Chronic nonmalignant pain

The rational use of opioid medication

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Every general practitioner has patients with chronic nonmalignant pain issues. At some point the possibility of using prescribed opioids is raised. General practitioners need to make the decision to initiate opioids cautiously, as a significant number of patients will gain little long term relief from these drugs, and some will exhibit problems resulting from dependence to the prescribed drug. For these reasons, patients and the prescriber should agree to a drug trial before agreement is reached to prescribe for the long term. All prescribing needs to be under strict control, with patients picking up medication from a pharmacy relatively frequently. If the GP feels they have lost control of the situation, urgent advice from a specialist in pain or drug and alcohol medicine should be sought.

Case study

Sally, 28 years of age, is in the fifth year of her university degree. She had used intravenous drugs on and off for several years, but has not used any drugs for 4 years.

Several months ago Sally was involved in a serious motor vehicle accident that almost severed her left arm. The arm was saved with a complex 9 hour operation which included extensive repair of the brachial plexus. The surgeon was optimistic about a good outcome with time. However, 2 months after the operation Sally was troubled by persistent neuropathic pain in the affected arm not responding to nonsteroidal anti-inflammatory drugs (NSAIDs), paracetamol/codeine preparations, or the more complex drugs used for neuropathic pain. There was no doubt that her pain was quite significant and she was not drug seeking as she and her general practitioner faced the decision whether to initiate stronger opioid medication.

Sally was prescribed MS Contin 20 mg twice per day, which initially gave very good pain relief. All appeared to be going well, but after 6 weeks, problems started emerging. There was the occasional lost prescription, attending too early for repeat prescriptions, and presentations to the pharmacist too early to pick up repeat medication. This was tolerated for a short time in view of her severe injuries, but matters continued to deteriorate and it became necessary to put strict containments in place for her medication (three times per week pick up of tablets from the pharmacy). This was initially successful, but opioid control continued to be a problem, and about 3 months after commencement of MS Contin, Sally admitted that she had re-commenced heroin use and was even occasionally crushing and injecting the MS Contin.

Sally was placed on a methadone program, which has been partially successful in that use of heroin has been reduced, however complete cessation of illicit opioids has not been achieved. It might therefore be concluded that the use of prescribed opioids in this case de-stabilised a patient who had been heroin free for 4 years. This patient now regrets starting the prescribed opioid.

What is the role of opioids in chronic pain and what can the general practitioner do to ensure that they are being prescribed appropriately and safely?

The use of oral opioid preparations in Australia has increased steeply over the past 10 years. These drugs are being used for a range of indications including back and other musculoskeletal pain, chronic headaches, and nonspecific pain syndromes. *Figure 1–3* show data from the Australian Capital Territory demonstrating the dramatic increase in prescriptions of long acting opioids. The same trends are seen when looking at national figures.[1] It is difficult to explain such a dramatic increase in the use of these drugs. Marketing by the manufacturers plays a small role, but other logical conclusions could be that:

- chronic nonmalignant pain in the past has been inadequately treated and is now being dealt with in a humane fashion using opioids, or

- the rapidly increasing use of opioids is not warranted by the literature and we may face a mounting burden of problems related to this prescribing pattern. The most worrying possibility is a large number of patients exhibiting prescribed drug dependence.

The use of opioids in chronic nonmalignant pain is a controversial issue. Most authors concur that there are very few studies showing that these drugs are effective for long periods.[2–6] General practitioners are familiar with the concept of 'tolerance'. Patients who consume alcohol regularly appear to be less intoxicated than alcohol naïve individuals and patients on long term methadone programs can take daily doses of methadone far in excess of the normal lethal dose. In some patients, tolerance to the analgesic effect of opioids appears to occur fairly early. It is therefore not uncommon in general practice to have patients on opioids who are dissatisfied with the pain relief they are experiencing. This may lead to dose escalation, whereupon analgesia is again briefly achieved until tolerance inevitably develops to the new dose. This merry-go-round of dose escalations may lead to alarmingly high levels of prescribing.

