

# PAIN MANAGEMENT IN PALLIATIVE CARE

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*The aim of palliative care is to provide relief from suffering and to improve quality of life for patients with incurable disease and their families. Palliative care encompasses a holistic approach, addressing not only physical symptoms but also the wider psychological, social and spiritual issues that contribute to a patient's wellbeing.*

*A multidisciplinary approach is needed to tackle all these issues and achieve good symptom control*



*Anticipation of side effects of strong opioids is important in maintaining the patient's quality of life*

The principles of palliative care are applicable to any progressive, incurable disease but currently co-ordinated palliative care services are usually available only to patients with cancer or progressive neurological disease. The majority of cancer patients spend their last year of life at home, but will spend at least some time in hospital or in a hospice.<sup>1</sup> This means that patients

are likely to be cared for by the primary care team, with support from palliative care specialists such as Macmillan home care nurses, and palliative care support teams.

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Many patients think that cancer and pain are synonymous. In reality, around a third of cancer patients, even with advanced disease, do not have severe pain. Pain is subjective and the patient's own description of the pain, whenever possible, should be the basis of any assessment.<sup>2</sup> It is essential to assess accurately the patient's pain to determine the origin and likely cause, which will influence the choice of drug therapy. Patients might have more than one pain and should be encouraged to report all pains. Pain from co-existing conditions, for example, arthritis, should be considered as well as pain from cancer.

Application of the principles of pain management laid out in the World Health Organization (WHO) programme for cancer pain relief<sup>3</sup> can provide satisfactory relief in 88 per cent of cancer patients who experience pain.<sup>4</sup> The principles are illustrated in the WHO analgesic ladder (Figure 1, p255). Patients should start at the step of the ladder most appropriate for the pain they report at assessment. If pain increases, drugs from the next step of the ladder should be prescribed. Pain should be reassessed on a regular basis. Other interventions, such as radiotherapy to bone metastases, might allow analgesia to be reduced.

Control of chronic pain in cancer requires constant therapeutic levels of anal-

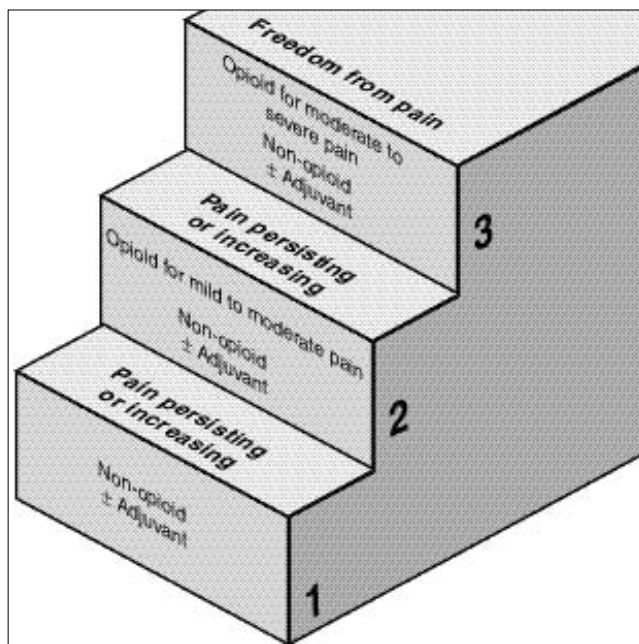


Figure 1 The WHO analgesic ladder (adapted from WHO guidelines)

gesics, so all drugs should be given at regular intervals appropriate for their duration of action. The oral route is preferable for drug administration and should be used unless the patient has significant swallowing or absorption problems.

**STEP 1: NON-OPIOIDS**

Paracetamol 1g taken regularly four times a day should be prescribed initially to patients with mild pain. To ensure adequate pain relief, regular rather than “as required” dosing is necessary.

Non-steroidal anti-inflammatory drugs (NSAIDs) may be considered both as step 1 analgesics, and as adjuvants used at any step of the ladder. NSAIDs have analgesic and anti-inflammatory properties in mild to moderate pain and are particularly useful in treating bone pain. The choice of NSAID depends on its side effect profile along with patient response and the local formulary.

**STEP 2: OPIOIDS FOR MODERATE PAIN**

Weak opioids such as codeine, dihydrocodeine and dextropropoxyphene should be considered where pain is not adequately controlled by regular paracetamol, given

alone or with NSAIDs. Paracetamol should be continued because its action enhances analgesia with weak opioids. Compound preparations of weak opioids and paracetamol can be useful in reducing the number of tablets prescribed. It is essential to use a combination that contains therapeutic doses of weak opiate (eg, co-codamol 30/500, co-dydramol 30/500 or co-proxamol).

