



Geriatric Pharmacotherapy

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Disclosure

- I have no actual or potential conflict of interest in relation to this presentation

Objectives

- Recognize general pharmacokinetic and pharmacodynamic changes in elderly patients
- Discuss drug-related risks in older adults, and review parts of the Choosing Wisely Campaign
- Describe the risks and treatment options for acute stroke and chronic pain in elderly patients
- Apply treatment modalities to specific patient cases



Optimizing Pharmacotherapy in Older Adults

Changes in physiology and oligopharmacy

Pharmacokinetic Changes in Older Adults

- Adsorption

- Increase in stomach pH
- Slowed gastric emptying
- Loss of subcutaneous fat layer

- Metabolism

- Decrease in liver mass and blood flow

- Distribution

- Decrease in total body water
- Increase in total body fat
- Decreased P-glycoprotein efflux transporters

- Excretion

- Cockcroft-Gault equations have been validated in older adults

Pharmacodynamic Changes in Older Adults

- Increased sensitivity
 - Benzodiazepines (BZDs)
 - Opioids
 - Antipsychotics
 - Tricyclic antidepressants (TCAs), α -blockers
 - Warfarin
 - Non-steroidal anti-inflammatory drugs (NSAIDs)
- Decreased sensitivity
 - β -blockers and agonists
- Impaired homeostasis
 - Diuretics and angiotensin-converting enzyme inhibitors

Patient Case

- Utilize this case to answer questions 1 & 2 on the next slide
- An 83-year-old woman (weight 65 kg) who resides at home with her daughter has a medical history significant for type 2 diabetes and hypertension, and 2 years ago, she sustained a right hip fracture after a fall. Her regularly scheduled medications include metformin 500 mg twice daily, glyburide 10 mg once daily, and aspirin 81 mg once daily. Her as-needed medications include melatonin 6 mg at bedtime for sleep, meclizine 12.5 mg three times daily as needed for dizziness, and docusate 100 mg twice daily. Her laboratory results show fasting plasma glucose 90 mg/dL, Na 138 mEq/L, K 4.5 mEq/L, Cl 102 mEq/L, CO₂ 25 mEq/L, BUN 30 mg/dL, SCr 1.8 mg/dL, and thyroid-stimulating hormone (TSH) 4.0 mU/L.

Patient Case Questions

1. Considering the potential for altered pharmacokinetics, which set of medications has the highest potential to cause problems for the patient?
 - A. Lisinopril and meclizine
 - B. Glyburide and metformin
 - C. Lisinopril and metformin
 - D. Aspirin and melatonin

2. Considering the potential for increased pharmacodynamics sensitivity, which set of medications has the highest potential to cause problems for the patient?
 - A. Lisinopril and meclizine
 - B. Glyburide and metformin
 - C. Lisinopril and metformin
 - D. Aspirin and melatonin

Irregularities in Medication Regimens

- Unnecessary drugs:
 - Excessive dose
 - Excessive duration
 - Without adequate monitoring
 - Without adequate indications for its use
 - In the presence of adverse consequences warranting a decrease in dose or discontinuation

Drug-related Risks in Older Adults

- Beers Criteria for Potentially Inappropriate Medications
 - Medications best avoided in older adults in general
 - Those with certain diseases or syndromes
 - Prescribed at reduced dosage
- Associated with poor health outcomes
 - Confusion, falls, and mortality
- Generally excluded patients in the hospice/palliative care settings

Drug-related Risks in Older Adults

- Examples to avoid:
 - Anticholinergics – meclizine, promethazine, antispasmodics
 - Cardiovascular – clonidine, doxazosin, digoxin, dronedarone
 - Central nervous system – amitriptyline, doxepin, barbiturates, BZDs (diazepam, clonazepam), zolpidem
 - Endocrine – sliding scale insulin alone, glyburide, estrogens
- Avoid in Drug-disease or Drug-Syndrome states
 - Heart failure – NSAIDs or COX-2 inhibitors, non-dihydropyridine calcium-channel blockers
 - Delirium – famotidine, corticosteroids, antipsychotics
 - History of falls – anticonvulsants, zolpidem, TCAs, SSRIs

