Dementia

Meded101.com

Major Types of Dementia

- Alzheimer's
  - Plaques in the brain
  - Most common form of dementia
- Vascular
  - Loss of blood supply to certain regions of the brain
  - Damaged vessels - Stroke, atherosclerosis can contribute
- Lewy Body
  - Usually associated with Parkinson's
  - Abnormal clumps of protein found in the brain

Dementia-Like Causes

- B12 deficiency
- Hypothyroid
- Mental illness
- Medications associated with dementia symptoms: Tricyclic antidepressants, benzodiazepines, opioids, antiepileptic agents, beta-blockers, antihistamines, Z-drugs, incontinence anticholinergics, sleepers

Vascular Dementia Treatment

- Hypertension
- Diabetes Care
- Statin Use
- Anticoagulation – Cardioembolic stroke and/or TIA hx
- Antiplatelet therapy for non-cardioembolic, ischemic stroke
- Acetylcholinesterase inhibitors
- Less evidence for memantine

NMDA Antagonists - Memantine

- Mechanism of Action: Blockade of N-methyl-d-aspartate (NMDA) receptors which helps reduce the activity of glutamate which is an excitatory amino acid that is proposed to contribute to brain cell death and dementia
- CNS side effects
- Used in moderate to severe Alzheimer's dementia
  - Less evidence in dementia with Lewy bodies, role unclear
- Dose adjusted with reduced kidney function
- Can be used in combo with acetylcholinesterase inhibitor particularly in advanced dementia
- 28 mg of XR is approximately equivalent to 20 mg of immediate release

Acetylcholinesterase Inhibitors

- Mechanism of Action: Inhibits acetylcholinesterase which is responsible for degradation of CNS acetylcholine (theorized to be a significant player in memory and brain function); ultimately leads to an increase in cholinergic function in the CNS
- **Donepezil** (Aricept), rivastigmine (Exelon), galantamine (Razadyne), tacrine (Cognex)
- Used in mild to moderate Alzheimer's dementia, Lewy Body Dementia
- GI side effects are most common (think opposite effects of anticholinergic medications)
  - Diarrhea, nausea, vomiting
  - Weight loss
  - Bradycardia
  - Rarely can cause insomnia
    - Donepezil is dosed at night in case patient gets GI side effects

Acetylcholinesterase Inhibitors

- Rivastigmine comes in a patch and oral formulation
  - Possibly less GI side effects
  - Rarely used due to cost $$$
  - Oral tablets are dosed twice daily
- Weekly patch formulation of donepezil (Adlarity) - $$$
  - Possible reduced GI adverse effects
  - Option for those with difficulty swallowing
- Interaction with anticholinergics (they can cause confusion and blunt effects of acetylcholinesterase inhibitors)

Dementia Related Behaviors

- Wandering
- Restless
- Agitation
- Physical Aggression
  - Hit, bite, kick
- Hallucinations
- Delusions

Behavior Identification

- Contributing factors
  - Individual person
  - Time of day
- Rule Out Causes
  - Pain
  - Infection
  - Medication changes

Solutions

- Solve underlying problem
  - Rule out B12 deficiency, thyroid issues, and possible medication(s), environmental factors contributing to memory loss
  - Medications associated with dementia symptoms: Tricyclic antidepressants, benzodiazepines, opioids, antiepileptic agents, beta-blockers, antihistamines, Z-drugs, incontinence anticholinergics, sleepers
- Non-drug approaches
- Make sure problem is distressing to patient before treating
- Medications last resort
  - Drugs don’t often “treat” behaviors effectively

Medication Management of Behaviors

- Antipsychotics
  - Black box warning for increased risk of death in dementia patients
  - Used off label in dementia
    - Only use for severe, distressing symptoms (aggression, paranoia, hallucinations, delusions)
  - Brexpiprazole received FDA approval for treatment of Alzheimer's agitation
    - Statistically significant reduction in behaviors but clinical significance can be debated
- Trazodone (Desyrel)
  - Tolerated ok in the elderly at low doses
  - Sedating (typically will dose at night)
  - In addition to sedation, orthostasis, dry mouth are common adverse effects

