Assorted Palliative Care

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Agenda

1. Case; using SDs to deliver anticonvulsants when oral route unavailable.

2. Alfentanil syringe drivers.

3. Transdermal buprenorphine and fentanyl.

Case background

-female, age 46, single.

-T4, N1, M0 ER-, PR-, HER2+ breast cancer 2021

-May 2023 resection R frontal metastasis, seizures.

-Aug 2023 Stereotactic radiosurgery

-May 2024 Recurrent disease R frontoparietal lesion, oedema

-June-Dec 2024; admissions with seizures, L sided weakness, lumbar spine metastases, T5 osteoporotic #.

Case; treatment/management

-Kadcyla 3 cycles

-Steroids; dose up/down

-Neurology input re AEDs; sodium valproate, levetiracetam, lacosamide, clobazam.

-MSW to support patient, Dad and daughter. POC.

-BHSCT OT & PT re ADLs, mobility

-SPC CNS and Dr @ Marie Curie (MST 20mg BD back pain)

Case early 2025

-Sleeping a lot

-seizures

-in bed, L sided neglect.

-variable @taking po meds

-wish to sit out bed.

-NBO, faecal impaction.

Dying?

Drowsy from seizures?

Case actions

-Move to Dad’s home (PPOC)

-OT organises hoist and riser recliner, but not alert enough to transfer.

-boost dexamethasone from 2mg to 8mg for 7 days.

-Change to sc route for levetiracetam, sodium valproate, BDZ,

-Change from MST to morphine sulfate csci.

Changing route of medications

Oral doses

-Levetiracetam 2g BD

-Na Valproate 1.4mg BD

-Clobazam 10mg, 10mg, 20mg.

-Lacosamide 250mg BD

-MST 20mg BD

Change to SC route

1. Levetiracetam 3g csci/24hrs
2. Levetiracetam 1g, morphine 20mg, midazolam 10mg csci/24hrs.
3. Sodium valproate 2.4mg csci/24hrs

Syringe driver considerations

1. Evidence of effectiveness & tolerability of SC infusions and bioavailability re conversion ratio.

2. Volume of medication for injection.

The maximum volume to be administered via a syringe pump, including diluent, is:

- 22mL for a 30mL syringe
- 34mL for a 50ml syringe.

3. Syringe driver drug compatibility.

Levetiracetam-see NIPCPG/BHSCT pdf (off license)

- PO to SC dose conversion =1;1

-Max licensed PO dose is 3g in 24 hours. Higher doses occasionally used following advice from neurology.

-Well tolerated if diluted (saline 0.9%)

-Volume; levetiracetam 500mg/5mL vials.

-Max dose in a 30mL syringe is 2g/24 24 hours

-Max dose in 50ml syringe is 3g.

-Compatibilities; morphine, oxycodone, midazolam, levomepromazine*, hyoscine butylbromide.

Sodium Valpraote-see OLH&CS pdf (off license)

-PO to SC conversion ratio 1:1

-'Clinical experience of up to 1.8g in SD', licensed IV up to 2.5g.

-0.4g reconstituted in 4mls WFI (100mg/ml) so up to 2.2g in 20ml syringe.

-No compatibility data-so not mixed with other drugs.

Changing route of medications

Oral doses

-Levetiracetam 2g BD

-Na Valproate 1.4mg BD

-Clobazam 10mg, 10mg, 20mg.

-Lacosamide 250mg BD

-MST 20mg BD

Change to SC route

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Clinical course

-leg pains managed by passive leg movements

-Ongoing seizures for approx. 1 week, midazolam increased 15mg to 25mg, seizure frequency reduced and started eating and drinking again.

-Able to take oral medications and to sit out of bed, transferring using hoist.

-Step-wise transition off SDs to po meds, reliable compliance po meds.

What if.... had changed from MST to alfentanil re constipation.....

-MST 20mg BD =40mg PO morphine /24hrs

-Alfentanil 1mg sc = 30mg PO morphine.

-MST 40mg/day =1.3mg alfentanil csci/24hrs.

Alfentanil in syringe drivers; why?

RENAL FAILURE

BOWEL OBSTRUCTION

INTRACTABLE OPIOID INDUCED CONSTIPATION

OPIOID TOXICITY WITH OTHER OPIOIDS

Increasing alfentanil SD

-Needing on average 3x morphine 3mg SC BT's per 24hrs with good effect.