Drug-related Risks in Older Adults

- Drug-drug interactions that should be avoided
 - Corticosteroids + NSAIDs
 - Lithium + loop diuretic/ACEIs
 - Peripheral alpha-1 blocker + loop diuretic
 - Warfarin + amiodarone/NSAIDs
- Dose-reduction or avoidance in varying levels of kidney function
 - Famotidine – CrCl < 50 mL/min → reduce dose
 - Tramadol – CrCl < 30 mL/min → IM: reduce dose/ER: avoid
 - Gabapentin – CrCl < 60 mL/min → Reduce dose
 - Duloxetine – CrCl < 30 mL/min → avoid

Drug-related Risks in Older Adults

- Choosing Wisely Campaign
 1. Antipsychotics in patients with dementia
 2. Target HbA_{1c} \geq 7.5%
 3. Avoid BZDs and sedative-hypnotics, for insomnia, agitation, or delirium
 4. Do not start antimicrobials to treat bacteriuria without symptoms
 5. Assess benefit vs. risk of cholinesterase inhibitors
 6. Appetite stimulants not helpful for anorexia or cachexia
 7. Drug regimen review is necessary for every new prescription
 8. Avoid lipid-lowering medications in patients with limited life expectancy

Patient Case

- Utilize this case to answer questions 3 & 4 on the next slide
- A 70-year-old woman (height 66 inches, weight 71.7 kg [158 lb]) is in the clinic for an evaluation by the clinical pharmacist for polypharmacy. She has complaints of fatigue, light-headedness, constipation, and “too many medicines.” Her medical history is significant for hypertension, coronary artery disease (drug-eluting stent 8 years ago), chronic obstructive pulmonary disease, diabetes mellitus, incontinence, frequent urinary tract infections, depression, and moderate dementia. Vital signs include blood pressure 160/82 mm Hg, heart rate 51 beats/minute, respiratory rate 16 breaths/minute, and O₂ saturation 99% on room air.
- Her current medications are as follows: Advair 250/50 1 puff twice daily, aspirin 81 mg daily, acetaminophen 650 mg three times daily, clopidogrel 75 mg daily, donepezil 10 mg daily, glipizide 5 mg twice daily, lisinopril 10 mg daily, loratadine 10 mg daily, metoprolol 50 mg twice daily, paroxetine 50 mg daily, ranitidine 150 mg twice daily, simvastatin 40 mg at bedtime, and tolterodine 2 mg at bedtime. Nitrofurantoin 50 mg twice daily x 10 days was initiated 3 days ago.
- Laboratory values from her physician visit 3 days before are as follows: sodium (Na) 130 mg/dL, potassium (K) 4.2 mEq/dL, chloride (Cl) 99 mg/dL, CO₂ 24 mEq/dL, blood urea nitrogen (BUN) 24 mg/dL, SCr 1.6 mg/dL, fasting glucose 67 mg/dL, A1C 6.3%, urinalysis negative except for: blood- small, pH 7.5, RBC 11–25/high-power field (HPF), WBC 0-2/HPF, bacteria 168/HPF.