Unlike morphine, weak opioids have an analgesic ceiling; if the maximum regular dose is insufficient to control the patients’ pain, step 3 analgesics should be prescribed. There is no advantage in substituting one weak opioid for another.

**STEP 3: STRONG OPIOIDS**

Morphine is the oral strong opioid of choice. Morphine is readily available in solid and liquid oral formulations, in sustained-release and immediate-release forms, and can be given rectally. For continuous subcutaneous infusion, diamorphine is preferred because of its greater solubility.

The dose of morphine required should be titrated using short-acting preparations. Morphine 2.5–5mg should be prescribed regularly every four hours, including throughout the night. A double dose may be given at bedtime to help stop the patient waking in pain.

Provision for extra doses to be given on an as required basis should also be made. The choice of starting dose is dependent on renal function, age and the dose of any previous opioids prescribed — codeine, dihydrocodeine and dextropropoxyphene are approximately 1/10 the potency of morphine.<sup>5</sup> Patients should be encouraged to use extra (“breakthrough”) analgesia whenever

they need it to allow the correct dose to be determined. Once the patient’s pain is stable on short-acting morphine an equivalent dose of a long-acting preparation should be prescribed to improve analgesia, reduce peak and trough effects and facilitate adherence. A breakthrough or rescue dose of 1/6 of the total daily morphine dose should also be prescribed in short-acting form. Patients should be encouraged to use this if necessary; regular need for breakthrough medication should be explored and the long-acting dose adjusted if necessary. Paracetamol may be continued regularly at step 3.

Patients might need reassurance that they will not become addicted to morphine, and that it will not lose its effectiveness leaving them with “nothing to use when the pain is really bad”.

Anticipation of predictable side effects of strong opioids is important in maintaining the patient’s quality of life (Table 1).

In the past few years, a number of different licensed opioid preparations have become available in the United Kingdom. These do not replace morphine as the drug of choice for the relief of moderate to severe pain but provide alternatives where the use of morphine is not possible.

Fentanyl citrate is a synthetic opioid that has a rapid onset and short duration of action when given parenterally. A fentanyl transdermal delivery system (Durogesic patches) avoids first pass metabolism and gives continuous plasma levels of fentanyl by forming a depot in the skin. Transdermal fentanyl has a long half-life; plasma steady-state concentrations are achieved 36–48 hours after application of the patch and the elimination half-life is 17 hours or more.<sup>6</sup> Care is needed when changing from oral or parenteral opioids to a fentanyl patch and when increasing the dose. Patients should also be given advice on how to use fentanyl transdermal patches (see Panel, 256).

Transdermal fentanyl is a good alternative if the patient cannot swallow or absorb medicines given by mouth, or if there are intolerable side effects from another strong opioid. It can avoid the use of a subcutaneous infusion, which is particularly useful in patients who are mobile and in their own homes. It is unsuitable for patients with unstable pain because of the length of time taken to reach steady-state. When the patch is removed, the remaining depot can take up to 72 hours to clear.

Hydromorphone (Palladone) is approximately 7.5 times as potent as morphine and has been widely used in the United States for the treatment of cancer pain. It is now licensed in the UK and is available as 1.3mg and 2.6mg immediate-release capsules and in a range of strengths as controlled-release capsules.<sup>7</sup> Patients who have reported confusion, loss of concentration, vivid dreams or hallucinations with minimal doses of morphine

TABLE 1: SIDE EFFECTS OF OPIOIDS AND SUGGESTED TREATMENTS	
Side effect	Treatment
Constipation	All patients should have laxatives co-prescribed regularly. A stimulant laxative and faecal softener are required (eg, lactulose plus senna or co-danthramer)
Nausea (rarely lasts beyond the first few days)	Anti-emetics can be prescribed to be taken if required (eg, metoclopramide, haloperidol)
Sedation (should resolve after a few days)	Patients should be advised that they might feel sleepy at first or when the dose is increased. They should avoid skilled tasks. Sedation persisting beyond a few days should be investigated as it might indicate toxicity
Dry mouth (occurs particularly where other anticholinergic drugs are co-prescribed)	Patients should be encouraged to practise good oral hygiene. The sucking of boiled sweets or ice chips, chewing gum, and taking frequent sips of water are helpful. Artificial saliva solutions might be needed. Avoid glycerine and lemon mouthwash as this can worsen dryness

