Pain management in palliative care: art or science

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Abstract

Pain management in palliative care is both an art and a science. Essential to good pain control is an understanding not only of the pathophysiology of the origin of the pain, but also the impact that the pain is having, as the palliative patient may have to live with the symptoms of disease for months or even years. Interventions can then be targeted and at various times, may include a range of pharmacological treatments, psychological or spiritual support and possibly the involvement of other specialties to alleviate a particular problem.

Keywords Multidisciplinary; opiates; palliative; routes of administration

Royal College of Anaesthetists CPD Matrix: 3E00

Learning objectives

After reading this article, you should:
- be able to explain a range of pharmacological and non-pharmacological options to optimize pain control in palliative care
- understand that pain may have a large psychological component
- understand that not all pain is opiate responsive
- understand different routes of administration and the rationale behind a particular choice
- recognize the need for a responsive individualized plan of care

It has long been debated whether medicine is an art or a science, and without doubt, the management of pain in palliative care uses both elements: a thorough understanding of the pathological processes underlying the pain, combined with the art and instinct of asking the right questions. ‘Palliative care’ can span months or even years, the aim of treatment being to improve quality of life rather than altering the quantity and may involve aggressive intervention to further that aim. It is distinct from ‘end of life care’ where the patient is in the last hours or short days of life, and the focus is purely on keeping comfortable with minimal medical intervention. Although the vast majority of pain control in palliative care is often focussed on cancer pain, there are significant areas of need in neurodegenerative diseases such as motor neurone disease and multiple sclerosis, as well as in chronic conditions such as chronic obstructive pulmonary disease.

Who decides what is pain – physiologist or patient?

Physiologists divide pain into nociceptive pain at the site of damage and neuropathic where the nerves are affected and the pain sensed at a distance from where the pathology lies. With the scientific element, if we consider a patient with a lumbar spine metastasis impinging on nerve roots, there will likely be pain from inflammation, pain from the destructive process in the bone, and also neuropathic pain because the nerves are being irritated. What the patient describes as pain is actually a combination of different aetiologies or ‘colours’ mixed together, and not infrequently, a cocktail of analgesics from different families is required to treat the different elements. The art is then of tailoring the various analgesics in the right quantities or ‘shades’ to treat the different pains, rather like an artist mixing paints to reach the perfect colour.

It is vital to be curious and obtain a clear understanding of the pain and how it is affecting the patient’s quality of life. While this takes time, it is usually time well spent as it also allows for the doctor–patient relationship to develop which in turn builds trust. The whereabouts and nature of the pain (stabbing, shooting, gnawing and so on) as well as precipitating and relieving factors may give some insight into the aetiology, and from that, how to manage the physical pain. However, knowing how that actually impacts on the person is just as important. Not infrequently there are a number of pains, and these may need to be addressed separately. Pain is a very individual sensation and is often a reflection not only of the underlying pathological process but also the patient’s previous experiences, anxieties and fears. It is important to acknowledge the pain and its impact, but also to be realistic in what is achievable. Someone who expects an instant resolution in their pain is likely to be disappointed and then the bond of trust and faith is destroyed. Hope can be given by an open discussion about aiming to make the pain tolerable if not completely resolved, and while this may take time, there are different options that can be tried to obtain the best outcome for the patient.

Which medications to choose and why?

The WHO analgesic ladder is well validated and is a good starting point for pain control. On step 1 the humble paracetamol is very easily overlooked, but is a mild anti-inflammatory, analgesic and neuropathic with relatively few side effects. Step 2 includes drugs such as codeine and tramadol, and step 3 is opiates of which morphine, oxycodone and fentanyl are the most commonly used.

The initiation of opiates requires a thorough explanation as there are many misconceptions and fears about it. Some patients have concerns about addiction, that it will make them feel drugged and confused, and others fear it might either prolong or shorten the life span. The National Institute of Health and Care Excellence (NICE) guidance advises using oral morphine as first line, provided the renal function is satisfactory, and converting to alternatives such as oxycodone or fentanyl if there are adverse effects such as hallucinations or opiate toxicity, or a different route of administration is preferable. In renal impairment, the

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half-life of morphine and oxycodone and their metabolites is prolonged causing an increased risk of opiate toxicity. Fentanyl relies less on the renal route and therefore has a greater safety margin in severe renal impairment.