Patient Case Questions

3. Which medication list best depicts potentially inappropriate medications for this patient according to the AGS 2015 Beers Criteria?
 - A. Paroxetine, ranitidine, donepezil, tolterodine
 - B. Donepezil, metoprolol, glipizide, simvastatin
 - C. Glipizide, donepezil, nitrofurantoin
 - D. Metoprolol, clopidogrel, ranitidine

4. Which medications would best be evaluated for discontinuation, according to the Choosing Wisely Criteria?
 - A. Paroxetine, ranitidine, donepezil, tolterodine
 - B. Donepezil, metoprolol, glipizide, simvastatin
 - C. Glipizide, donepezil, nitrofurantoin
 - D. Metoprolol, clopidogrel, ranitidine



Acute Ischemic Stroke (AIS)

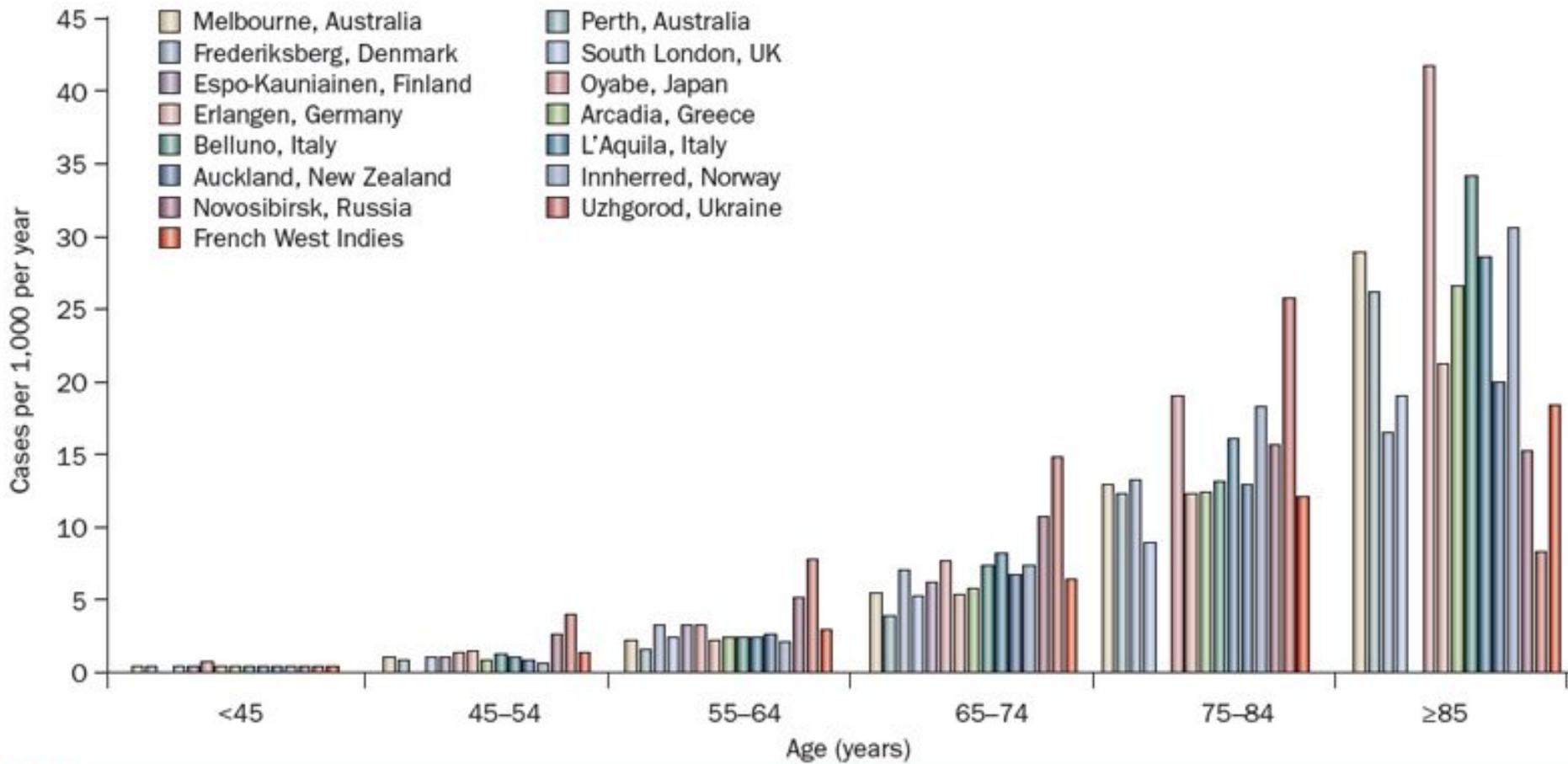
Changes in the elderly brain and increased risk of AIS

