INAPPROPRIATE PRESCRIBING PATTERNS OF TRANSDERMAL FENTANYL (DURAGESIC®)

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PHARMACIST OBJECTIVES

• Analyze, understand, and utilize the NM PMP
• Describe the recommended requirements for initiation or conversion of transdermal fentanyl
• Describe risks associated with the use of transdermal fentanyl
• Recommend a strategy for conversion from oral opioid regimens to transdermal fentanyl
• Describe how to transition between intravenous (IV) fentanyl and transdermal fentanyl
• Identify which fentanyl products are registered with the REMS program
• List the P450 3A4 inhibitors that potentially interact with fentanyl
• Outline and provide treatment recommendations for transdermal fentanyl overdose
• Outline the appropriate procedure for disposal of transdermal fentanyl

TECHNICIAN OBJECTIVES

• Analyze, understand, and utilize the NM PMP
• Describe risks associated with the use of transdermal fentanyl
• Define the relative potency of fentanyl compared to other opiates
• Identify which fentanyl products are registered with the REMS program
• Understand the medication utilized in the treatment of fentanyl overdose
• Outline the appropriate procedure for disposal of transdermal fentanyl

SHOUT OUT

Patient Case

• AG is an 88 year old male patient, residing at an assisted living facility (ALF). Fell and sustained multiple rib fractures.
• Discharged from emergency room with:
  Fentanyl 25mcg/hr TD patch
  1 patch every 72 hours

P450 3A4 inhibitors that potentially interact with fentanyl:

- Cimetidine
- Ketoconazole
- Ritonavir
- Indinavir

Outline and provide treatment recommendations for transdermal fentanyl overdose:

1. Stop fentanyl patch
2. Observe the patient and monitor vital signs
3. Provide support
4. Call for additional assistance

Outline the appropriate procedure for disposal of transdermal fentanyl:

1. Remove the fentanyl patch
2. Dispose of the patch in a sharps disposal container
3. Wash hands

DISCLOSURES

• No relationships to disclose
• No conflicts of interest
• I am not an expert in the field of opiate prescribing – I am merely a concerned community pharmacist wanting to share my knowledge and concern

PATIENT CASE

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Patient Case:
- Would you fill this?
  1. Yes
  2. No
- What steps would you follow to confirm the validity of prescription?

Question?
Compared to morphine, what is the relative potency of fentanyl?
- 1.50
- 2.35
- 3.100
- 4.60

Question?
Compared to morphine, what is the relative potency of fentanyl?
1. 50
2. 35
3. 100
4. 60

History of Fentanyl
- 1959: First synthesized by Paul Janssen (Janssen Pharmaceuticals)
- 1960: Created IV anesthetic (Sublimaze®)
- 1990: First form of transdermal fentanyl (Duragesic®) available

Fentanyl Today
- Synthetic pure mu opioid agonist
- Important difference
  - **75-100 times more potent than morphine**
- Lipophilic nature facilitates rapid diffusion across the blood brain barrier, resulting in quick onset of action

Fentanyl Today

<table>
<thead>
<tr>
<th>Drug</th>
<th>Parenteral</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.3</td>
<td>0.4(SL)</td>
</tr>
<tr>
<td>Cadaverine</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>0.1</td>
<td>N/A</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>N/A</td>
<td>30</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Meprobamate</td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>Metadone</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Oxycodeine</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Tramadol</td>
<td>100</td>
<td>120</td>
</tr>
</tbody>
</table>
QUESTION?
How many dosage forms of fentanyl are currently available?

- a) 7
- b) 9
- c) 4
- d) 11

FENTANYL TODAY

1. Intravenous-Fentanyl-various strengths
2. Transdermal-Duragesic®: 12mcg, 12.5mcg, 25mcg, 50mcg, 75mcg, 100mcg, etc.
3. Iontophoretic Transdermal Patch: IONSYS®-400mcg/hr
4. Lozenge: Actiq®-200mcg
5. Buccal Film: Omeprazol®-200mcg
6. Buccal Tablet: Fentora®-100mcg
7. Intranasal Spray: Lazanda®-100mcg
8. Sublingual/Sublingual Spray: Subsys®-100mcg*
9. Sublingual Tablet: Abstral®-100mcg*

FENTANYL TODAY
Transmucosal immediate-release fentanyl products (TIRF)
- REMS guidelines and criteria restricting use
  - Effective 2011

QUESTION?
Which CYP450 substrates may effect the metabolism of fentanyl?