Medication Management of Behaviors

- Buspirone (Buspar)
  - Generally well tolerated in elderly compared to other higher risk agents like benzo's and antipsychotics
  - Classified as antianxiety medication
  - Multiple doses generally required (BID/TID)
  - Takes a while to have a clinical effect
- Benzodiazepines
  - Can help with insomnia and anxiety symptoms, but lots of problems with side effects in the elderly
  - Fall risk
  - Can exacerbate patient's confusion
  - Disinhibition is a possible effect (i.e. it may make patients behaviors worse)
- Antidepressants
  - May help if they have depression
  - If OCD, anxiety and PTSD history, they may be helpful as well

Medication Management of Behaviors

- Mood stabilizers
  - Some clinicians will use these medications to help with anger/aggressive behaviors
    - i.e. valproic acid (Depakote), lamotrigine (Lamictal)
- Pimavanserin (Nuplazid)
  - Mechanism of Action: Antagonist at serotonin 5HT2A receptors, and to a less extent, an antagonist at 5HT2C receptors
  - May see used off-label in Alzheimer's dementia
  - Indicated for hallucinations/delusions associated with Parkinson's disease related psychosis
  - Crazy expensive
  - 3A4 inhibitors can increase concentrations
  - Non-dopamine blocking atypical antipsychotic

Nurse Management: Dementia Care

- Cognitive status and changes from baseline (memory, orientation, attention)
- Behavioral and psychological symptoms (agitation, aggression, hallucinations, wandering)
- Safety risks (falls, wandering, ability to perform activities of daily living)
- Medication effects and adverse reactions, especially with antipsychotics, sedatives, and cholinesterase inhibitors
- Nutritional status and hydration (weight changes, appetite, swallowing ability)
- Sleep patterns and changes in sleep–wake cycle
- Mood and mental health (depression, anxiety, apathy)
- Pain and discomfort, including nonverbal signs
- Elimination patterns (constipation, incontinence, urinary retention)
- Caregiver stress and ability to manage care needs

Headache

Meded101.com

Nursing Pearls

- Headache characteristics (onset, location, intensity, duration, triggers)
- Frequency and response to treatment or medications
- Red-flag symptoms (sudden severe headache, fever, neck stiffness, vision changes, focal deficits)
- Medication use and side effects, including overuse or rebound headaches
- Blood pressure, especially with severe headache or migraine therapies
- Nausea, vomiting, photophobia, and phonophobia
- Hydration status, sleep patterns
- Impact on daily functioning and quality of life

Types of Headache

- Tension
- Migraine
- Cluster
- Medication Overuse/Rebound

Tension

- Dull, constant pain
- Bilateral
- Milder pain/pressure
- Light and sound sensitivity
- Most common headache
- Usually relieved by OTC NSAID or acetaminophen

Migraine

- Intense, stabbing pain
- Typically one sided
- Aura (not all)
- High sensitivity to light/sound
- Nausea/Vomiting
- More common in females

Cluster

- Severe, recurrent
- More common in men
- Stabbing/burning pain around an eye
- Generally shorter in duration than migraine/tension
- “Attacks” – can happen multiple times per day and over a period of weeks to months

Medication Overuse

- Taking frequent analgesics (>15 days/mo)
- Symptoms can vary
  - Can be more tension type headache and/or migraine type symptoms
- Stopping drug is the intervention
  - Symptoms get worse for 1-2 weeks

Medication Overuse/Rebound

- Often precipitated by initial onset of headache
- Repeated use of medication over time to relieve headache
- Drug Causes
  - Caffeine
  - Opioids
  - Triptans
  - NSAIDs
  - Acetaminophen

Management of Tension Headache

- Non-pharmacologic
  - Reduce stress
  - Avoid triggers
  - Rest
- Pharmacologic
  - Acetaminophen
  - NSAIDs
  - Combination with Caffeine
  - Triptans
  - Opioids

Migraine Treatment

- Triptans (see next slide)
- Antiemetics can be used in patients with significant nausea/vomiting
  - Metoclopramide, prochlorperazine, chlorpromazine
- Dihydroergotamines
  - Generally avoided
  - Most dosage forms very expensive
  - Do NOT use if pregnancy is a possibility
- In general, avoid opioids and butalbital
  - Not that effective
  - Risk of dependence and medication overuse headaches
- Alternatives in patients with failure to triptans
  - Lasmiditan – selective serotonin 1F receptor agonist
  - Rimegepant, ubrogepant – CCRP antagonists

