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- If you think any information is wrong or out of date let us know.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'.

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INFORMATION PAGE: Understanding the effects of opioids

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.
- *Tolerance to analgesia is uncommon* (ie. pain relief does not wear off with time). Tolerance can be seen when opioids are used as the only treatment for neuropathic pain (resolved by adding anti-neuropathic agents), and a rare syndrome called opioid hypersensitivity (resolved by switching opioids).
- *Withdrawal symptoms* (usually colic and diarrhoea) are likely if morphine is stopped abruptly, 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 palliative care 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:

Opioid	Renal impairment	Liver impairment
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.

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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* 4th 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.

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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, 6th 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

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PCF6- Palliative Care Formulary, 6th ed. Twycross RG, Wilcock A, Howard P. www.palliativedrugs.com

Symptom Management in Advanced Cancer, 4th edition. Twycross RG, Wilcock A, Stark-Toller C. Oxford: Radcliffe Press, 2009

Wall and Melzack's Textbook of pain, 5th ed. McMahon SB, Koltzenburg M, eds. Edinburgh : Elsevier Churchill Livingstone, 2005.