- 1. Erythromycin
- 2. Ketoconazole
- 3. Nefazodone
- 4. All the above
Recommendations and Considerations for Healthcare Providers

- CYP450 3A4 inhibitors (eg: ketoconazole, erythromycin, nefazodone, diltiazem, or grapefruit juice) may result in an increase in serum plasma concentrations. Careful monitoring is recommend and adjustment of the fentanyl dose may be warranted.
- Before converting to TD fentanyl, insure patients pain is under relatively stable control. Titration of the TD formulation and chasing increasing pain is difficult. Steady state concentrations are normally achieved around 6 days.
  - NEVER USED FOR ACUTE POST-SURGICAL PAIN

*>Which of the following could a patient cut to fit the area where they would like to apply the patch?

A. Nicotine  
B. Butrans  
C. Lidocaine  
D. Fentanyl

Opiate Tolerant???

- The patient must have a history of using the below minimum milligram daily or equianalgesic opioid dose for one week or longer:
  - Morphine 60mg
  - Oxycodone 30mg
  - Hydromorphone 8mg
  - Oxydorphone 25mg

Clinical Pearls

1. ABSOLUTELY NO CUTTING
2. Do not directly apply patch to site of pain
3. Apply to intact non-irritated, not shaved, flat skin surface
   - Chest, back, or flank of upper arm
4. Caution when elevating body temperature
   - Use during hot baths, heating blankets or pads, hot tubs/saunas, etc
5. Remove patch prior to MRI procedures
6. Careful monitoring in elderly, cachectic, or debilitated patients
7. Renal and Hepatic impairment
   - Moderate impairment: decrease dose to 50%
   - Severe impairment: do not use

Question?

- Which of the following could a patient cut to fit the area where they would like to apply the patch?
  
  A. Nicotine  
  B. Butrans  
  C. Lidocaine  
  D. Fentanyl
Currently the package labeling states there has been no systematic evaluation of fentanyl as an initial opioid analgesic in managing chronic pain.

Author suggests the conversion table is to conservative.

Use ratio of 2:1 → 2mg oral morphine per day ~ 1mcg per hour.

The number of mcg/hr = half the number of milligrams of oral morphine/day.

Example: 50mg of oral morphine ~ 25mcg/hr patch.

Fentanyl TODAY

<table>
<thead>
<tr>
<th>Current Analgesic</th>
<th>Total Daily Dose (mg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Morphine</td>
<td>30.00</td>
</tr>
<tr>
<td>Oral OxyContin</td>
<td>15.75</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>9.16</td>
</tr>
<tr>
<td>Oral Codeine</td>
<td>3.7</td>
</tr>
<tr>
<td>Oral Hydromorphone</td>
<td>1.5-3.4</td>
</tr>
<tr>
<td>Oral Oxycodone</td>
<td>2.5-4.5</td>
</tr>
<tr>
<td>Oral Methadone</td>
<td>10.22</td>
</tr>
<tr>
<td>buprenorphine</td>
<td>10.22</td>
</tr>
<tr>
<td>Transdermal</td>
<td>95-135</td>
</tr>
</tbody>
</table>

Recommended Fentanyl dose:
- 42 mcg/hr
- 25 mcg/hr
- 34 mcg/hr
- 75 mcg/hr
- 100 mcg/hr

*Currently, the package labeling states there has been no systematic evaluation of fentanyl as an initial opioid analgesic in managing chronic pain.

Conversions

1. Global RxPh:
   - https://globalrph.com/medcalc/
2. Oregon Pain Guidance
   - https://www.oregonpainguidance.org/opioidmedcalculators/
3. Mathematical conversion factors (for nostalgia purposes?)

Hydrocodone example:
- JR taking Hydrocodone/APAP 5/325mg po q 4 hours for the past 2 weeks.
- Provider wants to convert to Fentanyl due to pill burden and reported increase in pain.

1. Would you recommend fentanyl TD?
2. What strength would you recommend?
3. Other options?
Conversions

Hydrocodone example:
1. 6 tablets of Hydrocodone/APAP 5/325mg = 30mg of hydrocodone
2. Conversion factor is 1:1
3. 30mg of Hydrocodone = 30mg of Morphine (MME)

Conversion example:
- Currently the package labeling states there has been no systematic evaluation of fentanyl as an initial opioid analgesic in managing chronic pain

Patient Case:
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- Discharged from emergency room with:
  - Fentanyl 25mcg/hr TD patch
  - 1 patch every 72 hours
  - #3
- Per allergy records, patient claimed allergic to codeine.