-You want to increase opioid in SD by equivalent of 2 xBTs (6mg SC morphine =12mg PO morphine).

-REMEMBER alfentanil 1mg sc = 30mg PO morphine

-Increase alfentanil by 12/30=0.4mg =total 1.4mg/24hrs.

-ALFENTANIL NOT USED FOR BREAKTHROUGH

-Diluent 0.9% saline or WFI. Compatible with many drugs.

Opioid Patches

Buprenorphine & Fentanyl

Patches; buprenorphine & fentanyl

- Indications; intolerance morphine/oxycodone, (ESRF BuTec & not removed by HD), poor compliance, diversion risk.
- Do not use in acute pain or if dose titration indicated. Fentanyl-only use in stable pain.
- Matrix patch; drug delivery proportional to patch size
- Switch from morphine/oxy can lead to withdrawal symptoms-use BT morphine/oxy to treat.

Patches, buprenorphine & fentanyl

CAUTION

- Slow onset and offset of analgesia & SEs
- Ensure patients know it is strong opioid, how to apply and safely remove, keep away from children. Driving.
- AVOID application of heat. Remove and seek medical advice if develop pyrexia.
- REMOVE BEFORE MRI SCAN and reapply new one after..
- Avoid irritated skin, apply to (non shaved) hairless skin
- Possibly reduced absorption in elderly and cachexia.

TD patch Case A

- 87 yrs, NH resident, bedbound, dementia, IHD, OA
- On BuTec 5mcg/hr for 6 months for pain related to OA.
- Developed acutely ischaemic foot 4 days ago
- Decision made for symptomatic management only, prognosis likely days.
- Rx morphine sulphate 2mg SC PRN and using on average 4 doses/24hrs with effect and no evidence opioid toxicity.

-You want to start a syringe driver

But what do you do with the patch??

Case A

-In a patient felt to be dying, continue with the patch and add the syringe driver

-Rx morphine sulphate 2mg SC PRN and using on average 4 doses/24hrs with effect and no evidence opioid toxicity.

So... 8mg morphine sulphate/24hrs CSCI....

But what about the breakthrough dose?

Case A-breakthrough dose

-On BuTec 5mcg/hr change every 7 days.

-morphine: buprenorphine ratio = 100:1

-remember 5mcg/hr BuTec =10-12mg OME.

-case 1 total daily OME= 10mg +16mg =26mg OME

-**BT dose ≤ 2mg SC**.

-Remember the patch but CAUTION caveat if high dose patch.

TD Buprenorphine

- TD patches; BuTec, BuTrans 5-20mcg/hr (7 day)
  - 20mcg =OME 40-48mg
- High dose TD patches: Transtec 35-75mcg/hr (4 day)
  - 75mcg/hr= OME 150-180mg
- Onset of action =18-24hrs
- Time to peak plasma concentration; approx. 3 days

Buprenorphine

- Lipid soluble; good for transdermal delivery.
- Partial opioid agonist
- Strong opioid or weak opioid?
- Less constipating than morphine
- Less impact on gonadal axis and immunity than morphine
- CYP 3A4 inhibitors increase levels; antiretrovirals

Case 3.

- 65 years, female, ovarian ca diagnosis, receiving palliative chemo, in hospital with C Diff and vomiting
- Pain well controlled on oxycodone 35mg CSCI/24hrs, but discharge planning and aiming to convert off SD.
- Son has moved home and has opioid addiction.

You want to change to a fentanyl patch

How do you do it?

Case 3.

-What is equivalent dose? Oxycodone 35mg SC=70mg PO= 140mg OME.

-morphine: fentanyl potency = 100;1 to 150:1 or use conversion tables-Adult-Opioid-Equivalence-Guide-HSC-2018.pdf

-Patient considerations, using minimal breakthrough.

-140mg/150 divide by 24= 38mcg/hr. 140/100 divide by 24 = 58mcg/hr.

-a 50mcg/hr patch would be reasonable, assess need for titration once steady state reached.