Morphine is available as a 12 hour slow release oral medication, with an immediate release form or top up boost, Oramorph, for break through pain, the dose of which is calculated as one sixth of the total slow release dose over 24 hours. If more than three break-through doses are required in a 24 hour period, an increase in the 12 hourly dose may be indicated. Oral oxycodone is generally used if the estimated glomerular filtration rate (eGFR) is between 30 and 50 ml/min, or if there have been previous adverse effects such as hallucinations with morphine and comes again in the two formulations. Fentanyl is available in patch form which needs changing every 72 hours, so it can also be the opiate of choice in people whose compliance with twice daily opiate regimes cannot be guaranteed, or who have issues with swallowing or absorbing oral medication. As it takes 24—48 hours to derive benefit from a change in patch strength, patches are not recommended when pain is unstable. By using the subcutaneous route, it is possible to stabilize the pain with an appropriate opiate (diamorphine, oxycodone or alfentanil) administered via a battery-operated syringe driver, the dose being reviewed every 24 hours and if necessary titrated until a pain control is achieved. At this point, the syringe driver doses can be converted to an equivalent dose in patch form or oral form, depending on the rationale behind originally starting the syringe driver (see Figure 1).

Adjuncts

While some patients gain significant relief from opiates alone, many do not, and in some situations opiates appear to have no effect at all. In the case of bowel colic secondary to constipation, opiates may even exacerbate the situation.

Depending on the suspected aetiology of the pain, additional or adjunct medications may be worth considering. The list commonly includes steroids or non-steroidal medications, neuropathic agents such as amitriptyline, gabapentin, or pregabalin, and sometimes anti-spasmodics.

It is important not to forget topical measures such as heat pads, TENs machines and also lidocaine plasters which can be of benefit. Infusions such as zoledronic acid can relieve bone pain from metastases when given monthly.

In selecting any adjunct, it is important to consider pre-existing medical co-morbidities such as renal failure or a previous gastro intestinal bleed, which may preclude the use entirely even if it were the ideal drug, or require a dose reduction in order to avoid toxicity. One should also be mindful that the addition of an adjunct, especially an anti-neuropathic agent, can have an opiate sparing effect, such that someone who has been long established on a stable dose of opiate, may become opiate toxic and require a dose reduction of opiate as the dose of anti-neuropathic agent increases.

In a few cases where the pain is severe, and a complex cocktail of opiates and adjuncts have not alleviated the symptoms, an inpatient trial of ketamine or methadone may be indicated, initiated under close specialist supervision. Many patients will recognize ketamine as a veterinary drug, and will need to be warned about the potential side effects of vivid dreams, for which a small dose of prophylactic haloperidol is often given. The risk of haemorrhagic cystitis although rare, requires immediate cessation of the drug. Methadone is a complex drug to initiate because of its pharmacokinetics, in particular its very long half-life and its wide distribution in the body before reaching a steady state.

