




Pain Management Tips and Tricks

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- ▶ This is meant to be more of a series of fast facts on pain-related subjects rather than one unifying talk about pain, so there may be a little jumping around from topic to topic.
 - ▶ My point is to have some answers to common scenarios you may run into with your patients who have various types of pain.
 - ▶ Please feel free to ask questions along the way!

Topical Pain Medications

- ▶ A 46 year-old male patient comes in to clinic with complaints of back pain. He tells you, “I don’t know what happened, maybe I slept on it wrong, but my back really hurts right now. I don’t want to take any pills, is there something like a cream or something you can prescribe me to put on it?”
- ▶ What would you consider for topical pain medication if he doesn’t want any oral medications?

Topical Pain Medications

- ▶ A few options to talk about:
- ▶ Lidocaine patch / jelly / cream
- ▶ Capsaicin cream / patch
- ▶ Diclofenac gel (Voltaren) (also available as patch)
- ▶ Menthol-based creams
- ▶ Topical opioids?
- ▶ Topical ketamine?

Capsaicin

- ▶ Derived from Capsicum chili peppers and used for centuries for pain relief
- ▶ TRPV1 receptor agonist (TRPV1 stands for transient receptor potential cation channel subfamily V member 1)
- ▶ Temporary TRPV1 activation causes heat or stinging sensations
- ▶ Prolonged TRPV1 activation causes loss of receptor functionality, leading to impaired pain sensation
- ▶ Proven to be helpful in various neuropathies (post-surgical, postherpetic, diabetic, HIV-related) as well as musculoskeletal
- ▶ With repeated uses over a course of weeks, can cause increasing pain relief, so think about this long-term!
- ▶ Don't put on a wound! Don't inhale! Consider using gloves when you apply it!

Topical NSAIDs

- ▶ A few different diclofenac formulations
- ▶ Minimal systemic absorption (<1% of systemic levels found vs PO)
- ▶ No association with renal failure or GI issues
- ▶ NNT of 4.5 to achieve 50% pain relief over 6-14 days (in a study of acute musculoskeletal pain)
- ▶ No studies done on lower back pain or chronic pain
- ▶ The main downside is expense (about \$36 for 100 gm)

Topical Lidocaine

- ▶ Reduces aberrant firing of Na channels on damaged pain fibers
- ▶ Very little is absorbed systemically (<5%)
- ▶ Some evidence that “deep” pain can be decreased, in addition to more superficial pain
- ▶ Patches are approved for postherpetic neuralgia specifically; studies on other types of acute pain show lidocaine patches to be no different than placebo
- ▶ Some possible evidence for use in neuropathic pain, chronic lower back pain, even compression fractures (though these studies are not high-quality RCTs, so interpret with caution)
- ▶ Downside: expense (about \$10 per patch)

Topical Opioids

- ▶ To be fair, you probably won't be prescribing this very often, or ever
- ▶ There are opioid receptors found in inflamed tissue and peripheral nerves
- ▶ No major studies done to show significant improvement in pain; a number of small studies or non-RCTs have showed some potential improvement
- ▶ Also potentially helpful for mucositis (used commonly in patients with cancer)
- ▶ Downside: ability to potentially abuse
- ▶ Downside: only available through a compounding pharmacy

Topical Ketamine

- ▶ Again, no high quality RCTs
- ▶ Also requires compounding pharmacy
- ▶ Generally expensive
- ▶ Anecdotal evidence of efficacy

Muscle Relaxants

- ▶ A 46 year-old male patient comes in to clinic with complaints of back pain. He tells you, “I don’t know what happened, maybe I slept on it wrong, but my back really hurts right now. My back muscle feels like it keeps spasming, is there any type of medication that can relax my back muscle?”
- ▶ After further evaluation, if you decide to proceed with a muscle relaxant, what would be your first choice?

