

THE USE OF ORAL OPIOIDS
IN PATIENTS WITH CHRONIC NONMALIGNANT PAIN:
MANAGEMENT STRATEGIES

Paul Graziotti and Roger Goucke
for the Directors of the Australian Pain Society

Paul J Graziotti FANZCA West Australian Director, Australian Pain Society, Visiting Specialist, Department of Pain Management, Sir Charles Gairdner Hospital PERTH WA 6009

C Roger Goucke FANZCA Secretary, Australian Pain Society, Head, Department of Pain Management, Sir Charles Gairdner Hospital, PERTH WA 6009

Correspondence to Dr Goucke.

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These management strategies were developed as a consensus view between the two authors. The strategies were subsequently reviewed by the Directors of the Australian Pain Society whose membership comprises, six anaesthetists specialising in pain management, a pharmacist, a rheumatologist, two rehabilitation physicians and an occupational therapist. A medline search dating back to 1966 produced 163 useable articles. Three randomised controlled trials with evidence levels II and III were identified.

INTRODUCTION

Patients with chronic nonmalignant pain present a number of challenges to their treating physicians. One such challenge is whether to use oral opioids in their treatment plan. The combination of poorly defined pathology, significant psychosocial factors, manipulative behaviour, dependence, tolerance and government regulations are formidable influences.

Because of these concerns many doctors may decide not to prescribe opioids for patients with chronic nonmalignant pain and certainly current legislation discourages it. Arguments against the use of opioids in these patients have also been published. (1,2). World wide though there is a growing body of opinion that a small sub-group of patients with chronic nonmalignant pain may improve their level of function whilst achieving improved analgesia in the absence of rapidly escalating doses and/or addictive behaviour.

Randomised controlled trials (3,4,5) are beginning to emerge which support the benefit claimed from published retrospective experience of patients who have had treatment with opioids for their chronic nonmalignant pain.(6,7) This evidence suggests that a proportion of patients report an improvement in their level of analgesia and/or level of function (8). The prevalence of drug abuse, dependence and addiction varies between 3.2-18.9% depending on definition. There is little evidence that addictive behaviours are common in the chronic pain population (9).

There is evidence however that an increasing number of Australian patients are receiving prescribed oral opioids for both malignant and non malignant pain.(10) This may be filling a previously unmet need. It is not clear though if the increased prescribing for nonmalignant pain is appropriate, whether there has been any increase in function,

reduction of pain, reduction in suffering, or if any of these drugs will enter the illicit market.

How then can we ensure the maximum benefit from the prescription of opioids for chronic nonmalignant pain. Who are the appropriate patients? Who are the appropriate prescribing doctors? How should the drugs be prescribed? Which drugs should be prescribed? How and when should they be ceased? The aim of this article is to explore these issues and provide guidelines to assist practitioners in the appropriate use of oral opioids.

WHICH PATIENTS?

It is essential that all reasonable attempts be made to achieve a diagnosis for the cause of the pain including nociceptive, neuropathic and psychological contributions. The demonstration of pathology commensurate with the degree of pain behaviour is desirable. However patients often have pathology which is difficult to interpret eg degenerative changes on spinal X-rays. Certain conditions result in neuropathic pain, which is usually a clinical diagnosis and may not be reflected in investigations such as radiographs or nerve conduction studies. This should not preclude a trial of opioids in these patients if otherwise appropriate.

A thorough history of previous conservative therapy (Table 1) should be taken before consideration is given to the medium to long term use of opioids. This may mean involvement in exercise programs, psychological therapy, attention to improving coping mechanisms, a multidisciplinary pain management program, reducing psychosocial stressors and the use of appropriate invasive physical treatments. Drug therapy should include, trials of non opioid analgesics, tricyclic antidepressants and, membrane stabilising medications (eg sodium valproate, carbamazepine).

Patients for whom opioids are being considered should be psychologically stable, although it is recognised that this is difficult to define. It is not uncommon for patients in chronic pain to develop psychological problems as a result of the pain and therein lies a dilemma for the physician. Will treating the pain reverse some of the psychological abnormalities? Or are the psychological abnormalities a significant contributor to the overall pain behaviour? Studies would suggest the former in most cases (11). For certain groups of patients a psychological assessment is essential, eg poorly defined pathology, younger patients, high levels of distress, previous or ongoing substance abuse. Consideration should be given to managing these patients in a multidisciplinary pain centre (see Table 2).

WHICH DOCTORS SHOULD PRESCRIBE?