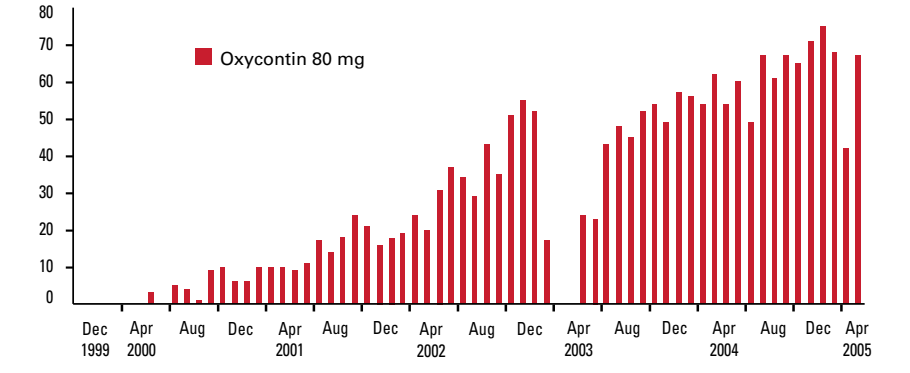

Figure 1. Oxycontin prescriptions in the ACT December 1999 to April 2005
Source: ACT Pharmaceutical Services

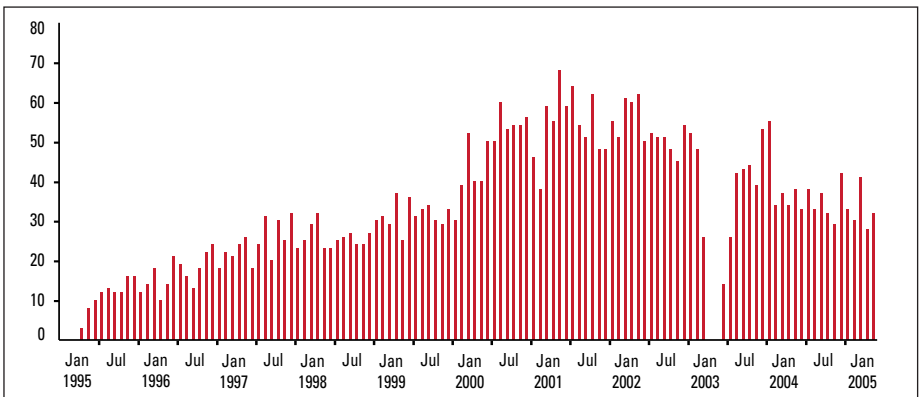

Figure 2. Kapanol prescriptions in the ACT January 1995 to May 2005
Source: ACT Pharmaceutical Services

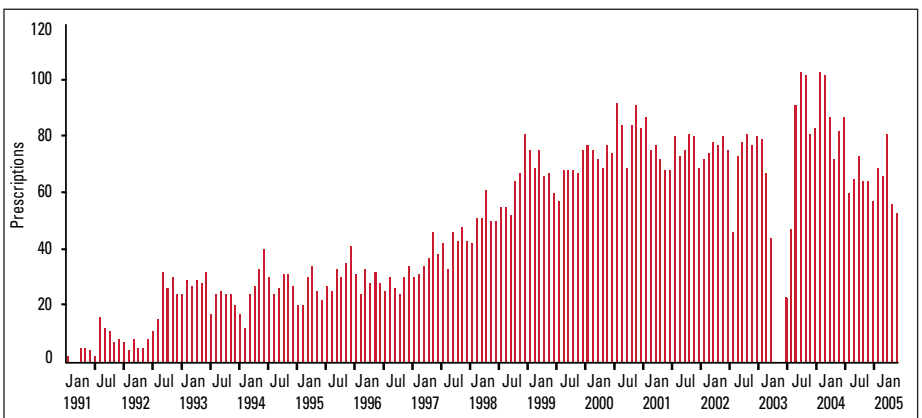

Figure 3. MS Contin prescriptions in the ACT January 1991 to May 2005
Source: ACT Pharmaceutical Services
Note: the gap in data from early 2003 is missing because the Pharmaceutical Services were burnt to the ground in the 2003 Canberra bushfires with consequent loss of data

In other patients, prolonged analgesic effect at a stable dose seems to be achievable. The individual response to opioids is therefore unpredictable and GPs are often cautious of when and in whom to try these drugs. What unfortunately remains unknown is the percentage of patients in whom a trial of opioids will be an ongoing success versus those in whom it will provide no respite from their problems.

In the absence of good evidence based trials, consensus statements have been published that at least provide guidelines that will assist the GP to prescribe these drugs rationally and safely.[7]

Summary of consensus statements

The treatment of chronic pain is a complex multidisciplinary effort. Most patients will benefit from an opinion from a pain clinic, and some will need drug and alcohol intervention. Nonopioid analgesia needs to be thoroughly explored before embarking on opioid medication. A 'step wise' approach will usually see the use of less potent and less potentially problematic medications such as tramadol tried at some point before a decision to initiate opioids. The World Health Organisation ladder of analgesia (*Figure 4*) is the most useful guide to progression of potency.

