Transdermal Opioids – Are we plastering over the cracks?

External Reviewer/Expert: S. Simpson
Transdermal Opioids – Where do they fit in?

- Niche market?
- Stable pain?
- Oral route not possible?
- Other opioid toxicity?
- Compliance issues?
- Patient preference?
Transdermal Opioids

• Are they safe and efficacious?
• For whom and how should they be prescribed?
• How should conversions to and from other opioids be managed?
• What knowledge do generalists have of Transdermal opioids?
Indications

- Mod-severe chronic pain (BNF)
- Stable severe pain
- Swallowing difficulties
- Intolerable side effects with morphine
- Renal failure
- ? Nil absolute contraindications
Is Transdermal Fentanyl Safe and Efficacious?

• Systematic review of literature 1966-2007. 3RCTs comparing TD Fentanyl with oral morphine.
• No difference in overall adverse effect profile, or efficacy.
• Reduction in constipation.
• Patient preference in favour of Fentanyl. (level 1+)

Transdermal Fentanyl - Concerns

- Informed prescribing is essential.
- 3 case reports of inappropriate prescribing of Transdermal Fentanyl by clinicians.
- 84 year woman commenced on 50mcg patch from paracetamol/codeine.

- **National Safety Alerts- FDA 2005**
  
  - Toxic Side Effects and deaths in USA.

- **FDA Update 2007**
  
  - Should not be initiated in opioid naive patients.
  - Equivalent of 60mg TDD oral morphine for > 1 week
  - Must not be initiated for titration

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**Can cause harm!**
Conclusions of Investigation into Deaths

- Lack of appreciation that Fentanyl is a strong opioid.
- Inappropriate use for acute pain.
- Lack of patient awareness of safe use, avoid heat sources, signs of overdose.
- Lack of awareness of potential drug interactions.
<table>
<thead>
<tr>
<th>UK Alerts</th>
<th>Key Factors Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Medicines and Healthcare products Regulatory Agency MHRA- Fentanyl Patches September 2008</td>
<td>• Dosing errors by healthcare professionals, patients or care givers.</td>
</tr>
<tr>
<td></td>
<td>• Accidental exposure.</td>
</tr>
<tr>
<td></td>
<td>• Exposure to heat resulting in increased absorption.</td>
</tr>
<tr>
<td></td>
<td>• Inappropriate prescribing in opioid-naive patients</td>
</tr>
</tbody>
</table>
Generalists Knowledge

- Survey questionnaire to GPs, hospital consultants and oncologists. Assessed knowledge of the use of Transdermal Fentanyl in clinical practice.
- Overall knowledge and confidence in using Transdermal Fentanyl was poor.

Summary

1. Effective
2. Side effect profile
3. Patient preference

1. Can cause harm
2. Inappropriate prescribing
3. Lack of generalist knowledge
Audit Results

- Prospective
- 6 months Oct 2009-April 2010
- 3 sites across Merseyside and Cheshire Cancer Network.
- 50 patients
What dose of Fentanyl was prescribed?

<table>
<thead>
<tr>
<th>Fentanyl Patch Strength micrograms/hr</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>6</td>
</tr>
<tr>
<td>25</td>
<td>14</td>
</tr>
<tr>
<td>37</td>
<td>4</td>
</tr>
<tr>
<td>50</td>
<td>3</td>
</tr>
<tr>
<td>62</td>
<td>1</td>
</tr>
<tr>
<td>75</td>
<td>2</td>
</tr>
<tr>
<td>87</td>
<td>2</td>
</tr>
<tr>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>125</td>
<td>1</td>
</tr>
<tr>
<td>200</td>
<td>2</td>
</tr>
<tr>
<td>300</td>
<td>2</td>
</tr>
</tbody>
</table>
Who was the original prescriber?

- GP
- Hospital Doctor
- Palliative Care Specialist
- Not Recorded
Is there a relationship to diagnosis?

![Bar chart showing the relationship to diagnosis across various categories: Breast, Colorectal, Head and Neck, Lung, Haematological, Upper GI, Genito-Urinary, Gynaecological, Non-Malignant, Not Recorded.]
Reason for use documented in only 26%

- Compliance: 2
- Renal Failure: 2
- Unable to swallow: 1
- Intolerance of other: 4
- Nausea/Vomiting: 1
- Patient Preference: 2
- Other: 1
Observer assessment of potential indications for Transdermal opioids
Did prescribed breakthrough medication correspond with equianalgesic guidelines

<table>
<thead>
<tr>
<th>TD</th>
<th>Fentanyl</th>
<th>Morphine</th>
<th>Oxycodone</th>
</tr>
</thead>
<tbody>
<tr>
<td>12mcg</td>
<td>5mg</td>
<td>2.5mg</td>
<td></td>
</tr>
<tr>
<td>25mcg</td>
<td>10mg</td>
<td>5mg</td>
<td></td>
</tr>
</tbody>
</table>
**Incorrect Oxynorm breakthrough medication prescribed**

<table>
<thead>
<tr>
<th>Fentanyl Dose</th>
<th>Oxynorm Dose Prescribed prn</th>
<th>Oxynorm “Correct” Dose prn</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 micrograms/hr</td>
<td>5mg</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>12 micrograms/hr</td>
<td>5mg</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>25 micrograms/hr</td>
<td>10mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>25 micrograms/hr</td>
<td>10mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>37 micrograms/hr</td>
<td>15mg</td>
<td>7.5mg</td>
</tr>
<tr>
<td>75 micrograms/hr</td>
<td>Oxynorm 5 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>75 micrograms/hr</td>
<td>Oxynorm 40mg</td>
<td>20 mg</td>
</tr>
</tbody>
</table>
Did the patient have any side effects?

- Varying degrees of opioid toxicity
- 1 case requiring naloxone

![Bar chart showing side effects]

- Yes: 26%
- No: 23%
- Missing: 51%
In opioid toxic patients who initiated introduction of Transdermal opioid?

Initiator of Transdermal Opioid

- Specialist Palliative Care: 0
- GP: 7
- Pain team: 1
- Hospital Doctor: 1
- Not known: 1
In toxic patients was breakthrough dose in line with equianalgesic recommendations.
Summary of key findings

- Reason for use poorly documented
- $\geq \frac{1}{4}$ patients suffered side effects – mainly opioid toxicity
- Toxicity appeared related to the transdermal opioid itself and not incorrect breakthrough doses.
- Poor prescribing of breakthrough medication
The key to safe appropriate prescribing?

Guidelines

Further Research

Education education education