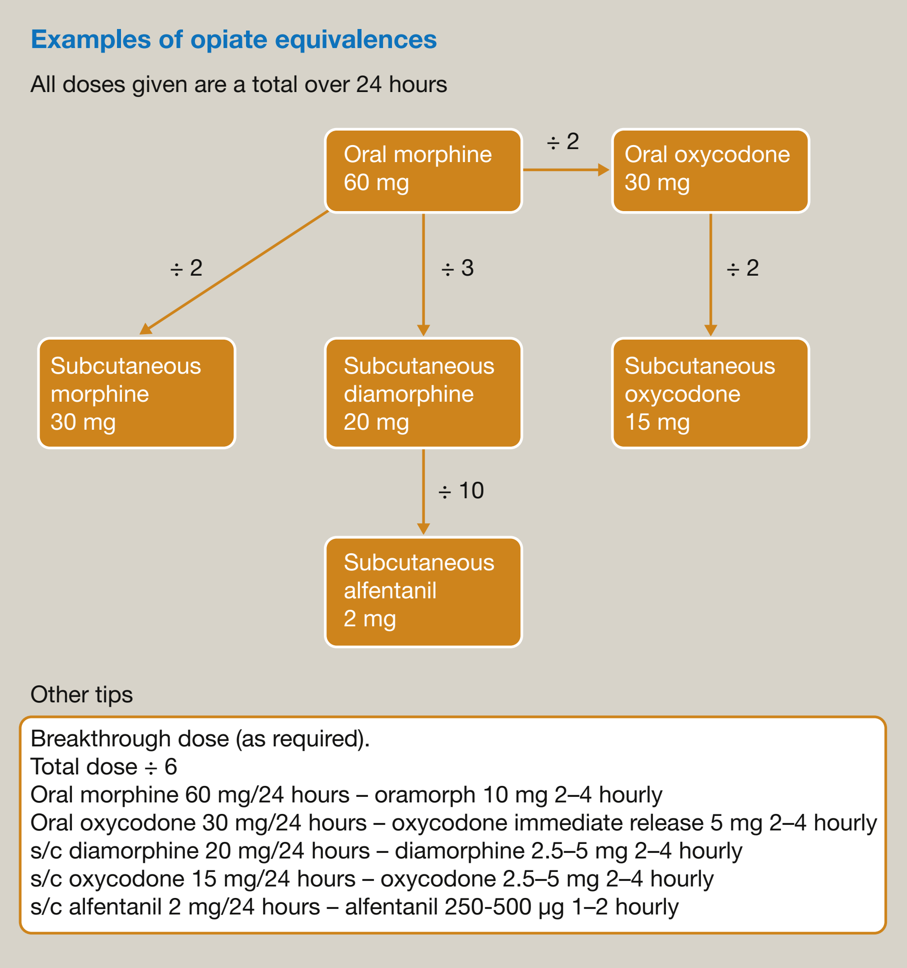
Team work

Finding the right balance of pain relief and side effects can only be done in conjunction with the patient; while one might choose to tolerate mild drowsiness or a dry mouth to achieve better pain control, another might prefer to endure a bit more discomfort but have fewer side effects. Families often struggle with this, and it is worth emphasizing that none of the medications are altering the course of the illness, just how well that life is experienced, and the only person who can judge their quality of life is the patient.

In order to achieve good symptom control, palliative care may involve considering active treatments such as further chemotherapy, or invasive interventions such as insertion of a venting percutaneous entero-gastronomy tube to relieve the symptom of vomiting from multi-level small bowel obstruction. Involvement of the multidisciplinary hospital team can be invaluable as careful consideration needs to be given to each situation and expert advice sought; is the procedure technically possible and even if it is, is this the right choice for that particular patient? Considerations include fitness and whether the patient will live long enough to benefit from the intervention as in the case of radiotherapy, as well as logistical and practical elements, such as whether they feel well enough to travel to another centre or are able to tolerate the procedure. A frank and open discussion of the pros and cons of the procedure or intervention can help a patient make an informed decision that is right for them. In addition to the medical considerations, the patient may decide that, for them, the benefits or outcome may not justify the investment in time and potential loss of quality of life, and decline the intervention.

Who are you going to call?

While palliative doctors are very good at identifying the problem, expertise from other specialities is often needed to improve or solve it. Oncologists may be able to offer palliative chemotherapy in certain instances, for example in an attempt to dry up recurrent ascites or to treat superior vena cava obstruction in small cell lung cancer. Radiotherapy can be used variously to treat a localized bone metastasis causing tenderness, to stop bleeding be it haemoptysis in a lung cancer, or a skin metastasis eroding through the skin. The gastroenterologists may well be able to stent a single level small bowel obstruction to relieve vomiting, while the surgeons might consider operating if there is a single level large bowel lesion or a troublesome fistula has formed. If the bowel obstruction is at multiple levels, then a venting gastronomy can be an effective treatment. The insertion of a biliary stent to relieve jaundice can palliate itching and pain from recurrent biliary sepsis. Urologists and radiologists may help relieve obstructive uropathy either with insertion of external nephrostomies or internal stents, with the intention of normalizing renal function thereby relieving the symptoms of renal


