

THE PALLIATIVE CARE NURSE

Palliative Care

medi+WORLD International 2013

Case Presentation



Mrs Hakouz was diagnosed with breast cancer six years prior to seeing you.

Her treating physician requests you provide at home care. She tells you her right hip has been painful for one week. You schedule a long home visit for that day.

There has been no history of trauma to Mrs Hakouz's hip. When the pain has been particularly bad, she has taken paracetamol tablets once or twice a day and they helped relieve the pain.

Your colleague saw Mrs Hakouz several days ago, when you were on leave and ordered an X-ray of her right hip. The X-ray findings were normal.

Given that Mrs Hakouz's pain has responded to prn doses of paracetamol, it is likely that 4 hourly paracetamol would control her pain. If 4 hourly paracetamol does not control her pain, then Mrs Hakouz needs to be told to report this to you.

If Mrs Hakouz's pain is not well controlled, initiate an opioid, such as morphine or oxycodone, rather than codeine. Morphine and oxycodone are much more flexible than codeine in terms of dose escalation.

Once the cause of the pain is established, appropriate adjuvant analgesics (e.g. corticosteroids) and other modalities (eg. radiotherapy) should be considered.

The bone scan confirms an isolated metastasis in Mrs. Hakouz's right hip.

Question

Which of the following statements about morphine are true?

One or more may be correct

1. Cancer patients commonly develop rapid tolerance to the analgesic effect of morphine.
2. There is a ceiling dose for morphine given to patients with cancer pain.
3. Oral morphine causes significant respiratory depression in the majority of cancer patients.
4. Morphine use in cancer patients carries a high risk of psychological dependence.
5. Under dosing with morphine is the main reason cancer patients suffer unrelieved pain.

Answers and Feedback

1. Cancer patients commonly develop rapid tolerance to the analgesic effect of morphine.

The authors disagree.

Increases in opioid doses in palliative care patients are probably due either to increasing nociceptive pain signals due to disease progression and/or tolerance. Tolerance is a pharmacodynamic property in which an increase in dose is required to produce the same level of effect. Some degree of tolerance probably occurs in most patients who receive opioids during the course of a terminal illness, so the therapeutic index may decrease. However this tends to be a gradual process rather than a rapid one. Tolerance is not considered to be a barrier to the provision of adequate analgesia.

2. There is a ceiling dose for morphine given to patients with cancer pain.

The authors disagree.

There is no ceiling dose for morphine in the management of cancer pain. The individual patient's analgesic needs should determine the way in which the morphine dose is titrated. The correct morphine dose is one that results in pain control without the presence of intolerable side effects. It is also important not to continue escalating the dose of morphine if the response is minimal or short term. In such cases, a different approach to pain management is required, ie. the use of other analgesic drug classes, route changes, interventions (eg. neurolysis) or treatment of the underlying disease.

3. Oral morphine causes significant respiratory depression in the majority of cancer patients.

The authors disagree.

In practice, significant respiratory depression is uncommon in patients where the morphine dose is gradually titrated according to individual needs. Respiratory pain can be reversed by giving naloxone, but this may precipitate severe pain.

Exceptions include:

- patients at risk of respiratory failure from other causes
- patients with impaired renal function
- opioid naïve patients
- patients receiving an excessive dose of morphine and/or too often
- patients who have had a procedure (eg. nerve block) to acutely relieve their pain.

4. Morphine use in cancer patients carries a high risk of psychological dependence.

The authors disagree.

As the risk of psychological dependence in cancer patients taking morphine is extremely low, fear of addiction should not be a reason to delay prescribing it. One needs to bear in mind that the majority of cancer patients will remain on a regular opioid until they die, so the issue of addiction does not arise. If the drug needs to be ceased, this can be done gradually (e.g. reducing the amount by 20-25% per day) so that effects of psychological dependence are avoided or minimised.

Exception: A small number of patients with a past history of drug abuse or psychiatric illness.

5. Under dosing with morphine is the main reason cancer patients suffer unrelieved pain.

The authors agree.

Unfortunately a varying degree of apprehension or reticence about using opioid drugs still exists amongst some doctors and patients. Doctors who still believe some or all of the common morphine myths may be reluctant to prescribe adequate doses.

Morphine, used appropriately, does not hasten death.

Morphine myths continued...

Question

Which of the following statements about morphine are true?

One or more may be correct

1. The early use of morphine for cancer patients reduces the likelihood of it being useful later.
2. A withdrawal syndrome is difficult to avoid if the dose of morphine is gradually reduced before complete cessation.
3. Severe pain requires parenteral morphine, even if a patient can swallow.
4. Morphine should be given on an 'as required' basis in chronic cancer pain.
5. Patients do not become tolerant to the sedative effects of morphine when it is used to treat chronic cancer pain.