Triptans

- Sumatriptan (Imitrex), rizatriptan (Maxalt), frovatriptan (Frova), naratriptan (Amerge), almotriptan (Axert), Eletriptan (Relpax), zolmitriptan (Zomig)
- Mechanism of Action: Selective 5HT1 receptor agonist, which potentially helps with vasoconstriction that contributes to headache symptoms
- May be used in combination with simple analgesics
- Adverse effects – CNS changes, dizziness, chest pressure
- Meant for acute relief, not prophylaxis

Triptans

- Potential for serotonin interactions (SSRI's, tramadol, MAOIs, etc.)
  - A patient being treated with an SSRI for depression is typically not a contraindication to triptan use
- Nonoral options for those with significant nausea and vomiting (i.e. nasal, injectable) – sumatriptan is the most commonly used agent and has oral, injectable (fastest onset), and nasal dosage formulations
- Generally avoided in patients with uncontrolled blood pressure, ischemic stroke or heart disease, Prinzmetal's angina, and pregnancy

Triptan Comparison Chart

Drug (Trade name)	Route	Typical dosing range (24 hr max dose)	Onset	Half-life	Tmax	Metabolizing enzymes
sumatriptan (Imitrex, Zembrace)	Oral tablet	25-100 mg x1, may repeat after 2 hours if needed (200 mg)	30 min	~1.5-3 hrs	2-2.5 hrs	MAO-A
	Nasal spray	5-20 mg x1, may repeat after 2 hours if needed (40 mg)	15 min	3 hours	10 min	
	Subcutaneous injection	1-6 mg x1, may repeat after 1 hour if needed (12 mg)	10 min	~1.5-3 hrs	12 min	
rizatriptan (Maxalt)	Oral tablet/orally disintegrating tablet	5-10 mg x1, may repeat after 2 hours if needed (30 mg)	30 min	2-3 hrs	1-2 hrs	MAO-A, CYP3A4
zolmitriptan (Zomig)	Oral tablet	1.25-2.5 mg x1, may repeat after 2 hours if needed (10 mg)	1 hr	3 hrs	1.5-3 hr	CYP3A4
	Nasal spray	2.5 mg x1, may repeat after 2 hours if needed (10 mg)	15 min	3 hrs	N/A	
naratriptan (Amerge)	Oral tablet	1-2.5 mg x1, may repeat after 4 hours if needed (5 mg)	1 hr	6 hrs	2-4 hrs	CYP3A4, MAO-A
almotriptan (Axert)	Oral tablet	6.25-12.5 mg x1, may repeat after 2 hours if needed (25 mg)	30 min	3-4 hrs	1-3 hrs	MAO-A, CYP3A4, CYP2D6
frovatriptan (Frova)	Oral tablet	2.5 mg x1, may repeat after 2 hours if needed (7.5 mg)	2 hrs	26 hrs	2-4 hrs	CYP1A2
eletriptan (Relpax)	Oral tablet	20-40 mg x1, may repeat after 2 hours if needed (80 mg)	30 min	4 hrs	1.5-2 hr	CYP3A4

Alternatives To Triptans

- Lasmiditan – selective serotonin 1F receptor agonist
  - 50-100 mg dose once every 24 hours (max)
  - Serotonin syndrome risk
  - Does not see same vasoconstriction effects due to 1000-fold affinity for 1F receptor – may be safe in patients with cardiovascular risk factors

Alternatives To Triptans

- Rimegepant (Nurtec ODT), ubrogepant (Ubrelvy), zavegepant (Zavzpret), atogepant (Qulipta) – CGRP antagonists (also see prevention below)
  - May be considered when triptans are contraindicated
  - CYP3A4 drug interactions may be problematic with some of these agents
  - Dose reductions and/or avoidance of these agents in severe CKD
  - Atogepant and rimegepant are approved for both acute management and prophylaxis of migraines
  - Ubrogepant, zavegepant – only indicated for acute management
  - Zavegepant – nasal option

Alternatives To Triptans

- Antiemetics
  - Used to help control N/V symptoms and pain associated with migraine
  - In addition to antiemetic effects, IV prochlorperazine or metoclopramide may have the best evidence to help reduce pain associated with migraine
    - Dopamine blocking action may increase risk for dystonic reactions so diphenhydramine may be given in combination with these agents
  - Other agents that may be considered haloperidol, ondansetron, chlorpromazine
    - Watch QT prolongation risk

Alternatives To Triptans

- Dihydroergotamines
  - Mechanism of Action: 5-HT agonist activity similar to triptans, but also may have other effects on dopamine, serotonin, and adrenergic receptors
  - Generally avoided, most dosage forms very expensive, warnings and risks
  - Do NOT use if pregnancy is a possibility
  - Boxed warning on interaction with CYP3A4 inhibitors like protease inhibitors, azole antifungals, and macrolides
  - Potential adverse cardiovascular effects (increase in blood pressure)
- In general, avoid opioids and butalbital
  - Not that effective
  - Risk of dependence and medication overuse headaches

When To Use Migraine Prophylaxis?

