CLIP

15 minute Worksheet

Helping the patient with pain

7: Alternatives to morphine

Advanced level

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Aim of this worksheet

To understand what other opioids can be used instead of morphine..

How to use this worksheet

- You can work through this worksheet by yourself, or with a tutor.
- Read the case study below, then work on the questions overleaf.
- The work page is on the right side, the information page is on the left.
- Work any way you want: you can try answering from your own knowledge (in which case fold over the information page), you can use the information page (this is not cheating- you learn as you find the information), or you can use other sources of information
- It should take you about 15 minutes. If anything is unclear, discuss it with a colleague.
- If you think any information is wrong or out of date let us know
- Use the activity on the back page and take this learning into your workplace

Case study

Linda is a 43 year old lady with myeloma. Despite some poor renal function initially, she did well with chemotherapy. Two months ago she relapsed and developed lytic bone lesions. While she was awaiting the treatment to take effect she was started on morphine for pain. This worked very well, and she has been on the same dose for several weeks and continued to work. Over the past week, however. she has become increasingly drowsy with pin-point pupils and myoclonic jerks, but remains pain-free.

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INFORMATION PAGE: Alternatives to morphine

Deterioration on a stable dose of opioid

There are four broad possibilities:

- The disease is advancing (unusual over a short time scale, having been relatively well before hand).
- There is a concurrent cause of drowsiness such as hypercalcaemia (common in myeloma)
- She has taken a higher dose than usual (an error would be the likeliest as suicide attempts with morphine are rare)
- She is not eliminating her morphine as efficiently as previously.

The pinpoint pupils, myoclonic jerks and the circumstances of her illness suggest the last cause. One of the active metabolites of morphine in morphine-6-glucuronide (M6G) which is water soluble and excreted by the kidneys. Any change in renal function will make the M6G accumulate. Renal impairment can occur in myeloma (indeed Linda had this problem originally), and a deterioration in renal function with an accumulation of M6G is a likely cause.

Alternative opioids

Morphine, diamorphine and hydromorphone have renally excreted metabolites, methadone and fentanyl do not.
Hydromorphone has fewer renally excreted active metabolites than morphine and may be safe in mild to moderate renal impairment, but in severe renal failure fentanyl is the opioid of choice.
Diamorphine is converted to morphine, and apart from greater solubility useful for small volume injections it has no advantages.
Methadone has a prolonged action and should only be used by specialist teams.

1. **F**. IV fentanyl has a short half life, but transdermally it can take up to 14 hours to reach steady blood levels.
2. **T**. Neither of these two opioids are known to have active metabolites that are renally excreted.
3. **F**. A pain unresponsive to morphine is unlikely to respond to these strong opioids.
4. **F**. Fentanyl in the body fat disappears slowly- it can take up to 30 hours for the effects to wear off.
5 **T**. Fentanyl produces less sedation and patients may need lower laxative doses.
6 **F**. The pharmacokinetics of both make them very difficult to adjust in an ill patient. In addition, diamorphine is converted to morphine, so would be unsuitable for Linda while she has renal impairment.

Steps in starting an alternative opioid

Dose conversion from morphine:

Hydromorphone: dose ÷ 5 . Oxycodone: dose ÷ 1.5

Fentanyl: a quick and safe conversion is oral morphine dose in **mg per 24 hours** ÷ 3 = fentanyl dose in **microg/hour**

Last dose of morphine:

Hydromorphone: give the first dose of hydromorphone in place of the next morphine dose.

Oxycodone: give the first dose of oxycodone in place of the next morphine dose.

Transdermal fentanyl: do not give a controlled release opioid formulation at the same time as starting fentanyl. Instead, a short acting opioid should be continued on an 'as required' basis for at least 12 hours after starting fentanyl to cover the time it takes for fentanyl to reach steady blood levels and to prevent a morphine withdrawal syndrome which can occur in some patients changing to fentanyl (most commonly diarrhoea).

Laxatives

Hydromorphone and oxycodone: continue the laxatives but adjust the dose to produce a comfortable stool.

Fentanyl: laxatives should be reduced or stopped for 24 hours before starting fentanyl and then retitrated.

Minimum delay between dose increases:

Hydromorphone and oxycodone: can be increased twice daily but are usually increased every other day to allow tolerance to develop to adverse effects.

Transdermal fentanyl: at least 24 hours is needed before the dose can be adjusted.

Influences on the blood levels of the opioid:

Hydromorphone: active metabolites are increased in severe renal failure.