It is important that only one doctor prescribes the opioids and assesses the response. Agreement between patient and doctor with respect to outcome assessment is required prior to the initiation of long term opioid therapy. Failure to reach these goals should be an indication to cease prescribing.

The prescribing doctor should have an established therapeutic relationship with the patient. This excludes casualty officers, specialists who see a patient on one occasion only, after hours locum services and in many cases junior medical staff working in outpatient departments.

All patients who are considered suitable for the long term use of opioids in nonmalignant pain should be assessed at some stage in a specialist pain management centre. Shared care with the general practitioner and the pain management centre is ideal. With a stable patient annual reviews by the centre are sufficient, otherwise more frequent assessments will be necessary. The prescribing doctor should review monthly. General

practitioners and other specialists should have access to advice and clinical input from a pain management specialist if problems occur.

WHICH DRUG?

Sustained release morphine preparations are the drugs of choice in patients with chronic nonmalignant pain, because of their single or twice daily dosage and stable blood concentrations as a consequence of their more predictable pharmacokinetics.

There is **agreement internationally(12) and within Australia(13)** that intra-muscular opioids should play no part in the treatment of chronic nonmalignant pain. In particular intra-muscular pethidine should be avoided. It has a short half life, a possible increased risk of dependence due to its psychomimetic effects, and the potential for excitatory central nervous system effects from accumulated nor-pethidine concentrations following repeated dosage.

Codeine phosphate is a short acting drug and as such has little place in chronic pain management. A controlled release preparation is available overseas and may prove useful.

Immediate release morphine as morphine mixture (5-10 mg/ml) may be used for dose finding prior to establishing sustained release morphine, but is generally unnecessary. It may be useful for breakthrough pain or exacerbations. Transdermal fentanyl patches may in the future, provide a useful alternative for patients intolerant to morphine. Methadone and oxycodone **rectal suppositories** are useful alternatives. Dietary advice should be given to minimise the problem of constipation and consideration given to the regular prescription of laxatives.

CONSENT

Patients prescribed opioids for the treatment of chronic nonmalignant pain should be fully informed as to the potential consequences of this therapy. There is increasing awareness that a written consent form is a valuable tool, particularly when treating patients who for any reason are difficult. (14)

Informed consent should include:

- a) Discussion regarding the likelihood of dependence and risk of addictive behaviour. That all patients will become dependent and are likely to experience withdrawal symptoms if opioids are suddenly ceased. That addictive behaviour occurs in a much smaller proportion of patients and may be minimised by appropriate patient selection.
- b) Currently, published data on long term outcome of the effects of medically prescribed opioids are lacking
- c) Patients should be informed as to the potential for cognitive impairment. In particular driving motor vehicles. Whilst there are few studies in nonmalignant patients assessing cognitive function in the presence of opioids (15), the studies in cancer patients would suggest that cognitive function is actually improved when adequate analgesia is provided. (16)
The potentiating effect of opioids on the sedative effect of other medication should be emphasised.
- d) Female patients should be aware of the possibility of physical dependence in children born to them, if they continue to take opioids in late pregnancy.

- e) Indications for the cessation of treatment with opioids should be outlined. Emphasis should be placed on the patient's responsibilities regarding the security of their medication. The consequences of aberrant behaviour (Table 3) should be identified as clearly as possible.
- f) Information regarding side effects should be given, eg. constipation, nausea, sedation, dry mouth.
- g) Clearly defined specific goals of the treatment programme can also be included.

(Copies of a sample consent form are available from the authors)

HOW SHOULD THESE DRUGS BE PRESCRIBED

TRIAL OF ORAL OPIOID

Before prescribing opioids on a long term basis, a trial should be undertaken. Goals from the trial should be identified, and the endpoint clearly stated. The trial should commence with the equivalent of sustained release morphine 10 to 50 mg bd and assessed at one week or earlier. Depending on response, the dose could be increased or decreased. The trial should last for 4 - 6 weeks. In general round the clock medication is the accepted regimen. However, in patients with fluctuating pain conditions it may be more appropriate to consider a variable dosing regimen with oxycodone or morphine elixir.(17)

It must be stressed that one doctor should institute and monitor the trial. Patients must accept the responsibility of ensuring their supply of medication does not run out after hours.

There is controversy regarding the expectation that patients will improve in function. Is it adequate for patients to achieve analgesia only? Is it adequate for patients to state that they feel better only? Certainly patients should demonstrate a reduction in other analgesics. Ideally patients should demonstrate an improvement of function. Perception of improved analgesia should be the minimal requirement and failure to achieve at least partial analgesia at a moderate dose should be considered a failure of the trial. Any further long term opioid treatment is contraindicated.

