

Pharmacotherapy of Pain Management in Palliative Care Part II

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New Developments in Palliative Care Pharmacotherapy

- Opioid Equianalgesic Conversions
 - Which patients are good candidates for conversion?
 - Equianalgesic Conversion Tools
- Advances in Breakthrough Pain Treatment
 - Determine Effective Opioid Doses For Episodic Pain
- Opportunities for Pharmacists
 - Suggest analgesic dose titration for uncontrolled pain
 - Suggest opioid conversion doses when needed
 - Suggest optimal opioid breakthrough pain dose

Opioid Conversion Concepts

- Identify Candidates For Opioid Conversion
- Opioid Conversion Calculators
- Equianalgesic Opioid Conversion Tables
 - Strengths/Weaknesses
 - Unique challenges with fentanyl
 - Updated to include:
 - Chronic fentanyl dosing vs. acute fentanyl dosing
 - Buprenorphine

Which Pain Management Patients are Candidates for Opioid Conversion?

- Patient on chronic opiates unable to take oral analgesics
 - Trauma
 - Abdominal Injury
 - Cancer Patient
 - Dysphagia
 - Severe Nausea/Vomiting
 - Chemotherapy

Which Pain Management Patients are Candidates for Opioid Conversion?

- Patients with pain that is not responsive to current opioid therapy
 - Disease Progression
 - Opioid Tolerance

Which Pain Management Patients are Candidates for Opioid Conversion?

Patient with intolerable side effects to an opioid

- Nausea
- Vomiting
- Sedation
- Dysphoria
- Delirium
- Myoclonus
- Hyperalgesia

Indications For Opioid Conversion

- Uncontrolled Pain resulting from:
 - Expensive Medication Regimen Noncompliance.
 - Poor absorption of oral opioid
 - Low Bioavailability of Transdermal Delivery System
 - Education on proper placement/use is critical