- Severe, long duration of headaches
- Frequent headaches per month
- Can’t tolerate acute therapies
- Impacting quality of life
  - Work
  - Family issues

Migraine Prophylaxis

- Topiramate
  - Cognitive slowing, weight loss, ammonia, metabolic acidosis, renal stones
- Propranolol
  - Sedating, pulse/BP monitoring, watch respiratory conditions
- Valproic Acid
  - Lab monitoring (CBC, LFTs), hepatic issues, weight gain, pregnancy risk, ammonia
- Tricyclic antidepressants
  - Highly anticholinergic
- SNRI’s
- CCB’s

Cluster Headaches

- Acute
  - Oxygen
  - Triptans
    - Consider ergotamines, intranasal lidocaine, or octreotide in non-responders to oxygen/triptan combination
- Prophylaxis
  - Calcium channel blockers first line (non-DHP)
    - Verapamil
  - Topiramate, steroids, CGRP antagonists, lithium as alternatives (weak evidence)

Parkinson’s Disorder

Meded101.com

Parkinson’s Symptoms

- Tremor (one-sided)
- Rigidity ”stiffness”
  - Pain
  - Alters range of motion
- Akinesia (loss of movement)
- Postural instability
  - Unable to remain in a stable (generally upright position)
- Can be challenging to diagnose
  - Trial Sinemet

Complications

- Falls
- Hypotension
- Dysphagia/swallowing difficulties
  - Aspiration risk
- Bowel/bladder problems
- Sleep disorders
- Psychosis/anxiety/depression
- Sexual impairment

Drugs for Parkinson's

- Sinemet
- Dopamine Agonists
- MAOI's
- COMT's
- Anticholinergics

Sinemet (Carbidopa-levodopa)

- Mechanism of Action: carbidopa inhibits decarboxylation of peripheral levodopa allowing levodopa to enter the brain before being broken down, this helps reduce risk of nausea; levodopa is converted to dopamine in the brain where it exerts its activity
- Frequent dosing, time sensitive
- GI (nausea)
- Psychosis
- Orthostasis
- Drug/Food interaction – protein
- Unusual obsessive behaviors
  - I.e. gambling, eating

Dopamine Agonists

- Ropinirole (Requip), pramipexole (Mirapex)
- RLS treatment
- Orthostasis
- Edema
- Unusual obsessive behaviors
  - I.e. gambling, eating

Amantadine (Symmetrel)

- Mechanism of Action: Dopamine agonist (also may has antiviral activity)
- Can be used for drug induced EPS
  - Has antiviral action (influenza)
- Tremor benefit in Parkinson’s
- Anticholinergic type SE’s
- DI’s – Antipsychotics, Anticholinergics, watch influenza (live) vaccine

Catechol-O-methyltransferase inhibitors (COMT)

- Entacapone (Comtan), tolcapone, opicapone
- Mechanism of Action: Inhibition of catechol-O-methyltransferase prevents further breakdown of levodopa which ultimately increases dopamine levels
- May have to reduce levodopa (Sinemet) dosing when initiating or at least monitor for signs of Sinemet toxicity - 25% reduction is an average figure and can vary from patient to patient
- Not effective if given alone (i.e. without levodopa)
- Tolcapone – rarely used, hepatotoxicity risk
- Adverse effects: look out for increased Sinemet concentrations (so adverse effects will look like Sinemet toxicity)

MAOI's (Type B)

- Selegiline, rasagiline, sufinamide
- Prevent the breakdown of dopamine
- Overlapping side effect profile with carbidopa/levodopa
- Possibly used alone in early disease where QOL is not impacted but symptoms are a nuisance
- Reduce Sinemet dosing – 10-30%
- Selectively target MAO – type B
  - Tyramine/food interaction (MAO – Type A) less likely than with traditional MAOIs used for depression
  - Hypertensive crisis
- Careful with SSRIs and other antidepressants