Answers and Feedback

1. The early use of morphine for cancer patients reduces the likelihood of it being useful later.

The authors disagree.

Morphine has a wide therapeutic range, so it can be titrated according to the need of each individual patient.

There are many cancer patients who take morphine for several years before their death. The dose of morphine is simply increased as/if required.

2. A withdrawal syndrome is difficult to avoid if the dose of morphine is gradually reduced before complete cessation.

The authors disagree.

The main reason for ceasing morphine in a cancer patient would be that pain relief had been successfully achieved by another treatment, eg. surgery or radiotherapy. If the patient's dose of morphine was gradually reduced by 20-25% per day, then withdrawal symptoms should be minimised or avoided.

3. Severe pain requires parenteral morphine, even if a patient can swallow.

The authors disagree.

Analgesics should be prescribed orally whenever possible.

Oral morphine is as effective in providing analgesia as the equivalent dose of parenteral morphine. (The oral to parenteral conversion ratio for morphine is 3:1).

4. Morphine should be given on an 'as required' basis in chronic cancer pain.

The authors disagree.

To effectively prevent pain, analgesia is best given regularly rather than as required.

Analgesia also needs to be prescribed on as as needed (prn) basis for breakthrough or incident pain eg. prior to showering.

5. Patients do not become tolerant to the sedative effects of morphine when it is used to treat chronic cancer pain.

The authors disagree.

It is not unusual for patients to feel drowsy during the first few days of commencing morphine, however the drowsiness is generally mild and tends to settle within several days.

Further information

In order to facilitate compliance, it is important patients be informed of this side effect. They should also be assured the drowsiness is likely to improve in 2-5 days and it is worth persevering with the treatment.

In summary, it is essential the treating doctor dispels any myths their patient may have regarding the taking of morphine. It is also important to emphasise that patients can live for a long time while taking morphine, and how it can improve quality of life by providing good pain control.

(continued next page)

Further history

Mrs Hakouz agrees to commence oral morphine after her concerns have been addressed. She also continues to take Naproxen tablets, 500mg bd.

Question

Given that Mrs Hakouz is "opioid naive" (is not currently taking any opioids), what dose of morphine mixture (immediate release morphine = IRM) would you prescribe for the next 24 hours, and how often should it be administered?

Authors' answer

Morphine mixture 5 - 10 mg 4 hourly

10mg morphine mixture is the usual starting dose for a 50 year old opioid naive patient.

Morphine mixture is available in the following strengths: 1mg/ml., 5mg/ml., 10mg/ml, 20 mg/ml and 40 mg/ml.

Effective management of cancer pain involves giving analgesia at regular intervals rather than when required.

The aim is to prevent the pain recurring before the next dose of analgesia is taken.

Question

Which of the following is/are TRUE of the dose of morphine mixture in an opioid naive patient?

An elevated creatinine of 300 mmol/L would not alter my starting dose of morphine.

Authors' answer

The statement is FALSE.

The major metabolites of morphine are dependent on renal excretion. Therefore a patient with impaired renal excretion needs a lower starting dose of morphine than a patient with normally functioning kidneys.

Question

It is appropriate to initiate a lower than usual dose of morphine mixture eg. 2.5 - 5 mg 4 hourly for a frail 75 year old lady

Authors' answer

This statement is TRUE.

Start with a lower dose in an elderly and/or frail patient. The major metabolites of morphine are dependent on renal excretion. An elderly frail patient is more likely to experience side-effects such as confusion or drowsiness if they are commenced on the standard morphine dose. Reasons for this could include renal impairment, low body weight and multiple drug interactions.

Question

It is appropriate to make the same percentage increase in the daily dosage of morphine mixture in a frail 75-year-old patient as for a 50-year-old patient.

Authors' answer

This statement is FALSE.

Increasing the dose of regular 4 hourly morphine mixture slowly and gradually by approximately 30% rather than the usual 50% is appropriate in managing a frail and/or elderly patient's pain. The major metabolites of morphine are dependant on renal excretion. An elderly, frail patient is more likely to experience side effects such as confusion or drowsiness if the regular dose of morphine is increased too quickly. Reasons for this could include renal impairment, low body weight and multiple drug interactions.

Question

What dose of morphine mixture prn (if any) would you prescribe for Mrs Hakouz's breakthrough pain on the day that you initiate regular morphine mixture ?