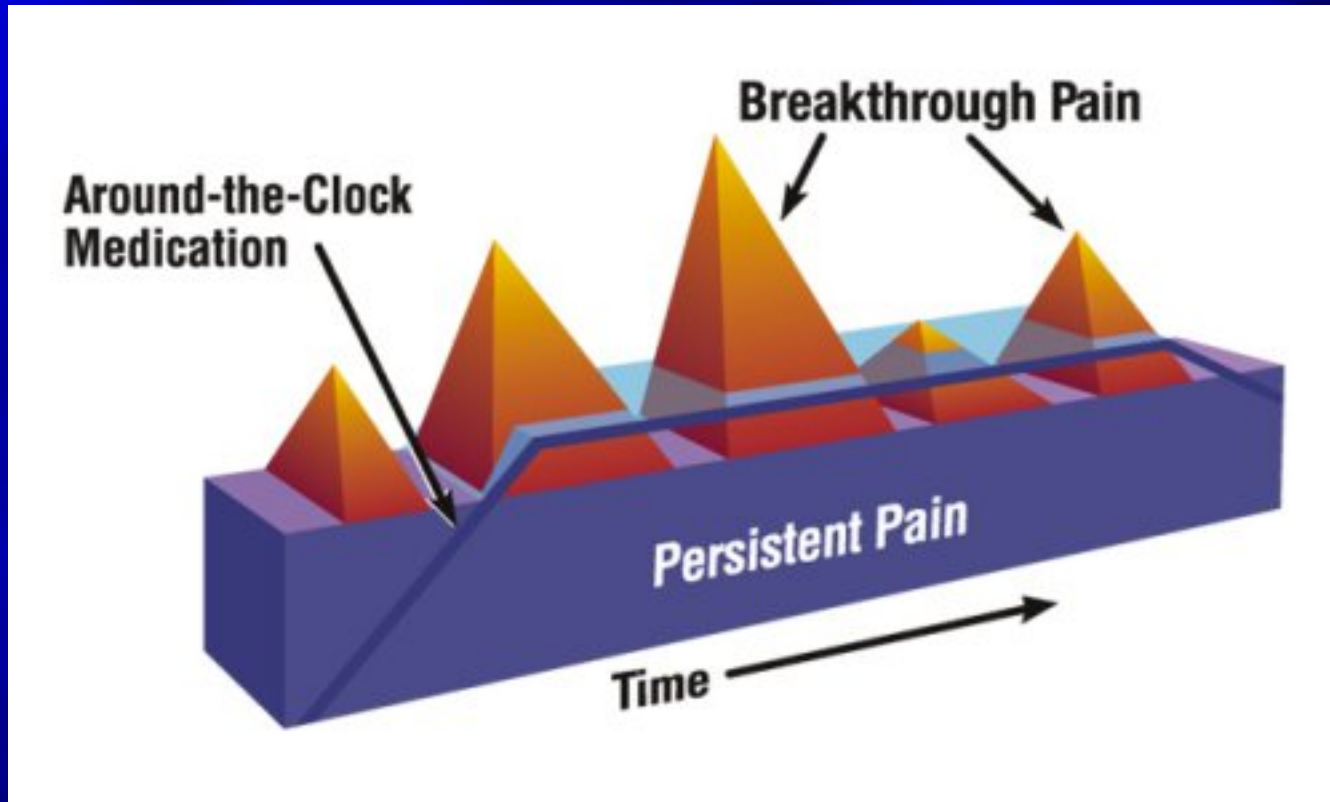
Indications For Opioid Conversion

- Patient Compliance/Quality of Life
 - Convert from short acting to long acting opiates
- Local Toxicity
 - Subcutaneous Route
 - Rectal Route
 - Transdermal Route

Opioid Equianalgesic Dose Tables

- Evidence Based Values for the Relative Potencies Among Different Opioids
- Most Opioid Conversion Studies involve Cancer Patients that are:
 - Clinically Stable
 - Experiencing Chronic Stable Pain
- Large Interindividual Variability
 - Pharmacokinetics
 - Pharmacodynamics

Breakthrough Pain Management Challenges



Breakthrough Pain Subtypes

- Incident, predictable
- Incident, unpredictable
- Idiopathic
- End-of-dose

Episodic (Breakthrough) Pain Dose Study

- Open Label Study Enrolling Patients on Oral Morphine
- Breakthrough Pain (BTP) Dose of Morphine IV Given Using Equianalgesic Ratio of 1/3 (IV/Oral)
- Pain Intensity Was Recorded at Start of BTP, at Time of Maximum Pain Relief, and one hour later

Equianalgesic Table

PO (mg)	Analgesic	SC/IV/IM (mg)
30	Morphine	10
10	Oxymorphone	1
4	Hydromorphone	1.5
20	Oxycodone	14
(2-8)	Methadone	(2-8)
-	Fentanyl	100 µg/hr parenteral or transdermal $\equiv$ 4 mg/hr morphine parenteral

Episodic (Breakthrough) Pain Dose Study

- In 162 Episodes, Pain Intensity Reduced 33% and mean time was 17.7 minutes from mean of 7.9/10 to 3/10
- In 136 Episodes, Pain Intensity Reduced Greater Than 50% and mean time was 16.6 minutes from mean of 7.9/10 to 2.6/10
- Twenty Episodes in Ten Patients Required an Additional Dose within 2 hours.

Episodic (Breakthrough) Pain Dose Study

Adverse Effects

- | | |
|--------------------------------------|-------------|
| • Drowsiness | 25 Episodes |
| • Moderate to Severe Nausea/Vomiting | 12 Episodes |
| • Confusion | 1 Episode |

Episodic (Breakthrough) Pain Dose Study Conclusions

- Morphine Administered IV at a Dose Equivalent to 20% of the basal oral dosage is safe and effective.
- This Dose Prevented the Occurrence of other Breakthrough Pain Episodes Within Two Hours in Almost All Patients.

Episodic (Breakthrough) Pain Dose Study

- Prospective Cohort Study to verify safety and effectiveness of breakthrough pain dose
- Breakthrough Pain Dose Equal To 20% of Total Daily Morphine Dose
- Enrolled 99 Cancer Pain Patients
- 945 Breakthrough Pain Episodes Were Recorded

Episodic (Breakthrough) Pain Dose Study

- Only 469 Breakthrough Episodes had complete assessment
- In 287 Episodes, Pain Intensity Was Reduced by greater than 33% at 15 minutes
- In 115 Episodes, Pain Intensity Was Reduced Greater Than 50%
- The mean pain intensity decreased from 7.2 (T0) to 2.7 (T15)
- In eight episodes no change in pain intensity was observed and an additional dose of morphine was given.