Anticholinergics

- Most benefit in tremor
- Rarely used due to adverse effect profile
  - Constipation
  - Dry eyes
  - Confusion/CNS changes
  - Dry mouth
  - Urinary retention
- Trihexyphenidyl (Artane)
- Benztropine (Cogentin)

Drug Induced Parkinson's

- Antipsychotics
  - Typicals – the worst
  - Quetiapine, clozapine – the best
- Metoclopramide
  - Used for GI problems, but DA blocking activity

Seizures

Meded101.com

Causes of Seizures

- CVD
- Dementia
- Trauma
- Cancer
- Withdrawal
  - Benzo’s
  - Barbiturates
  - ETOH

Medications that Increase Seizure Risk

- Bupropion
- Tramadol
- Cancer medications
- Hypoglycemia
- Antipsychotics
- Stimulants

Common Seizure Medications

- Phenytoin
- Levetiracetam
- Carbamazepine
- Lamotrigine
- Valproic Acid
- Topiramate

Phenytoin (Dilantin)

- Mechanism of Action: Not completely understood, but possible inhibition of voltage gated sodium channels
- Complex Kinetics
  - Dose depending increase in concentration
  - Small doses can lead to disproportionately large increases in drug levels
- Free versus total levels
  - 1-2, 10-20
- Vitamin D deficiency
- General toxicity symptoms similar to alcohol
  - Vertical nystagmus
- Enzyme inducer
- Gingival Hyperplasia

Carbamazepine (Tegretol)

- Enzyme inducer
- Hyponatremia
- Bipolar and trigeminal neuralgia
- Bone loss
- Levels
  - 4-12
- Cousin *oxcarbazepine

Levetiracetam (Keppra)

- Mechanism of Action: Binds to SV2A, inhibits presynaptic calcium channels and theorized to reduce neurotransmitter release
- Watch kidney function
- Drug levels not routinely done
- Adjust dose based upon SE’s/seizures
- Less drug interactions
- SE’s; sedation, confusion, GI, behavioral changes, increase in BP

Lamotrigine (Lamictal)

- Mechanism of Action: Blocks release of the excitatory neurotransmitter glutamate and inhibits voltage-sensitive sodium channels
- Very slow dose titration
- Interaction with Valproic acid and enzyme induces
  - Quicker titration with enzyme inducers like phenytoin
  - Slower titration with VPA
- Drug induced rash (SJS)
  - Life threatening

Topiramate (Topamax)

- Mechanism of Action: blocks voltage-dependent sodium channels and also may potential the effects of GABA; also may weakly inhibit carbonic anhydrase
- Cognitive slowing
- Weight loss
- Migraine indication
- Metabolic acidosis
- Kidney stone formation

Valproic Acid (Depakote)

- Mechanism of Action: Helps increase or stimulate the inhibitory neurotransmitter GABA
- Weight gain
- GI
- Hair loss
- Rare (ammonia elevations, LFTs, thrombocytopenia)
- Migraine, Bipolar indications, might also see off label for aggressive type behaviors versus use of antipsychotics

Status Epilepticus

Meded101.com

Potential Causes

- Epilepsy
- Hypoglycemia
- Acid/base disorder
- Toxicity

Medication Management

- Benzodiazepines
  - Lorazepam
    - Typically first line
    - May stay in CNS a little longer than diazepam
  - Diazepam
    - Most lipophilic
    - May get to CNS a little quicker, but may redistribute out of CNS quicker as well
- Likely going to load patient with tradition antiepileptic agent in addition to doing benzodiazepine

Anticonvulsants

- Fosphenytoin/phenytoin
  - Slower onset than benzodiazepines
  - Generally not used alone in status epilepticus
- Fosphenytoin
  - Can be administered more quickly
  - Reduced risk of purple glove syndrome and phlebitis compared to phenytoin

Refractory Agents

- Phenobarbital/pentobarbital
  - Likely will require intubation if using these agents
  - 3rd or last line agent
  - Slow onset to peak efficacy compared to benzodiazepines
- Propofol
  - Anesthetic agent
  - Ventilation/intubation
- Midazolam
  - Benzodiazepine
  - More water soluble, may take a little more time to get to CNS for activity