Opioids in palliative care: the NICE guidance

In this article...

- What to consider when using opioids in palliative care
- How to establish and maintain an effective dose
- Possible side-effects that may be experienced by patients

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Many life-limiting and progressive disorders require effective pain-management strategies. The use of opioids is one facet of pain management and the National Institute for Health and Clinical Excellence Clinical has produced guidance on this. One of the primary messages from the guideline is the need for careful assessment and excellent communication. This article discusses the various recommendations included in the guideline, covering issues of correct dosage, understanding patients’ expectations and fears, ongoing monitoring and management of the side-effects associated with opioids.

Providing holistic care to their patients includes ensuring they are comfortable and as free from pain as possible. In order to do this nurses need to understand pain physiology, pain assessment and the wide variety of pain-management strategies available.

Although pain management encompasses far more than the use of medication, it is a key tool and nurses must have a good understanding of each type of drug and how to use it effectively. Opioids are commonly used for palliative care pain management, either alone or in combination with other drugs such as paracetamol, antidepressants like amitriptyline, non-steroidal anti-inflammatories (NSAIDs), and anticonvulsants such as pregabalin.

The National Institute for Health and Clinical Excellence’s clinical guideline (2012) outlines the use of opioids for pain management in palliative care, which is defined by Sepulveda et al (2002) as:

“An approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychological and spiritual.”

Conditions requiring palliative care include cancer, heart failure, renal failure and neurodegenerative disorders such as motor neurone disease. The National Audit Office (2004) reported that there were 128,000 cancer-related deaths in England in the year 2000-01 and stated that one in four people will die from cancer. It is estimated that more than half of patients with cancer will have pain requiring treatment (Breivik et al, 2009).

More than 1.4 million people in England suffer from chronic obstructive pulmonary disease (Nacul et al, 2011) and approximately half will experience moderate to severe pain that reduces their quality of life and limits their daily functioning (HajGhanbari et al, 2012). Heart failure is also a relatively common condition with more than a third of people experiencing moderate to severe pain (Goebel et al, 2009).

Pain has also been identified as a major symptom in a number of neurodegenerative disorders such as motor neurone disease (Clarke et al, 2005), Parkinson’s disease (Broen et al, 2012), and multiple sclerosis (Hirsh et al, 2009), and is common in people with dementia (Zwakhalen et al, 2009).

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5 key points

1. Patients who require strong opioids for pain should be given oral sustained-release morphine in a dose of 30-40mg per day with 5mg immediate-release morphine available for breakthrough or episodic pain.

2. When oral morphine is not appropriate, consider using subcutaneous or transdermal opioids.

3. Some side-effects of opioid therapy tend to resolve over time but require aggressive management from the outset to improve patient adherence.

4. Nausea and vomiting can be caused by a number of mechanisms and may require a number of different treatment approaches.

5. There is a high risk of respiratory depression at the start of treatment so it is important to monitor patients carefully.
What are opioids?
Opioids are drugs that combine with opioid receptors, which can be found in most tissues of the body including the brain, the spinal cord, the gut and subcutaneous tissue. There are three main types of opioid receptors:

- Mu;
- Delta;
- Kappa.

The key receptors from the perspective of pain relief (analgesia) are the mu receptors. Activating these leads to an increased activation threshold of pain nerves and the production of endorphins – hence they “block” pain signalling. These receptors are also responsible for the production of respiratory depression, sedation, euphoria and dependence.

Opioids are extremely effective pain relievers when used correctly but a number of factors need to be taken into consideration. Pain related to damaged tissues (nociceptive pain) responds better to opioid medication than pain caused by damage or dysfunction of the nerves or nervous system (neuropathic pain). Although opioids can still be helpful in relieving neuropathic pain, larger doses may be required (Smith, 2012).

The initial and ongoing assessment of pain is a vital part of effective management and the nurse’s role is central to this. The initial assessment can be complex and will involve a number of members of the multidisciplinary team, whose aim is to discover the:

- Cause and mechanism(s) of the pain;
- Patient’s understanding, expectations and concerns;
- Efficacy of previous and current management strategies;
- Physical, social and psychological effects the pain is having on the patient and family.

NICE guidance
The NICE guideline (2012) covers a number of issues nurses should consider when using opioids in palliative care. Box 1 list common terms used in this area of care.

The patient’s beliefs and knowledge
Patients who need opioids may have fears about dependence, addiction and debilitating side-effects (Sullivan et al, 2010). They may also be concerned the use of these drugs signals the end of life. As such, one of the aspects the guideline addresses is good communication with the patient.

One of the common barriers to effective opioid use in long-term pain control is fear in both patients and staff about addiction.

Short-term treatment of pain with opioids almost never results in addiction, nor is it reported to be a problem in end-of-life care. However, trends to commence palliative care earlier in the disease course have led to longer-term use of palliative pain-management approaches, which has led to an increased risk of addiction; this could be compared to opioid use in chronic nonmalignant pain, about which there is a rapidly growing literature (Højsted and Sjøgren, 2007).