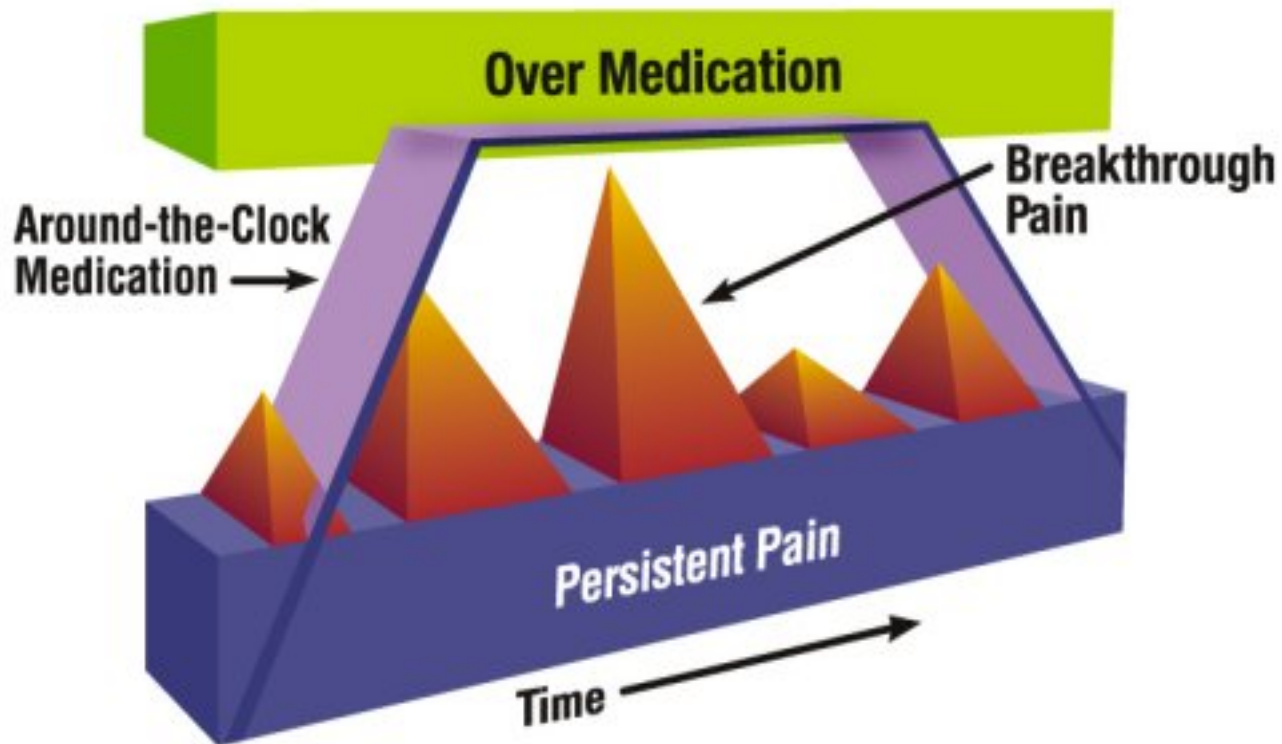
Episodic (Breakthrough) Pain Dose Advances

- We now have published studies to Guide the dosing ratios we use to treat Breakthrough Pain
- How Should We Apply This?
- Change Breakthrough Dose Ratio from 5 – 15% of Daily Opioid Dose to 10-20% of Daily Opioid Dose.