Muscle Relaxants

- ▶ Two main groups: antispastic vs antispasmodic
- ▶ Spasticity = increased muscular tone, exaggerated reflexes = MS, TBI, CP
- ▶ Spasm = sudden involuntary contraction of muscle groups = muscle strain, fibromyalgia, low back pain
- ▶ Think of it as spasticity is more likely to be treated in a neuro clinic and spasm is more likely to be treated in a primary care clinic
- ▶ Antispastic = baclofen (Lioresal)
- ▶ Antispasmodic = cyclobenzaprine (Flexeril), carisoprodol (Soma), metaxalone (Skelaxin), methocarbamol (Robaxin)
- ▶ Combination = diazepam (Valium), tizanidine (Zanaflex)
- ▶ So your first step should be determine if you want antispastic or antispasmodic

Muscle Relaxants

- ▶ General Precautions
- ▶ CNS depressants
- ▶ Risk of drowsiness, confusion, dizziness
- ▶ Higher likelihood of adverse events in those aged 65 or greater
- ▶ Most are metabolized by liver (except for baclofen) so use with caution in patients with liver issues

Muscle Relaxants

- ▶ No good evidence that one muscle relaxant works better than another in general
- ▶ Most of the antispasmodics have been proven to be moderately effective in back pain short term
- ▶ Insufficient evidence to continue past 2 weeks for antispasmodics
- ▶ Most sedating: cyclobenzaprine, tizanidine, diazepam
- ▶ Least sedating: methocarbamol, metaxalone
- ▶ Potentially can cause respiratory depression in combination with opioids and/or benzodiazepenes; less likely on their own

Muscle Relaxants

- ▶ Baclofen – lowers seizure threshold, can increase LFTs
- ▶ Cyclobenzaprine – caution when pt has known cardiac issues (can increase QTc), can have anticholinergic side effects
- ▶ Carisoprodol – significant abuse potential; the only muscle relaxant (besides diazepam) which is a controlled medication
- ▶ Metaxolone – avoid in liver failure
- ▶ Methocarbamol – possible urine discoloration
- ▶ Diazepam – obviously has abuse potential
- ▶ tizanidine – hypotension, dry mouth; contraindicated with CYP A12 inhibitors (like ciprofloxacin)

Muscle Relaxants

- ▶ The takeaway?
- ▶ Avoid baclofen unless you are specifically treating MS or CP or something similar
- ▶ Use with caution in ages 65 or older
- ▶ Use with caution in liver disease
- ▶ Use with caution in patients concurrently taking opioids and/or benzodiazepenes
- ▶ When using for muscle spasms, generally limit to 2-4 weeks
- ▶ In my opinion, just avoid carisoprodol (Soma)
- ▶ I generally start with methocarbamol; antispasmodic, least sedating, fewest side effects

Neuropathic Pain

- ▶ A 61 year-old female patient with long history of DM2 presents to clinic with bilateral foot pain. She tells you, “The pain in my feet feels like burning or tingling. I’ve tried ibuprofen and Tylenol – I even tried my spouse’s Norco, but nothing is helping. Can you help me?”
- ▶ If your examination makes you further suspect neuropathy, what could you consider for neuropathic pain?

Neuropathic Pain

- ▶ A very wide range of causes, including but not limited to:
- ▶ DM, sciatica, chemotherapy (and other medications), injury, muscle spasm, MS, herpes zoster, burn injuries, cancer, vitamin deficiency, ischemia, etc.
- ▶ Also a very wide range of medications that can be used to treat neuropathy
- ▶ Definition of neuropathy: damage to peripheral nerves which impair sensation, movement, function
- ▶ We will focus on the treatment of pain caused by neuropathy rather than other potential effects of neuropathy

Gabapentin (Neurontin)

- ▶ FDA approval technically only for postherpetic neuralgia and partial onset seizures
- ▶ Some clinical evidence as well for multiple types of neuropathic pain
- ▶ Mechanism and site of action unknown
- ▶ Doses should be reduced in patients with renal disease
- ▶ Other adverse reactions include sedation, confusion, dizziness; however, patients often can gain tolerance to these over the course of a few days
- ▶ I always warn patients about these side effects and usually also encourage them to stick with gabapentin for at least a few days to see if the side effects go away