The risk of addiction should not prevent the use of opioids for the management of pain in those who need it, but it is important that patient risk factors are identified and monitored. The management approach needs to be truly individualised in order to differentiate between pseudoaddiction, addiction and the use of opioids as part of an emotional coping strategy (Childers and Arnold, 2012).

It is important to assess the patient’s previous experiences with pain-relieving drugs and especially opioids. Some patients will have already experienced nausea and vomiting or constipation; these side-effects may be a source of concern that are serious enough to prevent them trying an opioid again.

Establish the optimal dose
When a strong opioid is commenced, the most appropriate dose needs to be determined. The right dose will balance the benefits of good pain relief with the side-effects of nausea and vomiting, and the risk of respiratory depression. Over a period of a few weeks patients can expect to feel less nauseous and will have a much lower risk of respiratory depression.

NICE recommends starting with 20-30mg per day of oral morphine in either sustained-release or immediate-release formulation. Some patients will not be able to take oral medication; in such cases, NICE recommends fentanyl transdermal patches. These add some complications, however.

BOX 1. GLOSSARY OF TERMS

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>Opioid</td>
<td>A substance, either naturally occurring or synthetic, that produces a morphine-like effect, which can be blocked by antagonists like naloxone. The group includes morphine, diamorphine, codeine, pethidine, fentanyl and oxycodone.</td>
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<tr>
<td>Activation</td>
<td>When a drug molecule combines with a receptor it produces a response and is such that we can say the receptor has been activated by the drug.</td>
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<td>Addiction</td>
<td>A primary, chronic, neurobiologic disease, with genetic, psychosocial and environmental factors influencing its development and manifestations. It is characterised by behaviours that include one or more of the following: impaired control over drug use; compulsive use; continued use despite harm; craving (British Pain Society, 2010).</td>
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<td>Antagonist</td>
<td>A drug that combines with a receptor, does not produce a response and blocks the receptor, preventing other drugs from binding with it.</td>
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<td>Dependence</td>
<td>A state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug or administration of an antagonist (BPS, 2010).</td>
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<tr>
<td>Drug receptor</td>
<td>A protein that evokes a response in the cell, to which the drug combines in order to produce a response by the cell.</td>
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<td>Equianalgesic</td>
<td>A means of converting the dose of Drug A to the equivalent dose of Drug B – for example, 10mg morphine given orally is equivalent to 0.2mg of fentanyl given transdermally.</td>
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<tr>
<td>Opioid naive</td>
<td>A patient who has recently started to use opioid medication and has not yet developed tolerance to the respiratory, sedative and nausea-inducing effects of the drug. This patient is at a higher risk of these toxic effects.</td>
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| Tolerance | Repeated use of a drug is associated with a gradual decline in its effectiveness, which leads to the need for a higher dose to control the pain. It can become noticeable within two weeks of the opioid being commenced. Patients also become tolerant to the side-effects of opioids such as respiratory depression, itching and nausea. There is no tolerance development in constipation or pupil constriction.

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“Recognise that care delivery of the highest quality is the essence of nursing”
Edward Alan Glasper  p24

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Fentanyl patches are not designed to be used in the titration process. Each patch delivers a specified dose of fentanyl over a 72-hour period and it can take up to 24 hours for the peak dose to be achieved after a patch is applied (Medicines Compendium UK, 2012). As a result of this, respiratory depression may not be apparent for some hours after the patch has been applied. The lowest dose a patch can deliver is 12mcg per hour – this is equivalent to more than 40mg of oral morphine per day, which makes it difficult to start on a low dose and build up. Patches should not be cut, and localised heat (including from fever) can increase the rate of absorption from the patch, thereby increasing the risk of respiratory depression and sedation in patients who are “opioid-naive” (Box 2).

The dose patients start on is rarely the dose they will stabilise at; very often it is insufficient. One of the nurse’s important roles is to continually assess the patient’s pain (Fig 1). Nurses must recognise that an absence of pain behaviour is not the same as an absence of pain. In addition to observation, they need to assess pain regularly using a numerical rating scale with at least 11 points (0-10), which has enough sensitivity to detect modest changes in pain intensity (Williamson and Hoggart, 2005).

The pain assessment should be carried out frequently in the early stages of opioid therapy and with increased frequency after changes in dose to determine the effect each dose of opioid has on the intensity of patients’ pain. The aims of this regular and frequent assessment are to determine whether the right quantity of opioid has been prescribed – too much and patients will experience toxic effects of sedation and respiratory depression, too little and they will be in pain. Nurses should also determine whether there is a daily pattern to patients’ pain and whether their opioid medication can be tailored to work better with that pattern.

Breakthrough pain is defined as a relatively brief increase in pain intensity above a baseline in patients who are taking regular analgesics (Mercadante, 2011). It can arise for no obvious reason or because of a triggering event. A patient’s pain might also “break through” because the opioid dose is not high enough or because it is the end of the dose. Assessment tools can help establish why such pain occurs and in this early titration phase it is useful to monitor the use of breakthrough medication. How frequently the patient requires it, in combination with some information about whether there is a trigger or not, can allow prescribers to decide whether the daily dose of morphine needs to be increased.