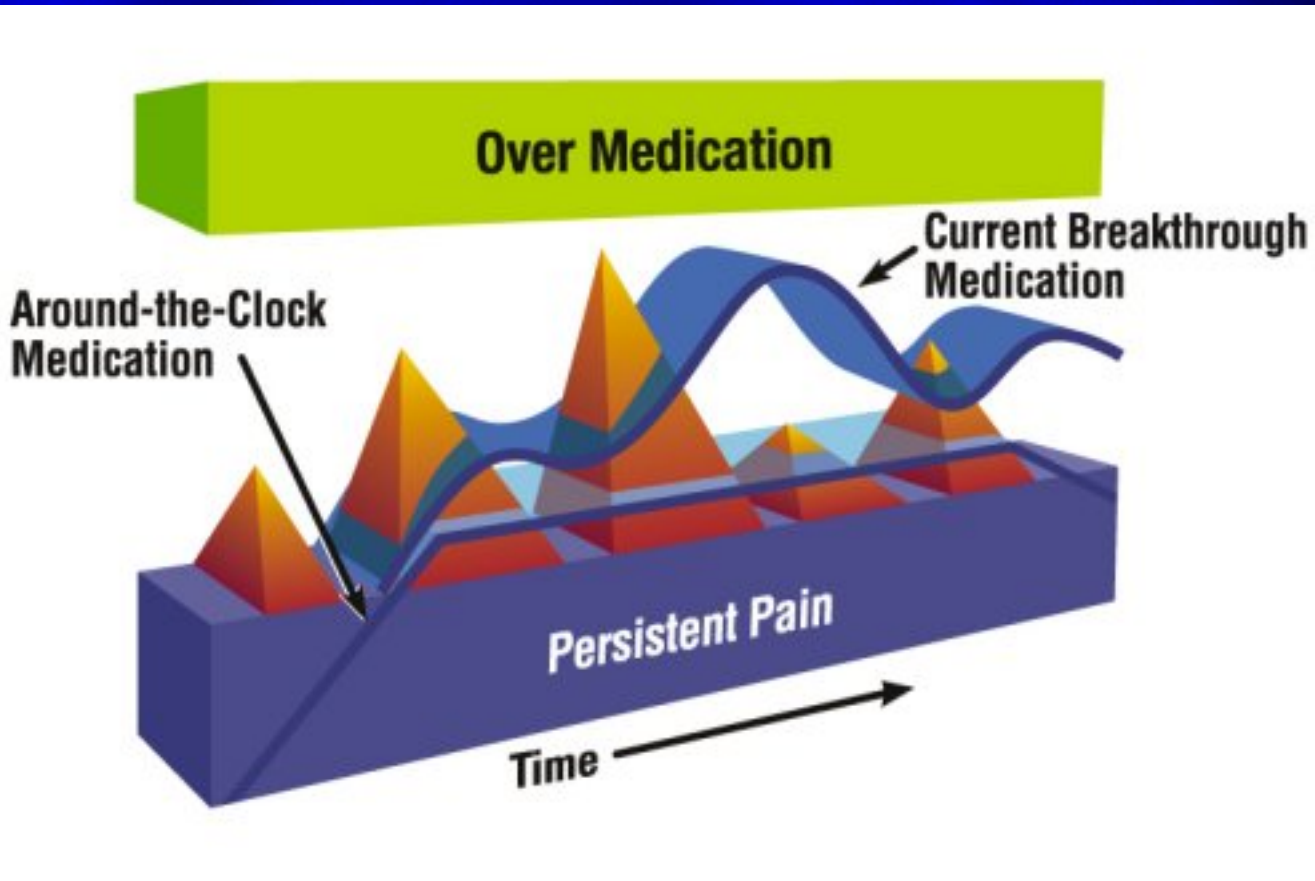
Episodic (Breakthrough) Pain Dose Example

- Patient with Breast Cancer Taking Morphine Extended Release 180 mg po Daily for Chronic Severe Pain.
- Breakthrough Pain Dose = 18 – 36 mg po
Morphine = 10 – 20 % of Daily Morphine Dose.
- Conservative Regimen: 20 mg po morphine now and repeat in 60 minutes if pain not decreased by 50%

