PAINWEEK

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

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Disclosures

- Nothing to disclose

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Learning Objectives

- Explain an index of suspicion regarding the potential of healthcare 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 pharmaceuticals)
- 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 2009;17 (2009): 485–490

Pharmacokinetic Considerations in Geriatric Patient

Parameter	Change With Normal Aging	Common Disease Effects
Absorption	• GI transit time ↓ • 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 ↑ V_d for lipophilic drugs and ↓ V_d for hydrophilic drugs • ↓ serum albumin results in ↑ drug free fraction	• Aging and obesity may result in ≥T1/2 β • ↑ toxicity with ↑ PPB pharmacotherapy
Metabolism	• Oxidation (variable and may ↓) • Conjugation often is = • First-pass effect often is preserved • Genetic enzyme polymorphisms; ↓ in hepatic blood flow and volume	• Hepatic events (pathologic) may negatively effect oxidation (conjugation preserved)
Excretion	• GFR Cl_{CR}↓ 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 ($CrCl_{CR}$ ≤ 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, $T_{1/2}$β	• Genetic polymorphisms CYP inhibition, induction, competitive inhibition
Plasma Protein Binding (eg. 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 Heroin Pethidine Diamorphine Dihydrocodeine Levorphanol Methadone Fentanyl Sufentanyl Alfentanil Tramadol Tapentadol	Naltrexone Naloxone Nalmefene Diprenorphine	Nalorphine Pentazocine Nalbuphine Butorphanol Dezocine	Buprenorphine Meptazinol

Table 4. *Approximate conversion charts for "opioid-naive" initial doses of opioids.*

Drug	Route	Equianalgesic Dose
Morphine	Parenteral PO	10 mg 30 mg (Chronic) 60 mg (acute)
Codeine	PO	200 mg
Fentanyl	Transdermal	12.6 to 25 mcg/hr
Hydrocodone	PO	20–30 mg
Hydromorphone	Parenteral PO	1.5 to 1.5 mg 7.5 mg
Meperidine	Parenteral PO	75 mg 300 mg
Methadone	Parenteral PO	Variable drug titration
Oxycodone	PO	20–30 mg
Oxymorphone	PO Parenteral	10 mg 1 mg
Tramadol	PO	undetermined
Buprenorphine	Parenteral	0.3 mg
Tapentadol	PO	100–130 mg

Note: In making conversions, patients may amalgamate euphoria and analgesia, consequently analgesia may be misrepresented by euphoria
• Use Conversion Guideline
• If switching to methadone, reduce the dose by 75% to 90% and titrate slowly
• Consider further changes to 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 (60%) 3A4 (60%)		
Hydromorphone	C/D	Phase II glucuronidation conjugated 6-OH minor metabolites (6H G>3H G)		
Levorphanol	B/D	Hepatic Phase II		
Meperidine	C/D	2D6, 2C19, 3A4		
Methadone	C/D	3A4, 2C8, 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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