Approximate equivalent doses of opioid analgesics for adult use

Read page 1 before using these equivalence tables

PO (Oral) to SC (Subcutaneous)

Oral Morphine to **Subcutaneous (SC) Diamorphine** – Divide by 3
E.g. 30 mg Oral Morphine = 10 mg SC Diamorphine

Oral Morphine to **SC Morphine** – Divide by 2
E.g. 30 mg Oral Morphine = 15 mg SC Morphine

Oral Morphine to **SC Alfentanil** – Divide by 30
E.g. 30 mg Oral Morphine = 1 mg SC Alfentanil

Oral Oxycodone to **SC Oxycodone** – Divide by 2
E.g. 10 mg Oral Oxycodone = 5 mg SC Oxycodone

Oral Hydromorphone to **SC Hydromorphone** – Divide by 2
E.g. 4 mg Oral Hydromorphone = 2 mg SC Hydromorphone

Specialist Palliative Care only. Oral Morphine to SC Fentanyl
Divide by 150 e.g. 15mg Oral Morphine = 100 micrograms SC Fentanyl

PO (Oral) to PO

Oral Morphine to **Oral Oxycodone** – Divide by 2
E.g. 30mg Oral Morphine = 15mg Oral Oxycodone

Oral Morphine to **Oral Hydromorphone** – Divide by 7.5
E.g. 30mg **Oral Morphine** = 4mg **Oral Hydromorphone**

Oral Tapentadol‡ to **Oral Morphine** – Divide by 2.5
E.g. 50mg Oral Tapentadol = 20mg Oral Morphine

Oral Tapentadol‡ to **Oral Oxycodone** – Divide by 5
E.g. 50mg Oral Tapentadol = 10mg Oral Oxycodone

Oral Tramadol‡ to **Oral Morphine** – Divide by 10
E.g. 100 mg Oral Tramadol = 10 mg Oral Morphine

Oral Tramadol‡ to **Oral Tapentadol‡** – Divide by 4

SC (Subcutaneous) to SC

SC Diamorphine to **SC Alfentanil** – Divide by 10
E.g. 10 mg SC Diamorphine = 1 mg SC Alfentanil

SC Morphine to **SC Diamorphine** – Divide by 1.5
E.g. 15 mg SC Morphine = 10 mg SC Diamorphine

SC Morphine to **SC Oxycodone** – Divide by 2
E.g. 20 mg SC Morphine = 10 mg SC Oxycodone
Note this may differ from other available conversions

SC Morphine to **SC Alfentanil** – Divide by 15
E.g. 15mg SC Morphine = 1mg SC Alfentanil

Transdermal to Oral

Buprenorphine Patch e.g. Butec®, BuTrans®
Replace patch EVERY 7 DAYS

Patch strength (micrograms per hr)	Oral dose over 24 hours (mg)		
	Morphine	Tramadol	Codeine/ Dihydrocodeine
5 micrograms/hr	~10 - 12	~100	~120mg/day
10 micrograms/hr	~20 - 24	~200	~240mg/day
20 micrograms/hr	~40 - 48	~400	

Buprenorphine Patch e.g. Transtec® Patch
Replace patch TWICE WEEKLY (every 3 or 4 days)

Transtec® Patch (micrograms/hr)	24 hour Oral Morphine Dose
35 micrograms/hr	~ 63 - 97mg
52.5 micrograms/hr	~ 95 - 145mg

Transdermal to Oral

Fentanyl Patch e.g. Mezolar®, Durogesic®
Replace patch every 3 days

Fentanyl Patch (microgram/hr)	Equivalent 24 hourly Oral Morphine Dose (mg)
12	30-59
25	60-89
37	90-119
50	120-149
The doses below are **not** recommended for persistent non-malignant pain.	
62	150-179
75	180-239
100	240-299
125	300-359
150	360-419
175	420-479
200	480-539
225	540-599
250	600-659
275	660-719
300	720-779

TD Fentanyl

- Onset action 3-24hrs
- Time to peak plasma levels 12-24hrs
- **Apply TD fentanyl 50mcg/hr and stop CSCI 8-12 hrs later.**
  - See Opioids-Changing-Routes-of-Administration.pdf

Opioids—Changing Routes of Administration

There is variation in practice when converting an opioid from one route of administration to another. The chart outlined below reflects the practice at Our Lady's Hospice and Care Services (OLH&CS). **THE INFORMATION OUTLINED BELOW IS INTENDED AS A GUIDE ONLY. RECOMMENDATIONS OUTLINED BELOW ARE SUBJECT TO CHANGE DEPENDING ON THE CLINICAL CONDITION OF THE PATIENT AND PATIENT SAFETY FACTORS.** The patient should be monitored very carefully during the route conversion period. Consider the need for breakthrough pain medication during the route conversion period.