The decision to commence a trial of opioids should not be taken lightly. The patient needs to be fully informed that opioids will inevitably cause physical dependence to some degree (not be confused with addiction or 'dependent behaviour'). It is a good idea to put the agreement in the form of a short 'contract' between the patient and the prescriber (*Table 1*). It is important to stress to the patient that the commencement of use will be on a trial basis, and that if the trial is deemed successful, prescribing will continue. If the trial does not succeed, the drug will be

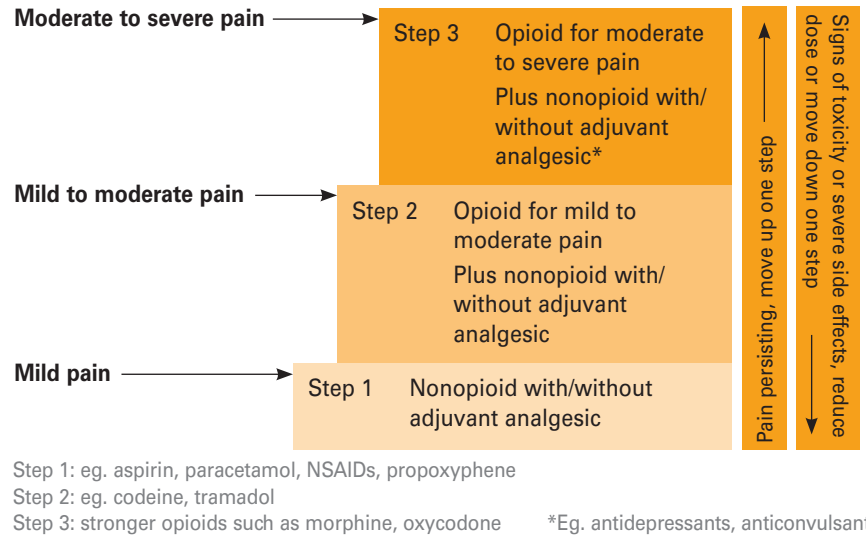

Figure 4. World Health Organisation analgesia ladder

Table 1. Sample opioid contract

Contract between _____ and _____

I (patient) hereby agree to the commencement of a trial of (drug) for the treatment of my medical condition. I agree that all prescribing will be done by (doctor's name) and that I will let Dr_____ know of any other medication I am receiving from any other sources. I agree that I will be dispensed and use the medication in accordance with my prescribing doctor. I am aware that the use of opioid medication is associated with a risk of physical and/or psychological dependence. The use of this medication will initially be for a period of ___weeks. At the end of that period, I and Dr _____ will make a decision as to whether the medication has been useful. The aims of the medication in my situation are:

1)

2)

3)

If it is thought that the medication has not been useful in my particular condition, I agree that Dr_____ will gradually reduce and cease the medication in a manner that will cause minimal discomfort to me. I also agree that if I am not compliant with any of the conditions of this contract, Dr_____ may make the decision to cease this trial of medication. I agree that the decision to cease or continue this trial always remains at the discretion of the prescribing doctor

gradually reduced and ceased in a way that will minimise physical withdrawal. The definition of what constitutes a successful or failed trial will need to be carefully explained to the patient. In general terms, a successful trial is one where there is lessening of pain to the extent that the patient functions better on several parameters. This improvement in functioning is more important than a report that pain has lessened. Assessment of function includes:

- increased activity level – ability to do activities previously not possible
- family and social interactions, and
- health care resource utilisation.

A failed trail usually means no real sense that pain relief is significant and no apparent improvement in function. There may have been unreasonable requests to escalate dose with no benefit from this, continued reports of poor analgesia, and possibly lost prescriptions or repeatedly running out of medication early. In the event of a failed trial, the prescriber needs to have the courage to abandon the trial.

A trial of opioids usually lasts a few months. The opioid chosen is commenced at a relatively safe (low) dose, and cautiously increased depending on response. A common starting dose might be 10–20 mg of long acting morphine twice per day or 10–15 mg twice per day of long acting oxycodone. This may then be slowly increased depending on response. It is the author's experience, that if good analgesia and improvement in function does not occur at moderate doses, an increase to higher doses is unlikely to be of benefit.

The opioid chosen should be a long acting oral agent. In chronic, nonmalignant pain, there are few indications for short acting opioids, and almost never an indication for parenteral opioids. A dose equivalent chart (*Table 2*) provides comparison of opioid potency. Preparations using 'dermal patch' delivery of fentanyl and, more recently, buprenorphine are also available.

Prescribing of the opioid should always be by the one practitioner, usually the patient's GP. Many patients find control of opioids difficult, and situations where the patient takes extra medication resulting in 'running out of medication early' are common. If a patient gets into this situation, the frequency of pharmacy pick up needs to be increased until control of the medication is regained. The prescribing practitioner needs to ensure that they abide by local regulations regarding gaining and regularly maintaining approval for ongoing S8 prescribing.