Examples of opiate equivalences

All doses given are a total over 24 hours

Other tips

Breakthrough dose (as required).
Total dose ÷ 6
Oral morphine 60 mg/24 hours – oramorph 10 mg 2–4 hourly
Oral oxycodone 30 mg/24 hours – oxycodone immediate release 5 mg 2–4 hourly
s/c diamorphine 20 mg/24 hours – diamorphine 2.5–5 mg 2–4 hourly
s/c oxycodone 15 mg/24 hours – oxycodone 2.5–5 mg 2–4 hourly
s/c alfentanil 2 mg/24 hours – alfentanil 250-500 μg 1–2 hourly

Figure 1

failure as well as possibly enabling further palliative treatments. Anaesthetic colleagues may be called on for nerve blocks which, though the effects are often short lived, may provide an analgesic window for a patient to have an essential scan or be transported home; for instance coeliac plexus blocks can be game changing for the neuropathic pain experienced in pancreatic cancer, and similarly for the complex pain in pleural mesothelioma, brachial plexus block or cordotomy can help.

The psychological impact

Allusion has already been made to the impact that the psyche and life experiences of a patient and their family can have on the patient's perception of physical pain. Early identification and involvement of appropriate support services such as clinical psychology, Macmillan advice and information, or spiritual support may be invaluable in untangling complex psycho-social situations which are having an overall impact on the patient and their family, at a time when the patient still has the time and energy to resolve issues. A person with significant unresolved issues in the terminal phase, be they practical such as the lack of a will, or spiritual and emotional, may well suffer more pain than someone who has had the opportunity to put their affairs in order and feels at peace. Complementary therapy and relaxation can provide relief of pain, and though often in short supply in acute settings, can make a huge difference to someone's outlook on life and ability to manage their pain.

Palliative to terminal care

In palliative care, death is not seen as a failure as the very nature of the speciality is one where people have incurable disease which they have to live with, and will likely die from, at some point. A bad death occurs when the patient or their family feel that things could have been done better. The main areas of complaint are about a perceived lack of communication and honesty, and a failure to identify when their loved one is dying.

As doctors, we are hard wired to 'fix' and our instinct is very much to 'do something' however fruitless, rather than admit to ourselves and the patient that there is nothing more that medicine can do to alter the situation. This is the stage when palliative care inevitably moves toward end of life care, and key in achieving a good death is recognizing this transition and preparing the patient and family for the change of focus.

In the final days, as a person becomes less able to manage oral medication, it is important to review the medication list and consider which are still essential to the patient's wellbeing and symptom control, (rather than a blanket crossing off of all oral medication) and whether there is an alternative route of administration. Liquid formulations may be easier to swallow than tablets, and this may prolong the use of the oral route. Some medications can be given subcutaneously, either as a bolus, but more commonly through a subcutaneous (s/c) syringe driver over a 24 hour period to achieve a steady state of medication in the system. Not all dying patients experience pain, and not every dying patient will need a syringe driver.

Symptom control in terminal care

The key area to consider in symptom control in a patient who is imminently dying is 'anticipatory' medications for pain, anxiety and breathlessness, agitation and also for excess secretions. It is important to recognize that agitation in the terminal setting is not necessarily due to physical opiate responsive pain, and judicious use of drugs such as midazolam for anxiety and haloperidol for mental distress may be more appropriate and effective. Urinary retention is very easily overlooked in this situation and must be excluded. Following on from the publication of the 2018 Gosport Independent Panel's findings into prescribing at the Gosport Memorial Hospital, there may well be concern in some quarters about the use and dosage of medication; the key point is that starting doses need to be proportionate, and that any subsequent increases are a reflection of the patient's requirements over the previous 24 hours. Careful documentation is essential.