Introduction

- Stroke is the leading cause of disability worldwide, second most common cause of dementia, and the third leading cause of death
- Classification
 - Ischemic
 - Occlusion of bloodflow to a focal region of the brain
 - Hemorrhagic
 - Focal collection of blood within the brain parenchyma, subarachnoid space, or ventricular system
- Non-contrast head CT helps to rule-out intracranial hemorrhage
 - Less specific for ruling-in ischemic changes

Acute Stroke and the Elderly Patient

- Age as a factor in risk of acute stroke
 - Stroke risk doubles every decade after 55 in both sexes
 - 75-89% of strokes occur in individuals >65 years old
- As the aging population increases, the incidence of acute stroke increases
 - Also increasing the need for better post-stroke management
- Increased vulnerability 2/2 brain changes in the elderly population
 - Decrease in Na⁺/K⁺ ATPase performance
 - Decrease in glutamate clearance
 - Decrease in surface area of blood brain barrier capillary systems



Medscape

Source: Nat Rev Neurol © 2010 Nature Publishing Group

Aging-related Risk Factors

- Sex
 - Mex aged 65-79
 - Women >80
- Atrial Fibrillation
- Congestive heart disease
- Physical inactivity
 - Increases risk from multiple factors
- Carotid artery disease
 - Atherosclerosis
- Hypertension
 - Less important >80 years old

Modifiable Risk Factors

- Hypertension
- Smoking status
- Heart disease
- Oral contraceptive use
- Dyslipidemia
- Obesity
- Physical inactivity
- Diabetes
- Alcohol consumption
- Drug abuse
- Inflammatory disease
- Sleep-disordered breathing

Treatment

- Reperfusion and neuroprotection
- Limited data on tPA treatment in patients >80 y.o.
 - 0.9 mg/kg IV (max dose 90mg)
 - 10% of total dose given over 1 minute
 - Remainder given as IV infusion over 60 minutes
- Over 1,000 drugs have been investigated for neuroprotection
 - Only ~100 have made it to trial

Contraindications for tPA

- Intracranial hemorrhage on CT
- History of intracranial hemorrhage
- Known intracranial arteriovenous malformation, neoplasm, or aneurysm
- Clinical presentation suggest subarachnoid hemorrhage
- Neurosurgery, head trauma, or stroke in past 3 months
- Uncontrolled hypertension (>185 mmHg SBP or > 110 mmHg DBP)
- Active internal bleeding
- Suspected/confirmed endocarditis
- Known bleeding diathesis
- Abnormal blood glucose (<50 or > 400 mg/dL)

Additional Warning to tPA 3-4.5 hr After Onset

- Age >80 years
- History of prior stroke and diabetes
- Any active anticoagulant use (even with INR <1.7)
- NIHSS >25
- CT shows multilobar infarction (hypodensity >1/3 cerebral hemisphere)

Secondary Prevention

- Other treatment options, early mobility, and correction of physiological variables:
 - Antihypertensive therapy
 - Antiplatelet therapy
 - Aspirin, clopidogrel, or aspirin/dipyridamole extended release
 - Anticoagulation only if patient has concurrent atrial fibrillation
 - Statin therapy
 - anti-inflammatory, anti-thrombotic, plaque stabilization, antioxidant effects

