

# CLiP

15 minute Worksheet



Helping the patient with pain

## 6: Understanding the adverse effects of opioids

Intermediate level

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### Aim of this worksheet

To understand the adverse effects of opioids and how to manage these.

### How to use this worksheet

- You can work through this worksheet by yourself, or with a tutor.
- Read the case study below, and then turn to the Work page overleaf.
- Work any way you want. You can start with the exercises on the Work page using your own knowledge. The answers are on the Information page - this is not cheating since you learn as you find the information. Alternatively you may prefer to start by reading the Information page before moving to the exercises on the Work page.
- This CLiP worksheet should take about 15 minutes to complete, but will take longer if you are working with colleagues or in a group. If anything is unclear, discuss it with a colleague.
- If you think any information is wrong or out of date let us know.
- Take this learning into your workplace using the activity on the back page.

### Case study

Pat is a 36 year old woman, married with two sons aged 12 and 9. She had problems with her bowels for several months before some rectal bleeding made her see her GP. Investigations revealed a carcinoma of the sigmoid colon with liver metastases. She copes, with some denial, and refuses to tell her sons.

A week ago she was started on morphine for her pain. Her husband telephones you to say her pain is better, but she's feeling sick, she hasn't moved her bowels and she keeps nodding off in front of the television. He says she wants to stop the morphine to keep her head clear and to keep the morphine in reserve until things get 'really bad'.

V8

**Morphine worries**

For example, *Will I feel drugged? Will it wear off? Will I get addicted? Won't I get badly constipated? Is this the end?*

- *Feeling drugged is unlikely* since tolerance to many side effects is rapid (ie. the effects wear off quickly). Once on a stable dose patients are usually safe to do many activities, including driving.
- *Tolerance to analgesia is not seen* (ie. pain relief does not wear off with time).
- *Withdrawal symptoms are likely* if morphine is stopped abruptly (usually colic and diarrhoea), but this is *not seen* if the morphine is reduced slowly over 5 days.
- *Addiction to morphine is very unlikely*. It is very unusual for pain patients taking morphine to develop a craving for the drug. The circumstances in which they take morphine do not encourage addictive behaviour, and patients have no difficulty stopping morphine if their pain is relieved by other means.
- *Constipation is very likely*: this occurs in 99% of people on opioids and does not wear off. However, using a combination of a stimulant (eg. senna, bisacodyl) and a softener (docusate or lactulose) means it is *very unusual* that a patient has to stop taking morphine because of constipation.
- *Hallucinations*, confusion, and nightmares are *very unlikely* at therapeutic doses.
- *Prognosis*: repeated studies have failed to show that strong opioids hasten death or shorten life when used in palliative care doses and titrated correctly.

**Opioid intolerance**

True intolerance to opioids is very unusual, while allergy to opioids is rare.

**Real intolerance**

*Fear of opioids* is the commonest cause of intolerance, but can usually be managed with explanation.

*Reduced drug clearance:*

<b>Opioid</b>	<b>Renal impairment</b>	<b>Liver impairment</b>
Morphine	Active metabolites accumulate (M6G, M3G)	Little effect unless impairment is severe
Hydromorphone	Active metabolites accumulate (H3G)	Little effect unless impairment is severe
Oxycodone	Oxycodone accumulates	Oxycodone accumulates
Fentanyl	Little effect	Fentanyl accumulates
Methadone	Little effect	Methadone accumulates

**Apparent intolerance:**

*Dose too high*: this is a common problem, and is probably the reason Pat had problems after her caesarean.

*Titration too rapid*: another common problem. 33-50% increases (usually every third day) is a reasonable rate.

*Conversion ratio incorrect*: it is easy to make a mistake with the large number of opioids and routes available (see CLiP worksheet, *Changing Opioids*).

*Other cause of confusion*: when used correctly opioids are an uncommon cause of confusion. Infection, other drugs and biochemical disturbances are much more common.

*Constipation*: this should nearly always be manageable.