Initiating subcutaneous opiates

Opiate-naïve patient (not already established on regular opiates):

- Consider renal function and select appropriate opiate.
- Prescribe 2.5–5mg diamorphine or 1.25–2.5mg oxycodone s/c 2–4 hourly as required.
- Daily review – if requiring three or more doses in 24 hours, start continuous infusion.
- If developing side effects – hallucinations, myoclonic jerks - consider alternative opiate.

Already on regular opiates:

Oral

- Review renal function if available.
- Convert oral sustained release dose to equivalent dose of same opiate s/c. (e.g. oral morphine converts to s/c diamorphine or s/c morphine, oral oxycodone to s/c oxycodone) unless renal function has deteriorated. (see opiate equivalence chart).
- prescribe s/c 'as required' dose, calculated as 1/6 of total 24 hour dose, 2–4 hourly as required.
- review daily and titrate depending on number of additional doses required over last 24 hours.

Transdermal

- Prescribe s/c 'as required' dose of appropriate opiate depending on renal function (patients will usually have been prescribed oral immediate release medication so use s/c version of their previous oral medication unless good reason to change).
- If requiring three or more additional doses in 24 hours, start continuous infusion of opiate but **continue** the patch.
- If eGFR is less than 30 ml/min/m,[3] alfentanil is the opiate of choice, with alfentanil as required for break through calculated in the same way (1/6 of total infusion dose).
- The breakthrough dose will be 1/6 of the total opiate dose which comprises the patch and the syringe driver. It is easy to overlook the presence of the opiate patch.

Some considerations and tips:

- Be aware that some people seem more sensitive to one opiate than another. When converting between opiates, particularly in higher doses, a modest dose reduction initially may be appropriate to avoid opiate toxicity.
- A slight under conversion may also be appropriate when converting from the oral to subcutaneous routes, particularly where there is a suspicion that the oral dose may not have been fully absorbed.
- After altering oral sustained release or continuous subcutaneous opiate infusions, remember to review the breakthrough dose so it is still proportionate (1/6 of total 24 hour dose)
- Alfentanil has a short half-life (1–2 hourly). Outside specialist inpatient settings there may be a relative lack of familiarity with its use. Cautious use of low dose oxycodone in poor renal function is sometimes used for break through doses particularly in the community.

Less common subcutaneous infusions

Other medications such as ketamine and methadone, if previously administered orally, should be converted to subcutaneous administration following advice from the specialist palliative care team. Dexamethasone if it is being used for pain control, for instance in headache from cerebral metastases, or if prolonged use could have caused adrenal suppression. Long term antiepileptics such as Levitiracetam can be administered subcutaneously, as can replacement doses of benzodiazepines with midazolam. A 10-mg stat subcutaneous dose of midazolam is recommended if there is the possibility of a catastrophic bleed or convulsions.

A case study: a truly multi disciplinary tale

Anne was a 51-year-old motorcycle enthusiast who was referred by the uro-oncologist for symptom control. Treated 18 months previously for a squamous cell cancer of the bladder with pelvic exenteration and formation of a urostomy, she now had pain radiating down her left leg. A staging CT had shown bone destruction around the left side of the pelvis and acetabulum with no distant metastases. She had no past medical history of note, and her renal function was normal. She disliked taking any medication of any kind. She had a partner who worked away, they lived 25 miles from the hospital, and logistically getting to clinic appointments was challenging.