Gabapentin

- ▶ Scheduled 1-3 times per day (if only once per day, generally given at night due to possible drowsiness)
- ▶ Generally start at 100-300 mg total daily dose, then titrate up by 100-300 mg every 1-3 days
- ▶ I take patient factors into account when titrating or starting, i.e. I'm a lot more likely to start with 100 mg QHS only in an elderly patient with balance issues, and higher doses for younger patients or patients who have more body mass
- ▶ Highest dose is 1200 mg TID; I generally titrate up until stopped due to pt's tolerance of medication / side effects, or until about 600-900 mg TID. If not having an effect by that dose, probably less likely to ever have an effect

Gabapentin

- ▶ Generally cheap (though not as cheap as TCAs)
- ▶ Can also be used for anxiety, insomnia, hiccups, hot flashes, chronic cough
- ▶ NNT of 5.8
- ▶ So strongly consider starting with gabapentin especially if the patient has any of those other symptoms concurrently

Pregabalin (Lyrica)

- ▶ Second generation antiepileptic
- ▶ Developed after gabapentin
- ▶ Binds to calcium channels, inhibiting release of excitatory neurotransmitters
- ▶ Needs dosing adjustment in renal failure
- ▶ Starting dose typically 150 mg per day, max dose 450 mg per day
- ▶ Typically given in 2 or 3 doses per day
- ▶ Side effects: dizziness, drowsiness, dry mouth, blurred vision
- ▶ Again, patients often develop tolerance to these side effects

Pregabalin

- ▶ NNT of 4 for 50% reduction in diabetic neuropathic pain
- ▶ Efficacy is quite on par with gabapentin
- ▶ Can also be used for anxiety, insomnia, etc
- ▶ Significantly more costly than gabapentin (3x), less often covered by insurance than gabapentin is
- ▶ More costly than amitriptyline (8-10x)
- ▶ During clinical trials, about 4% of people reported euphoria, which has led to it being classified as a Schedule V Controlled Substance (equivalent to promethazine+codeine cough syrup)

Anti-seizure medications

- ▶ Carbamazepine = classically known for relieving pain from trigeminal neuralgia
- ▶ NNT only 1.7! Sounds great, right?
- ▶ Adverse effects: leukocytosis, thrombocytopenia, drowsiness, agranulocytosis, aplastic anemia, Stevens Johnson syndrome. Not great! NNH of only 2.6
- ▶ Think of it this way...if you started 5 patients on carbamazepine, you would likely help three people, and harm two!
- ▶ Need to continue monitoring of lab values throughout treatment with carbamazepine
- ▶ Side effects are obviously very limiting here

Anti-seizure medications

- ▶ Oxcarbazepine = equal to carbamazepine for trigeminal neuralgia, but fewer side effects
- ▶ Valproic acid = insufficient evidence to strongly recommend (some small studies showed benefit)
- ▶ Topiramate = again, not great evidence; potential adverse events of bradycardia and seizure
- ▶ Lacosamide = weak evidence
- ▶ Phenytoin = no evidence
- ▶ Levetiracetam = no evidence
- ▶ Lamotrigine = weak evidence

Tricyclic Antidepressants (TCAs)

- ▶ As with most of the medications we are talking about for neuropathic pain, developed for one thing but can be used for neuropathic pain
- ▶ Mainly replaced by SSRIs and SNRIs at this point for depression
- ▶ Amitriptyline, desipramine, doxepin, imipramine, nortriptyline, and many others
- ▶ They hit lots of different receptors: block transport of serotonin and norepinephrine, to a lesser extent block dopamine transport, also antagonize histamine and acetylcholine receptors and sodium channels and calcium channels (can lead to cardiac issues)!
- ▶ So use with caution!

