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# The Right Drug, The Right Patient, the Right Time!

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## Disclosures

- None

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## Learning Objectives

- Explain an index of suspicion regarding the potential of health care prescribers' errors
- Recognize a heightened appreciation of adverse events experienced by the patient
- Differentiate appropriate standards of care and system performance failures
- Identify the pharmacokinetics of pain medication, the pharmacology of pain medications and the various pathophysiological aspects of an elderly patient which together influence prescribing
- Distinguish select opioid pharmacokinetics and selected opioid pharmacology

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## The Right Clinical Based Concepts Utilized in Patient-Specific, Patient-Centered, Patient-Focused, Personalized Care

- Right patient
- Right diagnosis
- Right medications
- Right dose
- Right laboratory indices
- Right tests (RFT, LFT, EKG, Hemato, radiology., etc.)
- Right location
- Right route (anatomic location)
- Right administration specifics
- Right time (hours)
- Right dosage forms
- Right CMP or current profile
- Right monitoring parameters
- Right information
- Right patient/advocate understanding
- Right dispensing
- Right communication
- Right generic equivalent
- Right interaction evaluation (food, OTC drugs, Rx drugs, phyto pharmacueticals)
- Right schedules
- Right need(s)
- Right analysis of challenges (physical, emotional, disability)
- Right to document allergies and/or side effects

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Clin. Geriatr Med 21 (2005) 465-490

Pharmacokinetic Considerations in Geriatric Patient

| Parameter | Change With Normal Aging | Common Disease Effects |
|---|---|---|
| Absorption | • GI transit time ↓<br>• Bowel dysmotility ↓ | • Disorders and pharmacotherapy altering gastric pH may reduce drug absorption; surgically altered anatomy may affect absorption, RnY, SLEVE, gastrectomy, ostomy |
| Distribution | • ↑ fat-to-lean body wt. ratio → in ↑ Vd for lipophilic drugs and ↓ Vd for hydrophilic drugs<br>• ↓ serum albumin results in ↑ drug free fraction | • Aging and obesity may result in ≥T1/2 β<br>• ↑ toxicity with ↑ PPB pharmacotherapy |
| Metabolism | • Oxidation (variable and may ↓)<br>• Conjugation often is ≈<br>• First-pass effect often is preserved<br>• Genetic enzyme polymorphisms; ↓ in hepatic blood flow and volume | • Hepatic events (pathologic) may negatively effect oxidation (conjugation preserved) |
| Excretion | • GFR ClCr↓ with age, resulting in ↓excretion; ↓ in renal clearance will ≥ effects of active and other metabolites | • Renal disease → to drug s/e, ADR's and toxicity (ClCr ≤ 30), presence of both functioning kidneys |
| Compliance | • Consider diminished esp. with polypharmacy | • Therapeutic end points not achieved |
| Interaction of Multiple Drugs (CYP 450) | • ↓ or ↑ in serum levels, AUC, CL, $T_{1/2}\beta$ | • Genetic polymorphism CYP inhibition, induction, competitive inhibition |
| Plasma Protein Binding (esp. albumin) | • ↑ serum levels of unbound active drug | • CMP, malnutrition |

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Pharmacology of Opioids

Table 3. *Classification of opioids.*

| Agonists | Antagonists | Agonist/antagonists | Partial agonists |
|---|---|---|---|
| Morphine Codeine<br>Oxycodone<br>Pethidine<br>Diamorphine<br>Hydromorphone<br>Levorphanol<br>Methadone<br>Fentanyl<br>Sufentanyl<br>Remifentanyl<br>Tramadol<br>Tapedolol | Naloxone<br>Naltrexone<br>Nalmefene<br>Diprenorphine | Nalorphine<br>Pentazocine<br>Nalbuphine<br>Butorphanol<br>Denocine | Meptazinol<br>Buprenorphine |

Table 4. *Approximate conversion chart for "equianalgesic" initial doses of opioids.*

| Drug | Route | Equianalgesic Dose |
|---|---|---|
| Morphine | Parenteral<br>PO | 10 mg<br>30 mg (chronic)<br>60 mg (acute) |
| Codeine | PO | 200 mg |
| Fentanyl | Transdermal | 12.6 to 25 mcg/hr |
| Hydrocodone | PO | 20-30 mg |
| Hydromorphone | Parenteral<br>PO | 1.3 to 1.5 mg<br>7.5 mg |
| Meperidine | Parenteral<br>PO | 75 mg<br>300 mg |
| Methadone | Parenteral<br>PO | Variable drug titration |
| Oxycodone | PO | 20-30 mg |
| Oxymorphone | PO<br>Parenteral | 10 mg<br>1 mg |
| Tramadol | PO | undetermined |
| Buprenorphine | Parenteral | 0.3 mg |
| Tapentadol | PO | 100-150 mg |

Note: In making conversions, patients may amalgamate euphoria and analgesia, consequently analgesia may be misrepresented by euphoria and its expectation for pain relief.
Dose Conversion Guideline:
- If switching to methadone, reduce the dose by 75% to 90% and titrate slowly.
- If switching to transdermal fentanyl it may be necessary to reduce the equianalgesic dose.
- Consider further changes in the adjusted equianalgesic dose based on pain source of medical conditions, patient activity, patient functionality and pain complaints, patient's pharmacokinetic profile, comorbidities, and pharmacotherapy.

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Table 2. Opioid metabolism. Pain Physician July/Aug 2011; 14:E343-E360

| Opioid | PG Risk Factor | CYP Substrate | CYP Inducer | CYP Inhibitor |
|---|---|---|---|---|
| Alfentanil | C | 3A4 | | |
| Buprenorphine | C | 3A4 , 2B7, Phase II | | 2D6, 3A4 |
| Butorphanol | C/D | | | 2D6 |
| Codeine | C/D | 2D6, 3A4 | | 2D6 |
| Dihydrocodeine | B/D | 2D6 | | |
| Fentanyl | C/D | 3A4 | | 3A4 |
| Hydrocodone | C/D | Phase II (40%) 3A4 (60%) | | |
| Hydromorphone | C/D | Phase II glucuronidation conjugated 6-OH minor metabolites (6HG<3HG) | | |
| Levorphanol | B/D | Hepatic Phase II | | |
| Meperidine | C/D | 2D6, 2C19, 3A4 | | |
| Methadone | C/D | 3A4, 2C9, 2C19, 2D6 ,2B6 | | 2D6, 3A4 |
| Morphine | C/D | Phase II, 2D6 (minor) | | |
| Nalbuphine | B/D | Hepatic | | |
| Oxycodone | B/D | 2D6 , 3A4 | | |
| Oxymorphone | C | Phase II glucuronidation | | |
| Pentazocine | C/D | Oxidation, glucuronidation | | |
| Propoxyphene | C/D | 2D6 | 2D6 | |
| Remifentanyl | C | Unknown CYP450 nonspecific esterases (blood) and tissue | | 2D6 |
| Sufentanil | C | 3A4 | | |
| Tramadol | C | 2B6, 2D6, 3A4 Phase II | | |
| Tapentadol | C | 85% Phase II; 15% CYP450 (13% 2C9, 2C19, 2% 2D6) | | |

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## References


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