Author's answer

Morphine mixture 5 mg orally pm for extra pain

The goal of treatment is to achieve the best possible pain control.

It is therefore necessary to prescribe a breakthrough dose of morphine to supplement the regular 4 hourly dose in case the patient experiences pain between the regular doses of morphine. This breakthrough dose is prescribed prn

and is an important strategy in managing pain. It enables a more rapid attainment of an effective dose of morphine and is important in managing incident pain eg. prior to showering. It is also likely to save you from being telephoned in the middle of the night by a palliative care nurse requesting a prn morphine order.

Some palliative care doctors choose to initiate oral morphine in opioid naive patients using sustained release preparations such as Kapanol or MS Contin.

Question

What dose of sustained release morphine would you prescribe for Mrs Hakouz?

Author's answer

Available sustained release of morphine are:

* kapanol 10, 20, 50, 100 mg capsules daily or bd.

* Ms contin 5, 10, 30, 60, 100, 200 mg tablets bd.

* Ms mono 30, 60, 90, 120 mg capsules daily

The standard starting dose of sustained release morphine for opioid naive patients is generally considered to be 20 mg bd or 40 mg daily.

Question

What dose of morphine mixture prn (if any) would you prescribe for breakthrough pain if you planned to initiate sustained release morphine in the form of Kapanol 20mg bd or 40 mg daily?

Author's answer

Morphine mixture 5 mg orally prn for extra pain.

It is essential to prescribe a top-up dose of morphine mixture to supplement the regular dose of sustained release preparations of morphine. The goal of treatment is to achieve the best possible pain control. It is therefore essential to prescribe a breakthrough dose of morphine mixture to supplement the regular 4 hourly dose in case the patient experiences pain between the regular doses of morphine. This breakthrough dose is prescribed prn and is an important strategy in managing uncontrolled pain.

Continuing history

In the past, Mrs Hakouz has experienced nausea from both pethidine (given during labour) and panadeine forte, prescribed for the pain of impacted wisdom teeth many years ago.

Question

Should a regular anti-emetic be prescribed for Mrs Hakouz when morphine mixture is initiated? Yes or No?

Author's answer

Yes. Given her past history of anusea from two different opioids, it would be appropriate to prescribe a regular prophylactic anti - emetic when morphine was initiated. Example of anti - emetic include: - maxolon (metoclopramide) 10 mg tablets qid - stemetil (prochlorperazine) 5 mg tablets tds or qid - Haloperidol 0.5 mg - 1 tablet tds.

The anti - emetic can be discontinued after 5 to 7 days, as the vomiting centre is likely to have settled by then.

Question

Would you prescribe a prophylactic laxative for Mrs Hakouz?

Author's answer

The aim of perscribing a laxative with opioids is to prevent the almost universal predictable side affect of constipation. Examples of prophylactic laxative are: -

Coloxyl with senna 1- 2 tablets daily, up to tds, or

Lactulose or sorbitol 20 mls daily up to tds.

(continued)

Continung history

Mrs Hakouz is commenced on 10mg morphine mixture 4 hourly (at 0630, 1030, 1430 and 1830). She is also ordered a double dose at 2230 with the aim of keeping her pain free overnight. She also takes four top up doses of 5mg morphine mixture over 24 hours.

Question

If after 24 hours, Mrs Hakouz's pain had improved by about 50%, how much morphine would you prescribe over the next 24 hours? (include your dose of morphine mixture prn).

Author's answer

15 mg morphine mixture 4 hourly (at 0630, 1030, 1430 & 1830) and 30 mg at 2230, plus morphine mixture 5 mg prn.

Mrs Hakouz took 80 mg morphine over the previous 24 hours (10+10+10+10 +20+5+5+5+5). It is usual to increase the regular 4 hourly dose of morphine by 30 - 50% depending on clinical observation, breakthrough requirements , incident pain and physiological parameters such as renal function.

Recommended dose escalations for regular 4 hourly morphine mixture are as follows:

5mg 10mg

10mg 15mg

15mg 20mg

20mg 30mg

The breakthrough range for morphine mixture 2-4 hourly prn is usually 30-50% of the regular hourly dose.

Some patients who are prescribed regular 4 hourly morphine mixture may not understand the concept of top-up/ breakthrough doses. This means they do not take any top-up doses, and their pain remains poorly controlled.

Question

If Mrs Hakouz was such a patient, what dose of morphine would you order for her over the next 24 hours if the original regular dose was 10mg morphine mixture 4 hourly?

Author's answer

15 mg 4 hourly, that is a 30 - 50% dose increase.