**Opioid adverse effects**

*Constipation* (usually, 99%) - little or no tolerance  
*Dry mouth* (often, 40%) - probably no tolerance  
*Nausea* (sometimes, 30%) - tolerance 5-10 days  
*Sedation* (sometimes, 25%) - tolerance 3-5 days  
*Poor gastric emptying* (sometimes, 20-25%) – no tolerance

*Respiratory depression* (uncommon) –tolerance in 1-3days  
*Confusion* (uncommon, 1-2%) - little or no tolerance  
*Myoclonic jerks* (uncommon)- no tolerance  
*Itch* (uncommon) – no tolerance

**Treatment of opioid adverse effects**

- *Constipation*: start a stimulant laxative (eg. senna). Usually this alone is sufficient (see CLiP worksheet on Constipation).
- *Dry mouth*: see CLiP worksheet on *Oral Problems*.
- *Nausea (area postrema- CTZ- stimulation)*: start low dose haloperidol (1 - 3mg at night)
- *Vomiting caused by gastric stasis*: start a prokinetic agent, eg. metoclopramide, domperidone.
- *Sedation*: this usually wears off by itself within 5 days, but if it persists consider using a different opioid.
- *Respiratory depression*: this is very unusual if palliative care doses and titrations are followed. If reversal is needed naloxone is titrated IV without reversing the analgesia. Give 400mcg in 10mls normal saline, in 1ml IV boluses until respiration improves. An infusion may be necessary, again at a level that does not reverse analgesia.
- *Confusion*: if due to drowsiness then the confusion will wear off, but with CNS stimulation it will be necessary to switch to another opioid or use other analgesia. Hallucinations are very uncommon at therapeutic doses.
- *Myoclonic jerks*: these are a useful sign of opioid toxicity and usually means a reduction in dose is needed.
- *Itch* is in all the books, but in practice is uncommon.

# Choose

Pat might have a number of fears about morphine. How likely is it that one of these fears may happen?

Fears about morphine	Likelihood of this effect happening in Pat – please ring your answer			
Feeling drugged (eg. being unable to drive)	Very unlikely	Unlikely	Likely	Very likely
Pain relief wearing off, needing dose increase	Very unlikely	Unlikely	Likely	Very likely
Withdrawal symptoms on stopping morphine abruptly	Very unlikely	Unlikely	Likely	Very likely
Addiction (ie. a craving for morphine)	Very unlikely	Unlikely	Likely	Very likely
Severe constipation	Very unlikely	Unlikely	Likely	Very likely
Hallucination	Very unlikely	Unlikely	Likely	Very likely

# Think

Pat's says that after a caesarean operation many years before, the doctor told her she was allergic to morphine because she became confused and vomited several times. Was she truly intolerant of the morphine?

Q. Think what could cause true intolerance to morphine?

Q. Think of situations that would cause morphine to be incorrectly blamed for a problem?

# Write

These are all possible side effects of morphine: complete the details

Side effect	Usually, often, sometimes or uncommon?	Does it wear off?	Treatment?
Constipation			
Dry mouth			
Nausea			
Sedation			
Poor gastric emptying			
Respiratory depression			
Confusion			
Myoclonic jerks			
Itch			

## FURTHER ACTIVITY: Understanding the effects of opioids

Review the protocols used by your team for prescribing and assessing the effects of morphine.

