Fentanyl Subcutaneous and Nasal - Palliative Care (Adult)

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1. Overview

Purpose

This protocol outlines the administration, prescribing and monitoring of subcutaneous and nasal fentanyl at Waitemata District Health Board.

Scope

All medical and nursing staff

Note: Fentanyl is a very potent drug and doses are charted in micrograms.

Subcutaneous fentanyl is useful in palliative patients with severe renal failure, in those who require low doses of opioids and in situations where transdermal patches are contraindicated because of unstable pain.

2. Presentation

Fentanyl 100microgram/2ml and 500microgram/10ml glass ampoules

- Fentanyl injection is a clear, colourless solution

Fentanyl nasal spray 50microgram/ml (20ml) (Manufactured by WDHB Inpatient Pharmacy)
3. Indications

Licensed:

- For narcotic analgesic action of short duration during anaesthetic periods, premedication, induction and maintenance, and in the immediate post-operative period (recovery room)
- As an adjunct to general or regional anaesthesia

Unlicensed:

- For moderate to severe pain responsive to opioids
- For use in patients with severe renal failure

Unlicensed routes of administration:

- Subcutaneous
- Transmucosal

4. Dose

4.1 Subcutaneous Fentanyl

There have been numerous studies which have lead to some controversy about the pharmacokinetics, conversion factors and therefore doses of fentanyl.

Note: The following doses and conversion factors are a guideline only and each patient must be assessed on an individual basis. Advice should be sought from the Palliative Care Team.

Table 1. Starting Doses if opioid naïve:

<table>
<thead>
<tr>
<th>Route</th>
<th>Fentanyl Dose</th>
<th>Equivalent Subcut Morphine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous PRN</td>
<td>25 microgram every 30 minutes PRN</td>
<td>2.5 mg morphine subcut every 30 minutes PRN</td>
</tr>
<tr>
<td>Continuous subcutaneous infusion over 24 hours (CSCI)</td>
<td>50 to 100 microgram over 24 hours titrating according to symptom control</td>
<td>5 to 10 mg subcut morphine over 24 hours titrating according to symptom control</td>
</tr>
<tr>
<td></td>
<td>Also chart 25 microgram subcut every 30 minutes PRN for breakthrough pain</td>
<td></td>
</tr>
</tbody>
</table>

Note: Do NOT administer more than 2mL as a single stat dose subcutaneously. Stat doses larger than 2mL must be administered in two different sites.

Note: Injectable fentanyl is only available at a concentration of 50microgram/ml. It is not possible to administer more than 22mL (1100 microgram) fentanyl in the 30mL BD Luer lock syringe recommended for continuous subcutaneous infusion at WDHB.

If the fentanyl volume required for continuous subcutaneous infusion exceeds 22mL, then draw up the required fentanyl dose in a 50mL BD Luer lock syringe and add diluent to make up to 34mL total volume.
Table 2. PRN fentanyl doses for patients on a continuous subcutaneous infusion

<table>
<thead>
<tr>
<th>Fentanyl subcut infusion 24 hours dose (microgram)</th>
<th>Fentanyl subcut q30mins PRN dose (microgram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>25</td>
</tr>
<tr>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>150</td>
<td>25</td>
</tr>
<tr>
<td>300</td>
<td>50</td>
</tr>
<tr>
<td>450</td>
<td>75</td>
</tr>
<tr>
<td>600</td>
<td>100</td>
</tr>
</tbody>
</table>

Note: If more than three PRN doses are used in a 24 hour period the background dose may need to be adjusted.

4.2 Dose Conversion

For the purpose of this protocol, the suggested conversion ratio of subcutaneous morphine to fentanyl is 100:1

1mg (1000 microgram) of subcut or IV morphine = 10 microgram of subcut or IV fentanyl

Table 3. Equianalgesic doses of morphine:fentanyl per 24 hours

<table>
<thead>
<tr>
<th>Morphine oral 24 hour dose (mg)</th>
<th>Morphine Subcut 24 hour dose (mg)</th>
<th>Fentanyl Subcut 24 hour dose (microgram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>30</td>
<td>15</td>
<td>150</td>
</tr>
<tr>
<td>60</td>
<td>30</td>
<td>300</td>
</tr>
<tr>
<td>90</td>
<td>45</td>
<td>450</td>
</tr>
<tr>
<td>120</td>
<td>60</td>
<td>600</td>
</tr>
</tbody>
</table>

Note: Provided the patient has stable pain, those using 300 microgram or more over 24 hours can be switched to fentanyl patches

Table 4. Equianalgesic doses of fentanyl patches and continuous subcutaneous infusions

<table>
<thead>
<tr>
<th>Fentanyl Patch (microgram/hr)</th>
<th>Subcut fentanyl (microgram/24hr)</th>
<th>Subcut Morphine (mg/24hr)</th>
<th>Oral Morphine (mg/24hr)</th>
<th>Subcut Oxycodone (mg/24hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5</td>
<td>300</td>
<td>30</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>25</td>
<td>600</td>
<td>60</td>
<td>120</td>
<td>60</td>
</tr>
</tbody>
</table>

Newly initiated patches may take up to 12 or more hours to reach adequate plasma levels.