Oxycodone: oxycodone itself is increased in renal or liver impairment.

Fentanyl: -increased by thin skin, pyrexia or local heat.
-decreased by thick skin or factors causing poor adhesion of patches (eg. hair, sweating)

Choosing the right opioid

Subcutaneous infusion: diamorphine.
Stable pain, unable to swallow: SC diamorphine or transdermal fentanyl
Afraid of using morphine: oxycodone or fentanyl.
Infection with pyrexia: any opioid can be used <u>except</u> transdermal fentanyl
Mild - moderate renal impairment: hydromorphone.
Severe renal failure: fentanyl
Liver impairment: morphine (with care).

A postscript on methadone

Methadone is an unusual opioid which can be more effective than other opioids. Although it has the same potency as morphine, it has a long action and accumulates over several days. Experience has developed special titration regimes which include starting methadone at one tenth of the daily morphine dose. For this reason it should only be used under specialist care or advice.

What could have caused her present problems?
Could the morphine be the cause?

Since her pain is still responsive to a strong opioid, an alternative opioid could help

1. Transdermal fentanyl has a fast onset of action. T F
2. Fentanyl and methadone are safer than morphine in renal failure T F
3. Hydromorphone, oxycodone and fentanyl could be used for morphine-resistant pains T F
4. In overdose, transdermal fentanyl is easier to treat than morphine T F
5. Transdermal fentanyl causes less sedation and constipation than morphine T F
6. Methadone and transdermal fentanyl are alternatives to diamorphine SC infusions in the last days of life T F

What steps would you take to convert Linda to an alternative opioid?

	Oxycodone	Hydromorphone	Transdermal fentanyl
What is the dose conversion from oral morphine?			
When do you give the last dose of morphine?			
Should you continue laxatives?			
What is the minimum delay before increasing the dose?			
What might affect the blood levels of the opioid?			

Which opioid(s) would you choose in the following situations?

Subcutaneous infusion =

Stable pain, unable to swallow =

Afraid of taking morphine =

Renal impairment =

Liver impairment =

Infection with pyrexia =

FURTHER ACTIVITY: Alternatives to morphine

In your clinical practice, review why patients are on opioids other than morphine.

FURTHER READING: Alternatives to morphine

Journal articles

Ashby M, Fleming, Wood M *et al* Plasma morphine and glucuronide (M3G and M6G) concentrations in hospice patients. *Journal of Pain and Symptom Management* 1997; **14**: 157 - 167.

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Kirvela M. Lindgren L. Seppala T. Olkkola KT. The pharmacokinetics of oxycodone in uremic patients undergoing renal transplantation. *Journal of Clinical Anesthesia*. 1996: **8**(1):13-8.

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Mazoit JX, Sardouk P, Zetlaoui P *et al*. Pharmacokinetics of unchanged morphine in normal and cirrhotic patients. *Anaesthesia and Analgesia*, 1987; **66**: 293-98.

Mannino R. Coyne P. Swainey C. Hansen LA. Lyckholm L. Methadone for cancer-related neuropathic pain: a review of the literature. *Journal of Opioid Management.* 2006: **2**(5): 269-76.

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Sarhill N. Walsh D. Nelson KA. Hydromorphone: pharmacology and clinical applications in cancer patients. *Supportive Care in Cancer.* 2001; **9**(2): 84-96.

Resource books and websites

A Guide to Symptom Relief in Palliative Care, 5th ed. Regnard C, Hockley J. Abingdon: Radcliffe Medical Press, 2004

Cancer Pain Relief and Palliative Care. Geneva : WHO, 1990.

Oral Morphine, Information for Patients, Families and Friends. Twycross R., Lack S.A. Beaconsfield Publishers. 1988.

Oxford Textbook of Palliative Medicine 3rd ed. Doyle D, Hanks G, Cherny NI, Calman K eds. Oxford : Oxford University Press, 2003.

PCF3- Palliative Care Formulary, 3rd ed. Twycross RG, Wilcock A. Oxford: Radcliffe Medical Press, 2008. Also on www.palliativedrugs.com

Symptom Management in Advanced Cancer, 3rd edition. 2001. Twycross RG, Wilcock A. Abingdon: Radcliffe Medical Press.

Wall and Melzack's textbook of pain, 5th ed. Stephen B. McMahon and Martin Koltzenburg, eds. Edinburgh : Elsevier Churchill Livingstone, 2006.