The case study describes a patient who has had a previous illicit narcotic dependence and now presents with a genuine chronic pain requirement. It is clear that such patients are more likely to run into problems with prescribed opioids than those who have never experienced illicit drugs. Diversion to others, sale of prescribed drugs, and injection of oral opioids preparations is not uncommon. While this does not mean that prescribed opioids are contraindicated in such patients, it does mean that extreme caution needs to be exercised before embarking on an opioid 'trial' and that close control of the prescribed opioid needs to be maintained from the outset. In the event of a failed trial in patients with previous drug dependence, transfer to a methadone or buprenorphine program can be offered as an alternative. It is not uncommon for patients with no prior history of illicit drug use to end up on such a program due to dependence problems from prescribed oral opioids. Indicators that problems of dependence might be present are listed in *Table 3*.

Table 2. Equianalgesic potency conversion

When changing opioid start at 50% of suggested equianalgesic dose then titrate according to response

Drug	Suggested dose equivalent to 10 mg IM/SC morphine[1]	Approximate duration of action (hours)[2]	Adjust dose in renal impairment	Comments
Agonists				
Codeine[3]	130 mg IM 200 mg oral	3–4	Yes	Mild to moderate pain, do not exceed 60 mg single dose
Dextropropoxyphene[3]	Unknown	4–6	Yes	Mild to moderate pain, avoid long term use
Fentanyl	100–150 µg IV/SC	0.5–1.0	No	Moderate to severe acute or chronic pain; preferred in renal impairment
Hydromorphone[3]	1.5–2.0 mg SC/IM 6.0–7.5 mg oral	2–4	Yes	Moderate to severe acute or chronic pain
Methadone	10 mg SC/IM 20 mg oral[4]	8–24 (chronic dosing)	No	Severe chronic pain, management of opioid dependence
Morphine[3]	30 mg oral	2–3; 12–24 (controlled release)	Yes	Moderate to severe acute or chronic pain
Pethidine[3]	75–100 mg IM	2–3	Contraindicated	Not recommended
Tramadol[3]	100–120 mg IM/IV 150 mg oral	3–6	Yes	Moderate to severe pain
Partial agonists				
Buprenorphine	0.4 mg IM 0.8 mg sublingual	6–8	No	Not recommended for analgesia; management of opioid dependence

1 = doses given are guidelines only
2 = duration of action depends on dose and route of administration; if pain occurs give more frequently (except for controlled release products)
3 = active metabolite
4 = based on single dose studies
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Conclusion

In the future, clinical trials will assist with the many unanswered questions regarding the use of opioids in chronic nonmalignant pain. Are they useful in the long term or does tolerance eventually develop with the majority of patients? How many will exhibit evidence of drug dependent behaviour?

In the meantime, if guidelines are adhered to, the GP can choose patients for whom opioids may be appropriate for the treatment of chronic pain, and should be able to control the use of the drug. This will minimise the eventual risk of problematic prescribed drug dependence.

Table 3. Indicators of possible problematic opioid use

- Persistent requests to increase doses
- Lost prescriptions
- Lost medication
- Running out of medication early
- Use of other practitioners without the knowledge of the primary practitioner
- Taking the medication in a manner other than prescribed (eg. injecting oral preparations)
- Use of illicit opioids in addition to the prescribed opioid
- Hazardous use of alcohol or other psychotropic medication (eg. benzodiazepines)
- Missing appointments (frequent attendance without appointment requesting medication)
- 'Sharing' medication with others
- Using the opioid to treat unrelated symptoms (eg. 'helps with my moods/anxiety')
- Frequent attendance at accident and emergency departments seeking opioids
- Reports from family members of intoxication/drowsiness that may indicate aberrant use of the opioid

Conflict of interest: none declared.

References

1. Bell JR. Australian trends in opioid prescribing for chronic noncancer pain. Med J Aust 1997;167:26–9.
2. Marcus DA. Treatment of nonmalignant chronic pain. Am Fam Physician 2000;61:1331–8.
3. Goucke CR. The management of persistent pain. Med J Aust 2003;178:444–7.
4. McQuay HJ. Opioids in chronic nonmalignant pain. BMJ 2001;322:1134–5.
5. Moloy AR. The role of opioids in chronic nonmalignant pain. Medicine Today 2003;(Suppl):4–11.
6. Antoin H, Beasley RD. Opioids for chronic noncancer pain. Postgrad Med 2004;116:37–40.
7. Recommendations for the appropriate use of opioids for persistent noncancer pain. A consensus statement prepared on behalf of the Pain Society, the Royal College of Anaesthetists, the Royal College of General Practitioners and the Royal College of Psychiatrists, March 2004.

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