Palliative care and community services

Seen the week before Christmas, Anne was describing a constant boring pain in her left groin punctuated by unpredictable shooting pains down her left leg. Her left leg would suddenly 'give way' and although she hadn't fallen, she was now walking with a stick. She was unable to sit normally for any period of time, she was being woken with the pain, and most important to her, was unable to ride her motorbike. She was already on paracetamol and slow release morphine but did not feel that the increase in opiate doses had made a significant difference, nor did she report much relief from Oramorph either. Non-steroidal anti-inflammatory drugs had also been tried without marked improvement, although she was still taking them. There seemed to be a clear neuropathic element to the pain, but following a discussion about neuropathic medications, Anne opted for a trial with a higher dose of Oramorph and taking break through doses more liberally than she had been, in case the current opiate dose was insufficient, rather than initiate pregabalin straight away. It was agreed for telephone review in 3 days' time, and if there was no improvement, then low-dose pregabalin would be initiated. A prescription was given in the clinic with a clear plan of how to titrate it upwards over the coming Christmas and New Year period. Phone contact was maintained, as there was a possibility that if the pain responded well to neuropathic medication, she might need a reduction of opiate dose to avoid opiate toxicity. Her GP and community specialist nurse were aware of the plan and were monitoring her locally.

Oncology and palliative care

In the first week of January, Anne was now on a reasonable dose of pregabalin, but again there was no huge improvement in the pain. She felt her leg had become weaker, and on repeat examination, there was an exquisitely tender area in her left iliac bone which, on discussion with the oncologist, was amenable to a fraction of radiotherapy and Anne felt that she could manage the 70 mile trip each way. She was also complaining of a new colicky abdominal pain and had been constantly nauseated, at times vomiting up her medication. She had normal bowel sounds, and it was felt that, despite the regular use of laxatives, the cause of this was opiate induced constipation. A subcutaneous syringe driver was started with an anti-emetic and oxycodone, the change of opiate being in case the pain responded better to this, and also to guarantee the absorption of the dose.

Palliative care, radiology and surgery

Two weeks later, following an improvement initially in both pain and sickness, Anne's pain in her leg and groin worsened and she was now passing faeces per vagina, as well as per rectum. Some of the pain eased when she opened her bowels. Following discussion with the radiologists and surgeons about how best to visualize the situation, a further CT confirmed a vagino-colic fistula and as her vaginal discharge was very distressing, urgent referral to the surgeons was made for further management. An outpatient barium enema was performed, and 2 days later, Anne was admitted onto a surgical ward with worsening abdominal pain since the barium enema.

Ever increasing doses of opiates and trials of additional neuropathic such as amitriptyline and clonazepam, which can also act as a muscle relaxant, had no impact on her pain. It was unclear how much of her pain was related to her intra-abdominal pathology, and whether a defunctioning colostomy would be technically possible and palliate symptoms. A surgical MDT discussion left the surgeons split about whether surgery was appropriate, but Anne was very keen to do anything that might improve her quality of life, even with the huge risks, as she felt she had little to lose. While the deliberations were ongoing, there were continued efforts to improve her pain control medically. A trial of ketamine seemed to help the pain a little, but the tricks that it played on her brain were such that she asked for it to be stopped.

Palliative care, surgery and anaesthetics

One brave surgeon, taking everything and especially Anne's thoughts into account, agreed to operate. She survived the surgery but the formation of a colostomy did not have the analgesic effect that had been hoped for, and there were no further pharmaceutical options available in a non-specialist unit. The chronic pain anaesthetist reviewed her for consideration of any kind of nerve block but the destruction of the pelvis was such that only a surgical or chemical ablation would be appropriate, and the procedure is offered only in certain specialist centres all of which were too far away for Anne to contemplate. Referral was made to her local hospice, but understandably, a period of postoperative stability was required before they felt it sensible to agree to a transfer. The day before the planned transfer, her stoma prolapsed and, on review, the surgeons felt there was nothing more they could offer to improve the situation.

Transition to end-of-life care

Frank discussions were held with Anne, who was becoming septic, and her family about the fact that she was going to die of sepsis secondary to bowel infarction indirectly caused by surgical intervention, and that increased analgesia and sedation were the only options available to keep her comfortable, a side effect of which would be that she would likely be less responsive. Owing to the honesty of the conversations with Anne and later, her family, when she died a week post-surgery of an infarcted bowel, the family were really grateful that she had been listened to throughout her palliative care journey. Even though her pain had never been perfectly controlled, the fact that no one gave up on her, and the surgery was a procedure that she dearly wanted, meant that they felt that everything possible had been done to give her the best chance. ◆

FURTHER READING

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