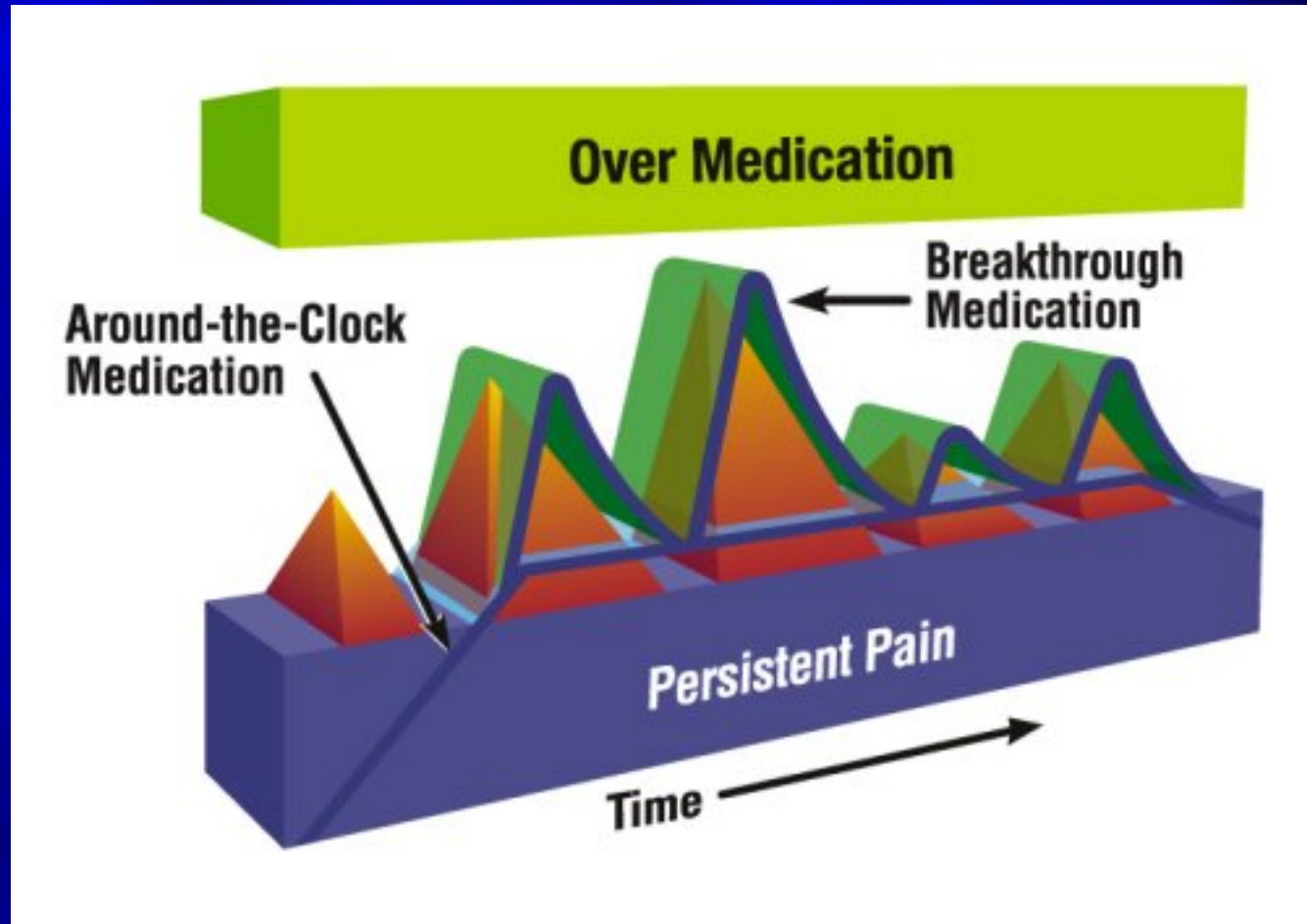
Breakthrough Pain Management Challenges



Breakthrough Pain Management Challenges



Breakthrough Pain Management Challenges



Episodic (Breakthrough) Pain Dose Advances

- We now have a published study to Guide the dosing ratios we use to treat Breakthrough Pain
- The Breakthrough Dose is 10-20% of Daily Opioid Dose when the breakthrough medication is morphine or oxycodone.

Why is oxycodone 5-10 mg often ineffective for breakthrough pain in patients on higher doses of scheduled long - acting opioids?

- Patient on MS Contin 240 mg per day
- Oxycodone 5 - 10 mg po q 4 hr prn pain
- Pain Score = 10/10 with movement

Equianalgesic Table

PO (mg)	Analgesic	SC/IV/IM (mg)
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20	Oxycodone	14
(2-8)	Methadone	(2-8)
-	Fentanyl	100 µg/hr parenteral or transdermal $\equiv$ 4 mg/hr morphine parenteral

Opioid Conversion Calculators

- <http://www.globalrph.com/narcotic.cgi>
- <http://http://www.hopweb.org>.
- <http://www.painphysicians.org/calc/Calculator.php>
- <http://www.lexi.com>
- <https://medicalconverters.net>

Why is oxycodone 5 - 10 mg often ineffective for breakthrough pain?

