Pharmacologic Options for Pain Control
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- Alpha 2 adrenergic agonists
  - Clonidine (acute and neuropathic pain)
  - Tizanidine (Zanaflex)
- Analgesics
  - Max APAP 4 gram/day and 3 gram/day for elderly
  - Vicodin (hydrocodone) now available with 300mg APAP (ES=7.5mg, HP=10mg)
- Anti-inflammatories
  - Caution with renal dysfunction and other renally cleared medications.
  - Cardiovascular (inc risk of MI and stroke) and GI (bleeding, ulceration, perforation)
  - Monitor for HTN, edema, worsening renal function, or GI bleeding
  - Add ASA 81mg and PPI for patients at high risk of thrombotic events (Selective more preferred)
  - Topical-diclofenac 1.4% patch (Flector), 1% and 3% gel (Voltaren and Solaraze), 1.5% soln (Pennsaid)
  - Ketorolac-should limit use to 5 days, max 40mg/day orally, usually only following IV therapy
- Anticonvulsants
  - Co-morbid anxiety (gabapentin (Neurontin), pregabalin (Lyrica))
  - Obese or sz history (topiramate (Topamax), zonisamide (Zonegran), levetiracetam (Keppra))
  - Co-morbid bipolar or sz history (oxcarbazepine (Trileptal), lamotrigine (Lamictal), carbamazepine (Tegretol), valproic acid (Depakote))
- Antidepressants
  - TCAs (amitriptyline, imipramine, desipramine, nortriptyline)-More sedating, hangover effect, weight gain, not recommended for the elderly (more NE, less 5HT, histamine)
  - SSRIs (paroxetine, citalopram, escitalopram)-increase anxiety initially, with tx later
  - SNRI (venlafaxine (Effexor), desvenlafaxine (Pristiq), duloxetine (Cymbalta), milnacipran (Savella) (3:1 NE:5HT)
    - Cymbalta SE-Neausa, dry mouth, insomnia, sleepiness, constipation, dizziness, fatigue (<1& suicidality, hepatotoxicity, allergic reaction)
    - 30mg to start (nausea). Limit to 60mg QD for pain (120mg max for GAD and MDD)
    - Savella-start 12.5mg QD x 1, 12.5mg BID x 2 days, 25mg BID x 4 days, 50mg BID (>200mg not recommended), need baseline sCr.
  - Atypicals (bupropion, mirtazapine, trazodone)
- NMDA antagonists
  - Ketamine (hypnotic, analgesic, amnesia, SE hallucinations, confusion, delirium)
  - Dextromethorphan (reduce opioid dose in surgery or for diabetic neuropathy)

- Opioid Agonists
  - Side Effects/Concerns
    - Dependence, sedation, respiratory depression, constipation, nausea, pruritis
    - Urinary retention, flushing, sphincter of Oddi pressure changes, hypotension
    - Hypogonadism, reduction of endogenous endorphins
  - Renal Dysfunction
    - Caution with Morphine (neurotoxic morphine-3-glucuronide), hydromorphone (moderate impairment)
    - AVOID meperidine (normeperidine)
  - Hepatic Dysfunction
    - Caution with morphine, hydrocodone (APAP), buprenorphine
    - AVOID meperidine, oxymorphone (mod-severe), methadone (severe)
  - CYP metabolism-increased drug interactions
    - Cyp3A4-fentanyl, buprenorphine
    - Cyp 2D6-codeine to morphine, hydrocodone to hydromorphone, tramadol, oxycodone to oxymorphone
  - Methadone
    - 5HT, NE, NMDA antagonist, Mu-opioid agonist
    - QTc prolongation-consider baseline EKG, 30 days, and annually
      - More if >100mg/day, seizures, or QTc 450-500ms (D/C at >500ms?)
    - T1/2 7-49 hours
    - Cyp 3A4, 2B6, 2C19
    - Monitor K+
    - Wait 5-7 days between dosage changes
    - Conversion not linear (higher morphine dose=less methadone needed)
    - 2.5mg Q12H for opiate naïve
  - Buprenorphine
    - Partial mu-opioid agonist, kappa antagonist
    - PO morphine:buprenorphine is 100:1 or 115:1
    - 20mcg/hr patch roughly equal to morphine PO 36-55mg/day
    - BUT start at 5mcg/hr and titrate (unless pt not opiate naïve, then 10mcg/hr)
    - Butrans Patch 7 day matrix patch
    - Available in 5mcg/hr, 10mcg/hr, and 20mcg/hr
    - **Increased respiratory depression with other CNS depressants
    - Adding opiates to buprenorphine patient-acceptable
    - Adding buprenorphine to opiates- CAUTION
    - Tolerance doesn't generally develop
    - CYP3A4 and CYP 2D6 metabolism to norbuprenorphine (Caution with amiodarone, ketoconazole, erythromycin, and ritonavir)
    - QTc prolongation (congenital, other QTc prolongation drugs, or >20mcg/hr patch)
  - Buprenorphine+ Nalaxone- Suboxone

- Skeletal Muscle Relaxants
  - Cyclobenzaprine-sedation, less effect, TCA-like structure
  - Baclofen- Intrathecal has best data, avoid abrupt withdrawal, use with caution with h/o sz
  - Tizanidine-sedation, hypotension (alpha 2 adrenergic agonist), possible hepatoxocity, refractory neuropathic pain, caution with ciprofloxacin and fluvoxamine
  - Carisoprodol (Soma)-active metabolite-meprobamate, max 8/day, serious GI effects, caution with h/o drug addiction, avoid in elderly, avoid with ketorolac, methadone, mirtazapine, ETOH, limit to 2-3 weeks of use, high abuse potential
  - Diazepam-high abuse potential, used with h/o sz, increased risk of resp depression and death with opioids
  - Metaxolone (Skelaxin)-Max 800mh QID, caution with hepatic and renal insufficiencies
  - Methocarbamol (Robaxin)-MAX 1.5g QID for 2-3 days, then 1g QID
- Sodium Channel Blocker
  - Lidocaine (local anesthetic, works in nociceptive (tissue) and neuropathic pain, Class 1b anti-arrhythmic)
  - Lidoderm-no more than 3 patches on dermatome, 12 hours on and 12 hours off
- THC
  - Marinol, Medical Marijuana-antiemetic and appetite stimulant
  - Similar to endogenous opioids (endorphins, enkephalins) in modulating pai
  - Neuropathy, fibromyalgia, OA, ankylosing spondylitis, PMS, gingival pain, migraine, phantom limb pain, Crohn's disease, IBS, CRPS)
- Topicals
  - EMLA
  - Capsaicin (Qutenza 8%)-medically supervised setting
    - delineate hyperalgesia site
    - apply topical anesthetic
    - apply up to 4 patches for 1 hour