Patient Case:
- Would you fill this?
  - Yes
  - No
- What steps would you follow to confirm the validity of prescription?

Common Problems:
- Patient allergies, pseudo-allergies, or ADEs?
  - Codeine*
  - True allergy??
  - <2% of the population
- Patient unable to tolerate PO
- Use your resources:
  - Contact facility
  - Contact patient's family members
  - Discuss with caregivers
**Patient Case**

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- Discharged from emergency room with:
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  - #3
- What tools can we use to help validate this prescription?

**NM Prescription Monitoring Program (PMP)!!!**

- **Mission:**
  - To provide practitioners, pharmacists, and other authorized users the ability to review a patient's controlled substance prescription history and assist in the prevention of diversion, abuse, misuse, and drug overdose deaths associated with controlled substance prescriptions.
- **Registration - any health care professional**
  - Delegates - up to 4
  - Law Enforcement

**NM PMP Registration**

- Create an account at [https://newmexico.pmpaware.net/login](https://newmexico.pmpaware.net/login)
- Verify your email
- Upload or email personal identification
  - Driver's license, state issued photo ID, or a passport
- Complete the required training at [http://nmpmp.org/Training.aspx](http://nmpmp.org/Training.aspx)

**Requesting PMP Patient Reports**

- [Access the PMP website at](https://newmexico.pmpaware.net)
- [How to Request a PMP Patient Report](https://newmexico.pmpaware.net)
PATIENT CASE-AG

Other potential ideas to manage AG prescription

1. Refusal of prescription
2. Recommendation of naloxone prescription
   • Prescriptive authority or DOH
   • Patient Relief Act [24-3D-1 NMSA 1978]

NARCAN

• Synthetic morphinan derivative of oxymorphone
• Racemic mixture of two enantiomers
  • Levo-naloxone and dextro-naloxone
  • This gives it the higher affinity potential for the Mu receptors
  • Antagonist at the opioid receptors; (delta, kappa, and Mu)
  • Achieves a brain-to-serum ration of 12-15 times greater than morphine

PATIENT CASE

QUESTION

True of False?

In the absence of an opiate, naloxone may have pharmaceutical activity and potentially cause harm?

FALSE!

NARCAN

• Highly lipophilic to enable its ability to penetrate the blood brain barrier
• Low oral bioavailability
  • Injection and nasal spray preferred in acute overdose management
• Short duration of action:
  • Half-life is 30 minutes to 2 hours
OPIATE REVERSAL

Support initiation with trag values result before providing reversal

Opiate Reversal

Fentanyl Reversal

NaRcan Today

Disposal

1. Medication take-back options
   - Take back day: April 27, 2019
   - 469 tons of unused medications collected
   - Pharmacies now accepting narcotics/unused medications
   - Permanent collection sites
     - https://www.cabq.gov/police/programs/pharmaceuticals

2. Disposal in household trash

3. Flushing

   * Only certain potentially dangerous medicines included

Disposal

List of medications recommended for disposal by flushing when take back options are NOT readily available:

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Tylenol</td>
</tr>
<tr>
<td>Aspirin</td>
<td></td>
</tr>
</tbody>
</table>
PATIENT CASE: REVIEW

1. Ran the PMP to find no past h/o of opiate use
2. Called to discuss with MD at emergency room
3. MD admits to prescribing TD fentanyl after IV fentanyl frequently, and patient has documented allergies to codeine
4. Verified with facility patient’s allergies were really nausea and stomach upset
5. Discussed further with MD and changed regimen to Oxycodone 5mg.

SUMMARY

✓ Review internal polices and procedures
   ❖ Create your own?
   ❖ Personal police and procedure
✓ Run manual PMP with ALL new fentanyl prescriptions

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   ❖ Identify if true allergy, pseudo-allergy, or ADE

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   ❖ Create your own?
   ❖ Personal police and procedure
✓ Run manual PMP with ALL new fentanyl prescriptions
✓ Review patient allergies
   ❖ Identify if true allergy, pseudo-allergy, or ADE
   ❖ Reach out to MD, patient family or caregiver
THANK YOU!!!