## Durogesic patches: patient education

- 1 The patch should be changed at the same time of day every three days
- 1 The replacement patch should be applied to a fresh area of skin after removal of the previous patch
- 1 Avoid sticking the patch to areas of irritated or irradiated skin, scar tissue, or to oedematous (swollen) skin
- 1 Avoid direct contact between the patch and hot water bottles or heat pads
- 1 Ensure that there is good contact between the patch and the skin. If adherence is poor, Micropore tape can be used
- 1 Used patches should be folded over, enclosing the drug reservoir, and disposed of in normal household waste

may benefit from a change to hydromorphone.<sup>8</sup>

Oxycodone is another step 3 opioid. It has been available as suppositories as a special order for many years and has now been launched as standard and controlled-release oral formulations (Oxynorm, Oxycotin). It has a high oral bioavailability and is twice as potent as oral morphine. No active metabolites that can accumulate in renal failure have been identified. The modified-release formulation of oxycodone has been shown in a randomised, double-blind crossover trial to be associated with fewer hallucinations and less sleep disturbance than oral morphine.<sup>9</sup> There is no commercially available injectable preparation.

### ADJUVANT ANALGESICS

Adjuvant analgesics are drugs whose primary indication is not analgesia, but which act as analgesics in certain situations. Such drugs include tricyclic antidepressants, anticonvulsants, and corticosteroids. They can be used at any stage on the analgesic ladder and are generally used for pains which respond poorly to opioids.

Tricyclic antidepressants have been shown to be effective for the treatment of neuropathic pain.<sup>10</sup> There are no preparations licensed for this use although amitriptyline is commonly used. The dose should be started low (10mg–25mg) and increased gradually; doses rarely need to exceed 75mg daily. Analgesic effects should be seen in three to seven days.

Anticonvulsants are also used in the treatment of neuropathic pain. Gabapentin is licensed for this indication although others, carbamazepine, sodium valproate and clonazepam, are also widely used. Gabapentin has been shown to be effective for neuropathic pain in a recent randomised controlled trial.<sup>11</sup> Gabapentin should be initiated at 300mg and increased by daily increments of 300mg to 900mg then more gradually to a maximum of 1,800mg.<sup>12</sup> Other anticonvulsants should be commenced at a low dose and increased

until analgesia is achieved or intolerable side effects are seen. There is no correlation between anticonvulsant plasma level and analgesic effect.

No measurable differences have been shown between tricyclic antidepressants and anticonvulsants in the treatment of neuropathic pain in efficacy, or adverse effects. Choice is based on relative contraindications, potential drug interactions and risk of side effects in an individual patient. Patients will vary in their analgesic response to various treatments and might require a combination of anticonvulsant and tricyclic antidepressant. It is good practice to introduce one drug at a time.

Corticosteroids are also used in the treatment of cancer pain. Dexamethasone is commonly used in palliative care because its potency, reduced mineralocorticoid effects and range of formulations make drug administration easier and improve compliance.

Clinical experience has shown dexamethasone to be a useful adjuvant in raised intracranial pressure, severe bone pain, nerve infiltration, soft tissue infiltration and liver capsule pain. The dose and duration of treatment are dependent on clinical response. High doses of up to 16mg daily might be required. The oral route should be used if possible with the last dose of the day given no later than 6pm to avoid insomnia.<sup>13</sup> High-risk patients, such as those over 60 years of age, those taking concurrent NSAIDs or anticoagulants, and those with a history of peptic ulcer, may require con-

comitant gastroprotection with a proton pump inhibitor.<sup>14</sup>

The management of pain in palliative care patients presents many challenges in pharmaceutical care. Drug therapy is central to the control of physical symptoms and pharmacists can advise on choice of analgesics and appropriate concurrent therapy. Palliative care patients present particular pharmaceutical care issues in that they might have frequent changes of medication, move between different care settings and require "specials" or drugs used outside the licensed indications. Communication between pharmacists in primary care, hospital and hospice can reduce discrepancies among medicines prescribed when the patient changes care setting.<sup>15</sup> Provision of good information, both verbal and written can significantly improve patients' understanding of therapy and improve adherence.<sup>16</sup> Pharmacists are ideally placed to offer advice on appropriate use of compliance aids, alternative formulations or routes of administration, and safe storage and destruction of medicines.

Good communication is essential to ensure continuity of therapy and consistency of advice because patients may have input from many health professionals in primary, secondary and tertiary care. Palliative care provision varies across the UK both in primary care and in hospitals. It is useful to be aware of the provision for palliative care in your own area and to liaise with your local specialist.

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