from other sources.

- Are misusing oxycodone or other addictive substances (including alcohol).

Opioid withdrawal symptoms
Abrupt cessation of any strong opioid can produce extremely unpleasant and distressing withdrawal symptoms, depending on the dose and the length of time the medicine has been used for. These symptoms reach a peak approximately three days after the opioid is stopped and may last for approximately 7–10 days. Although opioid withdrawal is very unpleasant for the patient, it is not usually associated with a risk of seizure or delirium, unlike abrupt cessation of such substances as alcohol or benzodiazepines.

Opioid withdrawal symptoms can include insomnia, dysphoria, yawning, rhinorrhoea, piloerection, perspiration, lacrimation, tremors, restlessness, poor sleep, nausea or vomiting, diarrhoea, muscle aches and twitches, abdominal cramps, anxiety and an increase in pain.

If required, medicines that may assist with the treatment of withdrawal symptoms include:

- Clonidine which decreases adrenergic activity and may relieve symptoms such as nausea, sweating, cramps and tachycardia: oral dose 50–75 micrograms up to three times a day, or alternatively a transdermal patch may be used if there are concerns about adherence to oral dose.

- A sedating antihistamine may help if the patient is restless and unable to sleep.
The role of strong opioids for chronic non-cancer pain

The use of strong opioids for chronic non-cancer pain is controversial and there is limited quality evidence to support or oppose their use for this type of pain. Principles for the use of opioid analgesics in people with chronic non-cancer pain have been developed by the Australian and New Zealand College of Anaesthetists. The principles aim to take into account both the widely varying individual response to opioids and the risks for an individual patient. The use of opioids for chronic non-cancer pain should be regarded as an "ongoing individual trial of therapy".

Assess all aspects of the pain
Consider factors that may influence the nature and intensity of pain and the patient's reaction to the pain. Ask about the patient's beliefs about the underlying problem, their mood, their fears and their expectations of pain treatment. Discuss the goals of treatment with the patient – a reduction in pain and an increase in function are realistic and achievable outcomes, while an expectation that the pain will be totally eliminated may be unrealistic.

Pain can be difficult to assess because it is subjective and is often influenced by factors such as mood, stress and the psychosocial support that the patient has. The most clinically useful pain scales include an assessment of the impact of the pain on daily life. Pain can have a significant effect on daily activities, e.g. altering sleep or appetite. It can induce or exacerbate depression and anxiety, it can influence social interactions, prevent work and impair relationships.

For further information about pain scales, see "Pharmacological management of chronic pain", BPJ 16 (Sep, 2008).

Ensure there has been an adequate trial of other treatments
The WHO analgesic ladder provides a step-wise approach to analgesia for the management of pain (Figure 3). Adjuvant treatments such as tricyclic antidepressants and anticonvulsants, can be included at every step of the ladder, especially for patients with neuropathic pain, and it...
is recommended that they are considered before the use of strong opioids, i.e. Step 3. Non-pharmacological treatment of pain is also important. This includes ensuring that the patient understands the underlying problem and the treatment plan, checking on family and social supports, promoting the benefit of healthy lifestyle choices (e.g. exercise, adequate sleep, balanced diet) and the involvement of other health professionals, e.g. physiotherapist, occupational therapist, psychologist, pain clinic specialist.

**Consider if a strong opioid is indicated and appropriate for the patient**

Prior to initiating a strong opioid for chronic pain in particular, consider the following questions:

- Have I identified the cause of the pain?
- What am I trying to achieve?
- Is this what the patient wants?
- To what extent are psychosocial factors contributing to the pain level and how can these factors be addressed?
- Is there evidence that a particular medicine will help this type of pain?
- Are there non-pharmacological alternatives?
- Do the potential benefits outweigh the harms of the treatment? Check if the patient has a history of addictive behaviour, alcohol or medicine misuse. If the patient has a current or past history of a psychological problem, a strong opioid may not be appropriate.
- Have I provided effective education about the most appropriate way to use analgesics?
- Have I considered how long a strong opioid may be required for?
- Have I made a plan for follow up?

**Reach an agreement with the patient regarding a trial of strong opioid analgesic**

If a strong opioid is indicated, ensure the patient has a good understanding of the type of medicine to be used and the goals of treatment, i.e. an increase in function rather than complete resolution of pain. The patient should be made aware of the potential problems with strong opioids, including adverse effects, safety issues and the potential for dependency and misuse. It is also recommended that an agreement is reached so that if the goals are not achieved, adverse effects are intolerable or there are concerns about misuse, the opioid will be discontinued. Any agreement should be clearly documented in the patient notes. This should include guidance about management if the patient requests or presents for an early repeat, if the medicine is reported as lost or there is a request for an increase in dose. When a strong opioid is prescribed, ideally there should be one prescriber and one pharmacy involved.

**Start with an appropriate dose and slowly titrate as required**

Choose a low starting dose of a long-acting or extended release preparation of a strong opioid, usually morphine as the first-line choice. Most patients taking opioids will also require a laxative, and possibly an anti-emetic (in the initial stages of treatment), as well as short-acting medicine for breakthrough pain. It is recommended that the dose be slowly titrated over several weeks if required, with a clinical assessment prior to each increase in dose. The Australian and New Zealand College of Anaesthetists recommends a “5A” assessment which includes a review of:

- Analgesia
- Activity
- Adverse effects
- Affect
- Aberrant behaviour

A suggested time frame for a trial of a strong opioid is four to six weeks. If the treatment has been of no benefit after this time, the dose of the opioid should be tapered and then stopped.

**Regularly review the patient**

Once the patient is established on an effective dose, regularly reassess them using the “5A” assessment. Check that the goals of treatment agreed initially are being achieved and that a strong opioid is still the most appropriate medicine for the patient. If the patient requests an increase in dose consider whether this may reflect:

- A change in the underlying condition producing pain
- The patient’s current mood, life stressors or other social circumstances
- The development of tolerance
- Opioid induced hyperalgesia (abnormal sensitivity to pain due to prolonged use of strong opioids)
- Aberrant drug taking behaviour
Learn from the mistakes of others. You can’t live long enough to make them all yourself.

References