Patient Case

- Utilize this case to answer questions 5 & 6 on the next slide
- A 76-year-old woman (weight 98 kg) was recently admitted to a long-term care (LTC) facility for rehabilitation after multiple falls at home. She had no loss of consciousness associated with any of the falls, and no head trauma resulting from them either. Her medical history is significant for hypertension, hypothyroidism, Alzheimer disease (AD), hyperlipidemia, and osteoarthritis (OA). She currently takes metoprolol succinate 50 mg daily, levothyroxine 75 mcg daily, atorvastatin 10 mg daily, and donepezil 10 mg daily.
- Her blood pressure is 126/80 mm Hg and heart rate is 66 beats/minute. Basic metabolic panel results were all within reference ranges; 25-hydroxy-vitamin D concentration was 20 ng/mL, TSH 1.89 mU/L, total cholesterol 180 mg/dL, low-density lipoprotein cholesterol 140 mg/dL, high-density lipoprotein cholesterol 35 mg/dL, and triglycerides 176 mg/dL. Her Mini-Mental State Examination (MMSE) score was 16/30, and her Geriatric Depression Scale (GDS) score was 2/15.

Patient Case Questions

5. What is the best intervention for reducing the incidence of ischemic stroke in this patient?
- A. Initiate aspirin 81 mg daily
 - B. Increase atorvastatin to 20 mg daily
 - C. Initiate hydrochlorothiazide 25 mg daily
 - D. Increase metoprolol succinate to 100 mg daily

Patient Case Questions

- One of the caretakers at the LTC facility notices that our patient is having difficulty forming her words, a noticeable right facial droop, and is unable to hold her drinking glass in her right hand. EMS is called and she is promptly taken to the closest stroke center emergency department. She arrives within 1 hour of last known normal, and within 30 minutes a head CT without contrast confirms an acute ischemic stroke. Her blood pressure is 170/97 mmHg and heart rate is 64 BPM on admission. Complete blood count results were as follows: white blood cells was $7.5 \times 10^3/\mu\text{L}$, hemoglobin was 15.4 g/dL, hematocrit was 40.2%, and platelet count was $232 \times 10^3/\mu\text{L}$. A point of care blood glucose was 124 mg/dL. NIHSS score was 16.

6. Is the patient a candidate for tPA administration?

A. Yes

B. No



Chronic Pain Management

Alternative options and multimodal therapy

Pain Management in the Elderly

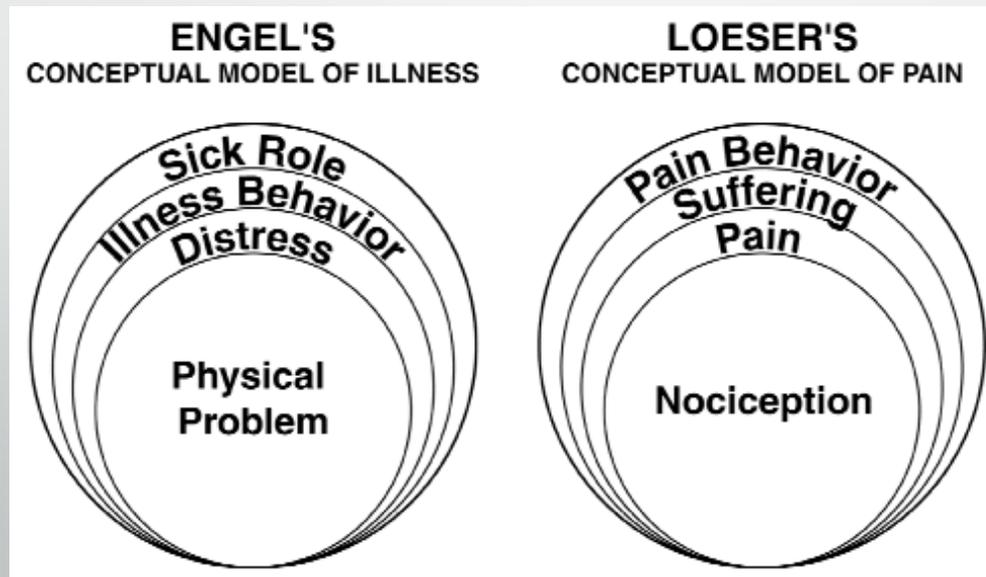
- Misconception that pain is an inevitable part of aging
- Fear of addiction, being labeled as weak, adverse drug reactions, loss of independence
- Comorbidities – depression, dementia, altered mental status
- Polypharmacy
- Biopsychosocial model