## FURTHER READING: Understanding the effects of opioids

### Journal articles

- Challand S, Frew K, Regnard C. Is there a problem with oxycodone? *Journal of Pain and Symptom Management*. 2008; **36**(6): e1–3.
- Chan JD et al. Narcotic and benzodiazepines use after withdrawal of life support: association with time of death? *Chest*. 2004; **126**(1): 286-93.
- Cherny N, Ripamonti C, Pereira J, Davis C, Fallon M, McQuay H, Mercadante S, Pasternak G, Ventafridda V. Expert Working Group of the European Association of Palliative Care Network. Strategies to manage the adverse effects of oral morphine: an evidence-based report. *Journal of Clinical Oncology*. 2001; **19**(9): 2542–54.
- Clemens KE, Quednau I, Klaschik E. Is there a higher risk of respiratory depression in opioid-naive palliative care patients during symptomatic therapy of dyspnea with strong opioids? *Journal of Palliative Medicine*. 2008; **11**(2): 204–16.
- Clemens KE, Klaschik E. Morphine in the management of dyspnoea in ALS. A pilot study. *European Journal of Neurology*. 2008; **15**(5): 445–50.
- Dean M. Opioids in renal failure and dialysis patients. *Journal of Pain and Symptom Management*. 2004; **28**(5): 497–504.
- Fallon M, Cherny NI, Hanks G. Opioid analgesic therapy. In, *Oxford Textbook of Palliative Medicine* 4<sup>th</sup> ed. Hanks G, Cherny NI, Christakis NA, Fallon M, Kaasa S, Portenoy RK. eds. Oxford : Oxford University Press, 2010, p661-98.
- Good PD, Ravenscroft PJ, Cavenagh J. Effects of opioids and sedatives on survival in an Australian inpatient palliative care population. *Int Med J*. 2005; **35**(9): 512-7
- Hanks GW, et al. Expert Working Group of the Research Network of the European Association for Palliative Care. Morphine and alternative opioids in cancer pain: the EAPC recommendations. *British Journal of Cancer*. 2001; **84**(5): 587-93.
- Harris JD. Management of expected and unexpected opioid-related side effects. *Clinical Journal of Pain*. 2008; **24**(Suppl. 10): S8–13.
- Hu WY, Chiu TY, Cheng SY, Chen CY. Morphine for dyspnoea control in terminal cancer patients: is it appropriate in Taiwan? *Journal of Pain & Symptom Management*. 2004; **28**(4): 356-63.
- 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.
- Lee MA, Leng ME, Tiernan EJ. Retrospective study of the use of hydromorphone in palliative care patients with normal and abnormal urea and creatinine. *Palliative Medicine*. 2001; **15**(1):26-34.
- Mazzocato C, Buclin T, Rapin CH. The effects of morphine on dyspnoea and ventilatory function in elderly patients with advanced cancer: a randomized double-blind control trial. *Annals of Oncology*. 1999; **10**(12): 1511-4.
- Medicines and Healthcare Products Regulatory Agency. Fentanyl patches: serious and fatal overdose from dosing errors, accidental exposure and inappropriate use. *Drug Safety Update*. 2008; **2**(2): 2–3.
- Morita T, Tsunoda J, Inoue S, Chihara S. Effects of high dose opioids and sedatives on survival in terminally ill cancer patients. *J Pain & Symp Manag*. 2001; **21**(4): 282-9.
- Portenoy RK, Thaler HT, Inturrisi CE et al. The metabolite morphine-6-glucuronide contributes to the analgesia produced by morphine infusion in patients with pain and normal renal function. *Clinical Pharmacology and Therapeutics* 1992; **51**: 422-431.
- Regnard C and Badger C. Opioids, sleep and the time of death. *Palliative Medicine*, 1987; **1**(2): 107-110.
- Sykes N, Thorns A. Sedative use in the last week of life and the implications for end-of-life decision making. *Arch Int Med* 2003; **163**(3): 341-4

### Further resources

- A Guide to Symptom Relief in Palliative Care*, 6<sup>th</sup> ed. Regnard C, Dean M. Oxford: Radcliffe Medical Press, 2010
- e-lfh: e-Learning for Healthcare* contains a range of online self-learning programmes, including several relating to end-of-life care (e-ecla). Registration is required but is free. <http://www.e-lfh.org.uk/projects/e-elca/index.html>
- Twycross RG. (1999) *Morphine and the Relief of Cancer Pain: information for patients, families and friends*. Beaconsfield: Beaconsfield Publishers.
- Oxford Textbook of Palliative Medicine* 4<sup>th</sup> ed. Hanks G, Cherny NI, Christakis NA, Fallon M, Kaasa S, Portenoy RK. eds. Oxford : Oxford University Press, 2010.
- PCF4- Palliative Care Formulary*, 4<sup>th</sup> ed. Twycross RG, Wilcock A. [www.palliativebooks.com](http://www.palliativebooks.com)
- Symptom Management in Advanced Cancer*, 4<sup>th</sup> edition. Twycross RG, Wilcock A, Stark-Toller C. Oxford: Radcliffe Press, 2009
- Wall and Melzack's Textbook of pain*, 5<sup>th</sup> ed. McMahon SB, Koltzenburg M, eds. Edinburgh : Elsevier Churchill Livingstone, 2005.



**Current Learning in Palliative care**  
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### 15 minute worksheets are available on:

- An introduction to palliative care
- Helping the patient with pain
- Helping the patient with symptoms other than pain
- Moving the ill patient
- Psychological and spiritual needs
- Helping patients with reduced hydration and nutrition
- Procedures in palliative care
- Planning care in advance
- Understanding and helping the person with learning disabilities
- The last hours and days
- Bereavement

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