Recommended dose escalations for regular 4 hourly morphine mixture are as follows:

5mg 10mg

10mg 15mg

15mg 20mg

20mg 30mg

Question

If Mrs Hakouz's pain was well controlled on the original total daily dose of 80mg immediate release morphine mixture, what dose of sustained release morphine mixture would you convert her to?

Author's answer

The total daily dose is 80 mg. So give kapanol 80 mg (10 + 20 + 50 capsules) daily or MS contin 40 mgbd (10 + 30 mg tablets).

Do not mix Kapanol and MS Contin as they have different pharmacokinetic profiles.

Do not forget to continue the 5mg top-ups of morphine mixture prn.

Question

Mrs Hakouz is having a total daily morphine dose of 80mg. What would be the equivalent dose of morphine if it was given as a continuous subcutaneous infusion?

Author's answer

Given that Mrs Hakouz's total daily dose of oral morphine is 80 mg and the oral bio-availability of morphine is effectively 30%, divide 80 by 3 = 27 mg per 24 hours in a syringe driver. This dose would then be rounded up to 30 mg per 24 hours. Some palliative care units divide the total daily dose of oral morphine by 2, rather than 3 when calculating an equivalent continuous subcutaneous infusion dose of morphine.

Continuing history

On the last day of her two-week radiotherapy course, Mrs Hakouz becomes progressively drowsy and is mildly nauseated on Kapanol 80mg daily. She is no longer on an anti-emetic.

Physical examination reveals the following signs:-

Right hip pain virtually gone.

Small pupils.

Decreased respiratory rate

Question

What is the likely explanation for these physical findings?

Author's answer

Mrs Hakouz has symptoms of a morphine overdose, her daily morphine requirement has reduced, because of the palliative radiotherapy's analgesic effect. The radiation response usually takes 2 - 3 weeks to occur.

Action: Mrs Hakouz's daily dose of morphine is reduced, and her daily dose of morphine is reduced and her daily dose of morphine stabilises on Kapanol 20mg bd.

Lesson: The dose of morphine does not necessarily need to be increased. Regular review of morphine doses is important, especially in patients who receive palliative radiotherapy.

Further Information

Let us assume Mrs Hakouz's pain is well controlled with morphine. However she subsequently develops intractable nausea, confusion and drowsiness. Her symptoms are assessed as being opioid related, after excluding other causes. (ie. brain metastases, hypercalcaemia and renal failure).

There are three different management options:

- Reduce the dose of morphine
- Change the route of morphine (eg. from oral to continuous subcutaneous infusion)
- Change morphine to a different opioid (opioid substitution)

Option one is likely to result in a return of Mrs Hakouz's pain. She is not keen to have a syringe driver at this stage, and you elect to do an opioid substitution. This involves changing a patient with unacceptable, refractory adverse effects of one opioid to a different opioid. The aim of this is to improve any adverse side effect(s) while maintaining an equivalent dose of analgesia.

Reference: Ashby M.A., Martin P., Jackson K.A. *Opioid substitution to reduce adverse effects in cancer pain management. MJA 1999; 70: 68-71.*

(continued)

Question

What analgesic could be used as an alternative to morphine, and in what form should it be administered ?

How do you convert the dose of Kapanol 20mg bd to the new analgesic?

Author's answer:

Oxycodone would be an appropriate alternative to morphine. Oxycodone is available in a sustained release formulation called oxycontin in the form of 10 mg, 20 mg, 40 mg, 80 mg tablets, given bd. The conversion ratio of morphine to oxycodone is 1 : 1. Therefore kapanol 40 mg bd could be changed to oxycontin 40 mg bd.

Each patch provides analgesia for 72 hours. Serum levels rise slowly and do not peak for 12-24 hours. It is therefore important that the previously used opioid is continued for the first twelve hours of introducing fentanyl.

Formulation of morphine**How to change to fentanyl patch**

Oral: slow release

Apply first patch at same time as final 12 hourly dose of morphine is taken

Oral: immediate release

Continue 4 hourly morphine liquid for next 8 - 12 hours

Continuous subcutaneous infusion

Continue subcutaneous morphine infusion for 8 - 12 hours

Question

If Mrs Green was taking 120mg of slow release morphine per day, what would be the equivalent dose of transdermal fentanyl?

Author's answer

The starting dose of transdermal fentanyl is calculated from the previous 24 hours dose of morphine or oxycodone (refer to product information).

To work out the dose of Fentanyl skin patch, multiply X by 25 ug/hr.

Answer $160/90 = 1.77$

Rounded off to the nearest whole number = 2.

$X = 2$

$X \times 25\text{ug/hr} = 50 \text{ ug patch}$