Pain Management in the Elderly

- **Dermatology** — pressure or ischemic ulcers, burns, scleroderma
- **Gastrointestinal** — constipation, irritable bowel disease, diverticulitis, inflammatory bowel disease
- **Cardiovascular** — advanced heart disease, peripheral vascular disease
- **Pulmonary** — advanced chronic obstructive pulmonary disease, pleurisy
- **Rheumatology** — osteoarthritis, rheumatoid arthritis, gout, pseudogout, polymyalgia rheumatica, spinal stenosis and other low back syndromes, myofascial syndromes, osteoporotic related fractures
- **Endocrine** — diabetic neuropathy, Paget's disease
- **Nephrology** — chronic cystitis, end stage renal disease
- **Immune** — herpes zoster, post-herpetic neuralgia, HIV/AIDS neuropathy
- **Neurology** — headache, peripheral neuropathies, compressive neuropathies, radiculopathies, Parkinson's disease, post-stroke pain
- **Oncology** — cancer
- **Miscellaneous** — depression, tendonitis, bursitis

Biopsychosocial Model

- Philosophy – understanding of how suffering, disease, and illness are affected by multiple levels of organization
 - Societal → molecular
- Practicality – understand patient's subjective experience
 - Essential contributor to accurate diagnosis, health outcomes, and humane care



Classification of Pain

- Nociceptive pain – activity in neuronal pathways caused by actual tissue damage or potentially damaging tissue stimuli
 - Ex. Post-operative pain, arthritis, mechanical pain
 - Physiologic and protective
- Neuropathic pain – activity stimulated by nervous system lesions or dysfunction
 - Ex. Multiple sclerosis, diabetic neuropathy, post-herpetic neuropathy, stroke
 - Pathophysiologic and harmful

Classification of Pain

- Acute pain – occurs immediately after an injury to the body and typically resolves when healing or the pain-producing stimulus is removed
- Chronic pain – occurs beyond the expected time for healing. Can persist for months to years, and be described as episodic, continuous, or a combination of both.

Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale

| Pain Questionnaire | Response |
|--|-------------------|
| Does your pain feel like strange, unpleasant sensations in your skin? Words like pricking, tingling, pains and needles might describe these sensations | No = 0 Yes = 5 |
| Does your pain make the skin in the painful area look different than normal? Words like mottled or looking more red or pink might describe the appearance. | No = 0 Yes = 5 |
| Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity. | No = 0 Yes = 3 |
| Does your pain con on suddenly and in bursts for no apparent reason when you're still. Words like electric shocks, jumping and bursting describe these sensations. | No = 0 Yes = 2 |
| Does your pain feel as if the skin temperature in the painful are has changed abnormally? Words like hot and burning describe these sensations | No = 0 Yes = 1 |
| Sensory testing | Response |
| Allodynia – pain or unpleasant sensation when lightly stroking cotton wool across the area without the same sensation on the non-painful area. | No = 0 Yes = 5 |
| Altered pin-prick threshold – difference in sensation of a 23 gauge needle placed gently on the skin in a non-painful area and in a painful area. (Either no sensation or very painful sensation) | No = 0 Yes = 3 |
| < 12 = likely nociceptive pain ≥ 12 = likely neuropathic pain | Total: |