Patients receiving opioids should have easy access to 5mg immediate-release morphine to manage breakthrough or undertreated pain. Fast-acting fentanyl is no longer recommended as a first-line treatment option for breakthrough pain; although it is effective, the guideline development group (GDG) did not find evidence to suggest it was any better than oral immediate-release morphine (NICE, 2012).

The maintenance phase
NICE recommends using oral sustained-release opioids in the maintenance phase for patients who can tolerate them. Patients should also have a supply of immediate-release morphine for episodic and breakthrough pain. If they cannot take oral medicines then it may be appropriate to consider an equivalent dose of fentanyl or buprenorphine delivered transdermally. In either case prescribers must carefully calculate the dose required based on equivalence tables.

An alternative to using patches is subcutaneous delivery of opioids via a pump. This is a better option for patients whose pain is unstable. This can be quite expensive as nurses must make home visits so it is not recommended when patches would be appropriate. Morphine, oxycodone and diamorphine can all be used for continuous subcutaneous infusion; the GDG (NICE, 2012) found no evidence to suggest the superiority of one over another.
In the maintenance phase it is important to continue monitoring pain, the effectiveness of the analgesia regimen and the occurrence of side-effects or signs of toxicity. Toxic effects of morphine are sedation and respiratory depression, and both tend to become less likely as the patient becomes used to taking the opioid medication. However, in the early stages of opioid therapy these can be dangerous and close patient observation is required.

Sedation usually precedes respiratory depression and as the respiratory rate naturally falls when the patient is asleep it is important the nurse does not confuse drug-induced sedation with normal drowsiness. Drug-induced sedation usually leaves patients unable to sustain a conversation – they will doze off after they have been woken. If you suspect this, administer oxygen, continue to monitor closely and be prepared to administer naloxone.

**Side-effects**

**Constipation.** This is the main side-effect from the long-term use of opioids for pain management. It causes significant physical and psychological distress, including interference with activities of daily living, anxiety and depression, and it can reduce adherence to the medication regimen (Dhingra et al, 2012). Constipation is caused because opioids reduce bowel motility, leading to an increased transit time for faeces, which allows greater re-absorption of water and dehydration of the faeces. Managing constipation should aim to increase gastric motility, the amount of water in the faeces and the ability of the faeces to retain water (Box 2).

Twycross et al (2012) produced an algorithm of a recommended treatment plan starting with senna and adding lactulose if that is not successful. NICE guidelines recommend all patients are prescribed laxatives as soon as they start opioid therapy on the grounds that nearly everyone experiences opioid-induced constipation.

**Nausea.** Up to 40% of people taking opioids experience nausea because of a reduction in gastric emptying and reduced gastric motility, as well as the effect of opioids in the chemoreceptor trigger zone, vomiting centre and other areas of the brain. Nausea and vomiting are dose-dependent and although these side-effects tend to fade over time, they can make patients reluctant to take their opioid.

Nausea can be managed by using antiemetic medication that targets the:

- Gut (for example, metoclopramide);
- Chemoreceptor trigger zone (for example, prochlorperazine, droperidol or ondansetron);
- Vomiting centre of the brain (for example, cyclizine).

Nurses should assess patients to determine what mechanism is causing the nausea and so ascertain the most appropriate medication.

Other ways to control nausea and vomiting include switching to a different opioid or reducing the dose and adding a different class of drug such as an anti-inflammatory. Although NICE recognises these are common methods of managing nausea and vomiting, it did not find a great deal of high-quality evidence to directly support their use.

**Drowsiness.** This is common when patients start taking an opioid. Like nausea and vomiting drowsiness is relatively transient but can be very disabling for patients. Those who are experiencing drowsiness may fall asleep easily and rouse readily with minimal stimulation but it can be more severe and result in hallucinations, agitation or even coma (NICE, 2012).

The GDG recommends patients are told that starting opioid treatment and dose increases often cause fatigue or drowsiness and, for most, this passes. It states that if this side-effect is severe or does not reduce over time, it may be necessary to change the opioid being taken or reduce the dose.

**Conclusion**

The GDG recommends that patients who require strong opioids for pain are given oral sustained-release morphine in a dose of 30-40mg per day with 5mg immediate-release morphine available for breakthrough or episodic pain. The quantity and pattern of use of immediate-release morphine can help to establish the effective dose of morphine to be used in the maintenance phase. When oral morphine is not appropriate, subcutaneous or transdermal opioids should be considered.

Some side-effects of opioid therapy tend to resolve over time but require aggressive management from the outset to improve patient adherence. The guideline’s message is that excellent communication with patients is fundamental to effective opioid pain management in palliative care.

**References**


Medicines Compendium UK (2012) Durogesic. tinyurl.com/mcuk-durogesic


**BOX 2. MANAGEMENT OF OPIOID-INDUCED CONSTIPATION**

- Increasing gastric motility: exercise, stimulant laxatives (for example senna), osmotic laxatives (for example lactulose)
- Increasing faecal water: osmotic laxatives, stimulant laxatives
- Increasing ability of faeces to retain water: docusate, fibre (for example bran, Fybogel), osmotic laxatives