Most patients who experience minimal or no analgesic effect will cease the drug themselves prior to the end of the trial. Similarly many patients who experience adverse side effects, such as severe nausea or constipation will determine that these outweigh the analgesic benefits and cease the drug. Opioid naive patients whose dose rapidly escalates in a one month period after the commencement, should in general be considered inappropriate for the long term use of opioid therapy.

At the end of the trial period, if the expected outcomes have not been achieved, the drug should be tapered over a few days and ceased.

ONGOING REVIEWS

Patients who are then prescribed opioids on an ongoing basis should be reviewed at first fairly frequently then monthly. A detailed review by the pain management centre should be undertaken annually. At each review analgesic efficacy should be assessed as should any improvement in the level of function. The responsible federal or state health department must be notified.

Evidence of aberrant behaviour should be assessed. Aberrant behaviour is variable in its importance and relevance. Table 2 indicates factors which Portenoy (18) has considered more or less predictive of the development of addictive behaviour. Patients

identified with behaviour in the less predictive column indicate a need to assess the dose of drug, the psychological factors of relevance, the patient's expectations or the type of medication.

Those patients identified with features in the more predictive column should result in a serious reassessment of the appropriateness of opioid prescription. In many cases it will be necessary to reduce and then cease the opioid over a one week period. In other cases, a more regulated supply such as daily or weekly prescriptions may be appropriate. An initial written consent form indicating those factors for which supply will be weaned and ceased will make this easier.

SUMMARY

There is growing evidence that a small group of patients with chronic nonmalignant pain may benefit from the use of oral opioids.

The challenge facing the medical profession rests with identifying this group and alleviating suffering without significantly increasing illicit use, addiction or medication induced suffering. We have attempted to provide some guidelines for the careful and constructive use of opioids in patients with chronic nonmalignant pain.

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Table 1

Treatment options to consider before Opioids

<p>MEDICATION</p> <ul style="list-style-type: none">• Simple analgesics• NSAIDS,• Tricyclic antidepressant drugs• Membrane stabilisers <p>EXERCISE PROGRAMMES</p> <p>TENS</p> <p>PSYCHOLOGICAL THERAPY</p> <ul style="list-style-type: none">• relaxation• cognitive behavioural therapy• hypnosis• coping strategies <p>INVASIVE PROCEDURES</p> <p>MULTIDISCIPLINARY PAIN MANAGEMENT PROGRAMMES</p>

Table 3

Aberrant drug related behaviour

More predictive features	Less predictive features
Selling prescription drugs	Aggressive complaining about the need for more drug
Prescription forgery	Drug hoarding during periods of reduced symptoms
Stealing or borrowing drugs from others	Requesting specific drugs
Injecting oral formulations	Openly acquiring similar drugs from other medical sources
Obtaining prescription drugs from non medical sources	Unsanctioned dose escalation
Concurrent abuse of alcohol or illicit drugs	Unapproved use of the drug to treat other symptoms
Multiple non sanctioned dose escalations	
Multiple episodes of prescription loss	
Repeatedly seeking prescriptions from other physicians or emergency departments without informing the prescriber or after warnings to desist	
Evidence of deterioration in function, at work, in the family, or socially that appear to be drug related	
Repeated resistance to therapy changes despite clear evidence of adverse physical or psychological effects from the drug	

Table 2

PATIENTS IDEALLY REFERRED TO A MULTIDISCIPLINARY PAIN MANAGEMENT
CENTRE BEFORE OPIOIDS COMMENCED

1. History of previous drug addiction
2. Previous opiate use resulting in problems
3. Psychologically unstable
4. Young patients with obscure pathology
5. Complex compensable patients

Box

Questions to ask before prescribing opioids for chronic nonmalignant pain

1. Has the patient tried opioids for this condition before?
2. Is the diagnosis established? (If not are further investigations required?)
3. Does the patient have neuropathic (nerve damage) pain? If so have non opioids, membrane stabilisers and antidepressants been tried?
4. Has the patient had a reasonable trial of nonpharmacological treatment including assessment and treatment of psychosocial factors contributing to pain behaviour?
5. Is the patient well known to you and psychologically stable?
6. Does the patient have a history of previous drug, alcohol or substance abuse?
7. Does the patient understand the implications of long term opioid therapy - is written consent necessary?
8. Do I have back-up resources if required?