Pharmacotherapy for Nociceptive Pain

- Acetaminophen (APAP)
 - Caution in liver failure and chronic alcohol use
 - 2-3 gm max for liver dysfunction
- NSAIDs
 - Monitor for hypertension, gastrointestinal issues, renal issues
 - Contraindicated in renal disease, congestive heart failure, and patients on anticoagulation
 - Interfere with cardioprotective effect of aspirin (except naproxen)
- Tramadol
 - Causes dizziness
 - Decreases seizure threshold, increases serotonin syndrome risk
 - Synergistic effect with APAP

Alternative Therapies for Neuropathic Pain

- Anticonvulsants
 - Gabapentin
 - Start low, titrate slowly
 - Pregabalin
 - Doesn't require lengthy titration
 - Lamotrigine
 - Not considered first line
- Antidepressants
 - Duloxetine
 - Venlafaxine

Alternative Therapies for Neuropathic Pain

- Local anesthetics
 - Lidocaine
 - Up to 3 patches at one time
 - Maintain 12 hr on/off periods
- Topical analgesics
 - Capsaicin
 - Requires several weeks of use for effectiveness

Opioid Therapy

- Generally used if non-opioid treatment ineffective
- Common AEs – constipation, cognitive decline, increased fall risk, hip fracture, exacerbation of sleep apnea
 - Recent articles showing increased risk of overdose, heart disease, and GI bleed if >65
- The analgesic effect of opioids is preserved while tolerance develops to most AEs
 - Except constipation

| Drug Name | Parenteral Dose (mg) | Oral Equivalent (mg) | Adult Oral Starting Dose (mg) | Comments |
|------------------|----------------------|----------------------|-------------------------------|---|
| Pure Agonists | | | | |
| Morphine | 10 | 30 | 15-30 | Active metabolites can accumulate in renal impairment |
| Fentanyl | 0.1 | -- | -- | Transdermal fentanyl should not be used in opioid naïve patients |
| Hydrocodone | -- | 30 | 10 | Abuse deterrent products available |
| Methadone | Variable | Variable | 5-10 | *See next slide* |
| Meperidine | 100 | 300 | -- | Toxic metabolite accumulates with repeated dosing, causing CNS excitation |
| Oxycodone | -- | 20 | 10-20 | Abuse deterrent products available |
| Hydromorphone | 1.5 | 7.5 | 4-8 | Physical barrier on ER tablets |
| Central Agonists | | | | |
| Tramadol | -- | 300 | 50-100 | Maximum 400 mg/day. Dose adjustment required in renal dysfunction |

Methadone

- Use with extreme caution in the elderly patient
- Long and variable $t_{1/2}$ - 8 to 59 hours
 - Difficult to predict serum levels
- Increased drug-drug interactions
- Ventricular arrhythmias – torsades de points

Mental Health Considerations

- Alzheimer's Disease:
 - Baseline cognitive decline make assessment and treatment more difficult
 - Debate on level of pain felt by these individuals as compared to neurologically normal adults
 - Possible sensory changes accompanying the cognitive decline
- Dementia:
 - Similar to Alzheimer's in the difficulty to vocalize pain
 - Opioid treatment is the most studied modality of therapy
 - Increase risk of dementia as total standardized daily doses increase >91

Useful Resource

- Pain Assessment and Management Initiative
 - University of Jacksonville College of Medicine
 - Pain Management and Dosing Guide Includes:
 1. Principles of Pain Management, Discharge and Patient Safety Considerations, Analgesic Ladder
 2. Non-opioid Analgesics, Opioid Prescribing Guidelines and Equianalgesic Chart, Opioid Cross-Sensitivities, Intranasal Medications
 3. Nerve Blocks, Neuropathic Pain Medications, Muscle Relaxer Medications, Ketamine Indications
 4. Topical and Transdermal Medications
 5. Procedural Sedation and Analgesia (PSA) Medications
 6. Stepwise Approach to Pain Management and PSA
 - http://americanpainsociety.org/uploads/education/PAMI_Pain_Management_and_Dosing_Guide_02282017.pdf



Questions?

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