- Patient on MS Contin 240 mg per day
- Breakthrough pain dose is 10-20 %
- Dose is 24-48 mg Morphine q 2-3 hrs
- 10 mg oxycodone = 15 mg morphine
- Thus any patient requiring >15 mg oral morphine may suffer

Pain Management in Patient with Breast Cancer

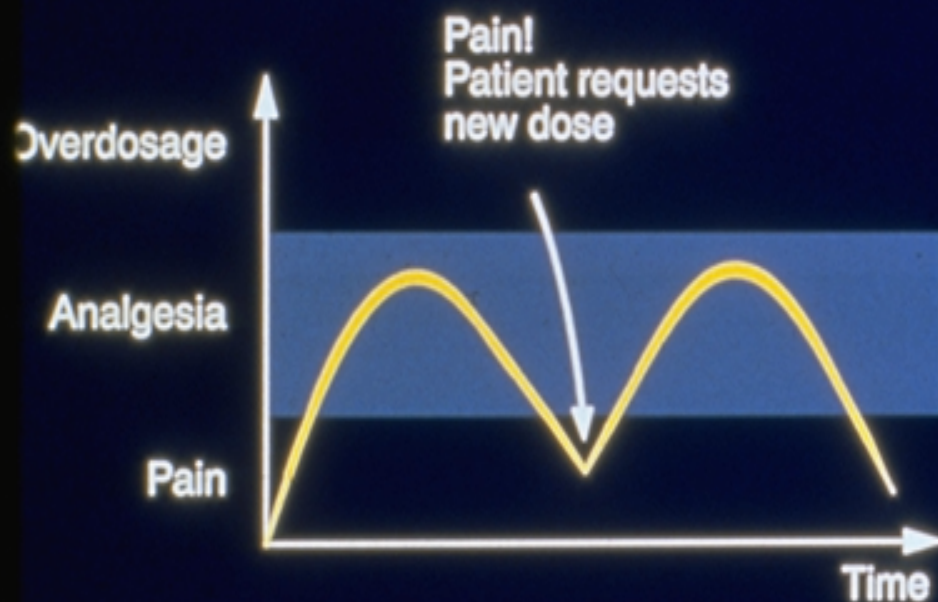
- Patient S/P Mastectomy of left breast with severe pain. She is taking oxycodone 20 mg Q 4 Hours for Chronic Severe Pain X 4 months. Pain Score = 3-5/10 She reports being nauseated at home with vomiting multiple times in past 24 hours.
- Patient is scheduled for radiation therapy.
- Patient appears fatigued.
- Important PMH: Patient with poor renal function (Cr = 2.8)
- Recommend analgesic plan for this patient.

Pain Management in Patient with Breast Cancer

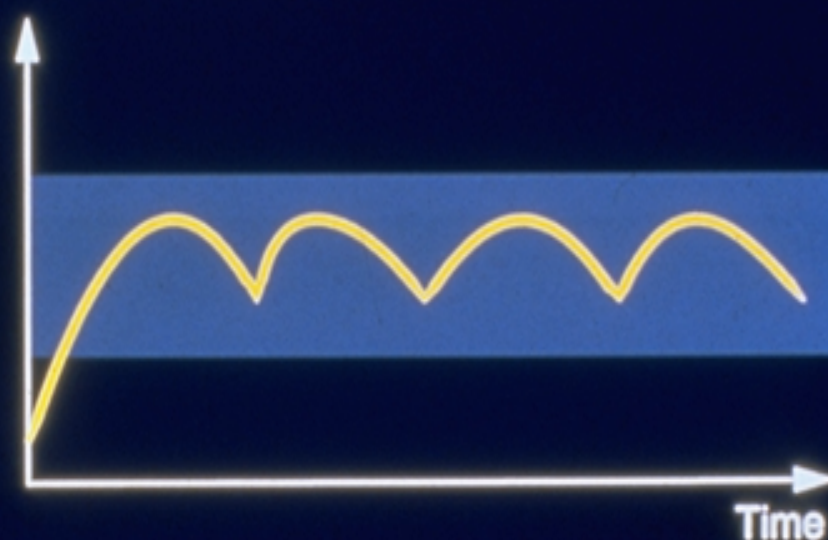
- Mechanism of Pain
 - Inflammatory
 - Neuropathic?
 - Spasm?
- Important Factors
 - Poor Sleep due to pain
 - Decreased Renal Function
 - Opioid tolerance
 - Nausea/Vomiting

Principles of Analgesic Dosage

PRN drug regimen



Continuous prophylactic pain therapy



Tønnessen TI: *Control of Pain and Other Symptoms in Cancer Patients*. New York, Hemisphere Publishing, 1990, p 51, adapted from Twycross, 1982.