Recommendations tabulated below do **not** apply to fentanyl CSCI or methadone. Specialist palliative care advice should be sought for fentanyl CSCI, methadone and any other opioids.

SR=sustained release **CSCI**=continuous subcutaneous infusion

Converting To → **Converting From ↓**	**Oral SR opioid** MST®, OxyContin® & Palladone SR®.	**Fentanyl Transdermal patch**	**Buprenorphine Transdermal patch**	**Opioid CSCI** Morphine, Oxycodone, Hydromorphone, Alfentanil
Oral SR opioid MST®, OxyContin® & Palladone SR®.		Administer the last dose of the SR opioid and apply the transdermal fentanyl or buprenorphine patch at the same time.		The CSCI should be started about 4 hours before the next oral dose would have been due in order to maintain analgesia.
Fentanyl Transdermal patch	#Remove transdermal fentanyl patch and administer SR opioid after 10—12 hours.	Specialist palliative care advice should be sought on switching between transdermal patches.		**Option 1:** Leave the fentanyl or buprenorphine transdermal patch in place and supplemental opioid should be administered through the CSCI. **Option 2:** #Remove the fentanyl transdermal patch and commence the CSCI 12 hours later. Monitor for worsening of pain for up to 24 hours.
Buprenorphine Transdermal patch	#Remove transdermal buprenorphine patch and administer SR opioid after 24 hours.			**Option 1:** Leave the fentanyl or buprenorphine transdermal patch in place and supplemental opioid should be administered through the CSCI. **Option 2:** #Remove the buprenorphine transdermal patch and commence the CSCI 12-24 hours later. Monitor for worsening of pain for up to 24 hours.

TRANSDERMAL PATCH CONVERSIONS: #A reservoir of buprenorphine and fentanyl accumulates in the body, particularly in adipose tissue. Significant plasma levels persist for at least 24 hours after discontinuing a patch. Caution, careful monitoring and an individualised decision is required on timing of the introduction of an opioid via a different route depending on patient's clinical factors and care setting. Breakthrough pain relief should be considered during the transition period.

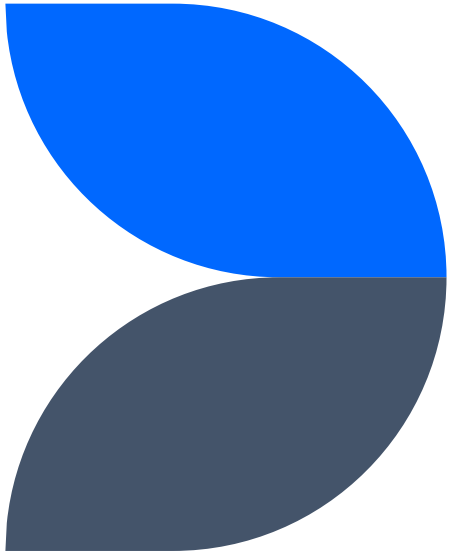
Fentanyl

- Also lipophilic
- Less constipating than morphine
- 2 ratios-can choose to use more conservative or not depending on patient situation (e.g caution if titrating off patch, less if uncontrolled pain and no toxicity).
- Although fentanyl as drug via CSCI is good option in ESRF and liver failure, avoid TD formulation in renal/liver failure.
- Also metabolised by CYP 3A4-inhibitors can increase levels-macrolides, azoles, others.

Referenced Resources

- SC levetiracetam in Palliative Care *BHSCT & NIPCPG*
- SC alfentanil in Palliative Care for adults *BHSCT & NIPCPG*
- The use of subcutaneous sodium valproate in Palliative Medicine *Our Lady's Hospice & Care Services*
- Opioids-Changing route of administration *Our Lady's Hospice & Care Services*
- Syringe Driver Compatibility Checker *Palliative Care Matters*

Questions??



Thank you

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