Note: For patients on patches, a PRN dose of subcut fentanyl or alternative opioid must also be charted for breakthrough pain [Refer to WDHB Fentanyl Patches - Palliative Care (Adult) Protocol].
4.3 Fentanyl Nasal Spray (transmucosal fentanyl)

Several transmucosal fentanyl products are available although none are licensed or subsidised in New Zealand. The administration of injectable fentanyl via the buccal, oral or intranasal route has been widely described. The parenteral form of fentanyl for injection can be used as an alternative, however the preparation available in New Zealand is a low concentration, which makes the nasal spray unsuitable for patients requiring moderate or high doses of opioids for breakthrough pain.

There is no commercial preparation of fentanyl nasal spray available in New Zealand. It is compounded for each patient by pharmacy. The amount delivered in each spray depends on the spray bottle used.

For WDHB a 50microgram/ml, 20mL intranasal spray is manufactured. Each spray delivers 0.1ml of solution = 5microgram of fentanyl.

Advice should be sought from the Palliative Care Team when prescribing fentanyl nasal spray

Nasal Spray Dose:
The dose required is patient and indication dependent

- In opioid naïve patients start with **ONE spray into each nostril and repeat after 15 minutes if inadequate response.**
- Opioid experienced patients are likely to need 25 to 50 mcg or more (5 to 10 sprays)

Doses higher than 100mcg (20 sprays) may be poorly tolerated because of the volume of drug that is required.

Storage on ward

- Fentanyl nasal spray is a controlled drug (CD). It must be stored in the controlled drug safe on the ward.
- When the patient requests a dose, write the dose out of the ward CD register in **milliliters** (1 spray = 5microgram = 0.1ml) e.g. if a patient uses 3 sprays in each nostril, write 0.6ml in the out column.
- After use, return bottle to ward CD safe until needed again (i.e. do not leave at patient’s bedside).

5. Administration

5.1 Diluent

- For subcutaneous bolus administration fentanyl does not need to be diluted.
- When added to a syringe driver the recommended diluent is water for injection.

5.2 Additional equipment

- Subcutaneous Saf-T-Intima single lumen [ADM140] (refer WDHB Policy Palliative Care- Subcutaneous Site Selection, Insertion and Monitoring of BD Saf-T-Intima Cannula)
- Continuous subcutaneous infusion pump (Niki T34) if required
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5.3 Compatibility

Compatible with:
Water for injection, 0.9% sodium chloride, metoclopramide, midazolam, haloperidol, hyoscine butylbromide, hyoscine hydrobromide, dexamethasone, ketamine, octreotide, levomepromazine, glycopyrrolate.7,9,10

Variable compatibility with:
Cyclizine (this combination should be avoided)7,10

Do not use if the solution is cloudy or a precipitate is present.

5.4 Administration Procedure

Subcutaneous administration

• Should be injected through a BD Saf-T-Intima single lumen or directly via subcutaneous needle.
• The Saf-T-Intima should be flushed with 0.2mL of water for injection after administration of medication.
• Can be administered via a continuous subcutaneous infusion pump (Niki T34).

Intranasal administration

• Patients should sit up, hold head and bottle upright, and press nozzle.
• There is no need to breathe in/inhale the spray.
• Avoid blowing nose for 1 hour after a dose.

6. Observation and Monitoring

• Monitor for excessive drowsiness.
• Monitor for respiratory depression.

7. Mechanism of action

Fentanyl is a potent narcotic analgesic with a rapid onset and short duration of action. The principal actions are analgesia and sedation. Fentanyl is a selective μ-receptor agonist. It may cause less constipation, sedation and cognitive impairment than morphine.1,2

8. Contraindications and Precautions

Contraindications

• Intolerance or hypersensitivity to fentanyl
• Myasthenia gravis
• Bronchial asthma1

Precautions

• Respiratory impairment
9. Adverse Effects

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory depression and apnoea</td>
<td>Dizziness</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Muscle rigidity</td>
<td>Blurred vision</td>
<td>Laryngospasm</td>
</tr>
<tr>
<td>Myoclonic movements</td>
<td>Bradycardia</td>
<td>Euphoria</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Itching</td>
<td>Sedation</td>
</tr>
<tr>
<td>Constipation</td>
<td>Confusion&lt;sup&gt;1, 3&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

10. Drug Interactions

- Monoamine oxidase inhibitors
  - Non-selective MAOIs intensify the effects of opioids which can cause anxiety, confusion and significant respiratory depression sometimes leading to coma
  - Avoid concomitant use and for 2 weeks after stopping MAOIs

- Additive effects with central nervous system depressants e.g. benzodiazepines, tricyclic antidepressants, other opioids, general anaesthetics and alcohol

- Use with SSRIs may increase the risk of serotonin syndrome<sup>4</sup>

11. References

8. WDHB Fentanyl Patches – Palliative Care Protocol