Pain Management in Patient with Breast Cancer

- Which analgesics may safely reduce pain?
 - NSAIDs (Cr = 2.8)
 - PCA
 - Fentanyl vs Morphine
 - Acetaminophen
 - Oral Acetaminophen

Equianalgesic Table

PO (mg)	Analgesic	SC/IV/IM (mg)
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20	Hydrocodone	NA
4	Hydromorphone	1.5
20	Oxycodone	14
(2-8)	Methadone	(2-8)
-	Fentanyl*	100 µg/hr parenteral or transdermal = 4 mg/hr morphine parenteral
	* chronic	

Equianalgesic Conversions

Example:

- **Patient with a total 24-hr dose of oxycodone 120 mg PO**
- **What is the equivalent 24-hour dose of PO morphine?**
- $$\frac{\text{Morphine 30 mg PO}}{\text{oxycodone 20mg PO}} = \frac{X}{\text{oxycodone 120 mg PO}}$$
- **X = morphine 180 mg PO per 24 Hours**

Equianalgesic Conversions

Example:

- **Patient with a total 24-hr dose of Morphine 180 mg PO**
- **What is the equivalent 24-hour dose of IV morphine?**
- $$\frac{\text{Morphine 30 mg PO}}{\text{Morphine 10mg IV}} = \frac{\text{Morphine 180 mg PO}}{X}$$
- **X = morphine 60 mg IV per 24 Hours**

Which Fentanyl Patch dose would you suggest for this patient utilizing the equivalent of 60 mg IV morphine per day or 2.5 mg/hr IV morphine?

1. Fentanyl Transdermal Patch 12.5 mcg/hr
2. Fentanyl Transdermal Patch 25 mcg/hr
3. Fentanyl Transdermal Patch 50 mcg/hr*
4. Fentanyl Transdermal Patch 75 mcg/hr
5. Fentanyl Transdermal Patch 37.5 mcg/hr

What medication and settings would you select for this patient's PCA utilizing the equivalent of 60 mg IV morphine per day or 2.5 mg/hr IV morphine?

1. Fentanyl PCA: PCA Dose = 25 mcg, Continuous Infusion = 25 mcg/hr, lockout = 10 minutes

Pain Management in Patient with Breast Cancer

- Follow - up on PCA Utilization with the Fentanyl PCA 10 mcg/ml settings: Basal = 25 mcg/hr, PCA dose = 25 mcg, lockout = 10 minutes
 - EMR Data shows:
 - 60 Attempts and 50 injections over 24 hours
- **Important Discrepancy**
 - PCA Pump interrogation provides following data:
 - PCA doses (injections) = 20 over 24 hours

Equianalgesic Conversions

Example: 50 PCA Doses (Charted in error by Nurse)

- **Patient with a total 24-hr dose of fentanyl 1850 mcg IV**
- **What is the equivalent 24-hour dose of IV morphine?**
- $\text{Morphine 1 mg IV} = \frac{\text{X}}{\text{Fentanyl 1850 mcg IV}} \text{ IV}$
- $\text{Fentanyl 25 mcg IV}$
- **X = morphine 74 mg IV per 24 Hours**
- **X = morphine 222 mg PO per 24 hours (Wrong!!!)**

Equianalgesic Conversions

Example: 20 PCA doses (Actual per pump)

- **Patient with a total 24-hr dose of fentanyl 1100 mcg IV**
- **What is the equivalent 24-hour dose of IV morphine?**
- $$\frac{\text{Morphine 1 mg IV}}{\text{Fentanyl 25 mcg IV}} = \frac{X}{\text{Fentanyl 1100 mcg IV}}$$
- **X = morphine 44 mg IV per 24 Hours**
- **X = morphine 132 mg PO per 24 hours (Correct!!!)**
- **Consider starting Fentanyl Patch 50 mcg//hr or OxyContin 40 mg PO Q 12 Hours plus**
- **Oxycodone 10 – 15 mg PO Q 3 Hours prn BTP**



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