Tricyclic Antidepressants

- ▶ Precise mechanism of action unclear for neuropathic pain relief
- ▶ Likely due in part to their ability to affect multiple different receptors
- ▶ Proven to be more effective than non-TCA antidepressants for treatment of neuropathic pain
- ▶ Could certainly be considered if patient has significant depression concurrent with neuropathic pain
- ▶ NNT of 2-3!

Non-TCA antidepressants

- ▶ SSRIs, SNRIs, others
- ▶ Generally less effective than TCAs or any of the other neuropathic pain medications we've already discussed
- ▶ Probably less effective than TCAs due to their more specific pharmacodynamic profiles

SSRIs

- ▶ Generally not effective for neuropathic pain
- ▶ Mild benefit with paroxetine and citalopram in HIV-related and diabetic neuropathy?
- ▶ Not many studies

SNRIs

- ▶ Actually a couple good options here!
- ▶ Duloxetine NNT of 5.2 (in diabetic neuropathy)
- ▶ Duloxetine takes about one week to actually work, with max effect in about 4 weeks; so tell patients to be patient on this one
- ▶ Venlafaxine NNT of 4.6 (in diabetic neuropathy)

Other antidepressants

- ▶ Bupropion (dopamine and norepinephrine reuptake inhibitor) shown to have mild analgesic effect in one study
- ▶ Mirtazapine with no known analgesic effects

So how should we treat neuropathic pain???

- ▶ Clearly very complicated, numerous classes of medications, with numerous side effects and efficacies
- ▶ My general algorithm:
- ▶ Start with gabapentin, titrate up to 900 mg TID if possible
- ▶ If no improvement, titrate down and start pregabalin or duloxetine (or venlafaxine)
- ▶ If that doesn't work, try one of the others in that second group
- ▶ If that doesn't work, I usually go to TCAs next if it's a patient who I'm less worried about side effects
- ▶ If a couple of TCAs don't work, I'm looking into anti-seizure meds
- ▶ Neurology consult? Pain or palliative consult?

Cannabis and Related Products for Pain

- ▶ A 59 year-old male patient presents to clinic with ongoing shoulder pain for the past 3 months. He states that his friend has been telling him to “try marijuana” for the pain, since his friend uses that for pain all the time. Patient says, “I would use it if I knew it would help, but I also heard that there are prescription marijuana pills? Could I try one of those?”
- ▶ What would you tell this patient about the role of cannabis in pain management?

Cannabis and Related Products for Pain

- ▶ While being legalized in many states now, is still not FDA-approved for any conditions
- ▶ Technically still Schedule I drug at the federal level
- ▶ Medically available even in states that haven't legalized it for recreational use yet
- ▶ Please note that there are many cannabis strains and obviously no centralized way of obtaining CBD products, etc., so outcomes may vary depending on where it is supplied from
- ▶ The endocannabinoid system impacts many things (including movement, appetite, mood, etc.) in addition to pain

Cannabis, etc.

- ▶ Side effects: Nausea, confusion, euphoria, dysphoria, anxiety, etc.
- ▶ Ingestion of actual cannabis raises risk of MVA
- ▶ Due to Schedule I label for cannabis, is obviously still difficult to get good RCTs of comparison between cannabis and another medication
- ▶ A recent multicenter RCT (360 patients), showed efficacy for breakthrough cancer pain in subjects who were already on a long-acting opioid...
- ▶ Inhaled cannabis had significant analgesia effect in HIV neuropathy (NNT 3.38)
- ▶ Also potentially helpful with nausea/vomiting, appetite, cachexia (?)

CBD Oil

- ▶ Cannabis plant produces more than 100 cannabinoids, including CBD and THC, which both have potential for pain management
- ▶ THC also can alter CNS, CBD oil generally non-intoxicating
- ▶ May be legal in some states where cannabis itself is not legal
- ▶ Technically CBD still Schedule I drug as well
- ▶ So you can't prescribe it, but you could write a "recommendation letter" for CBD (or cannabis)

CBD

- ▶ No RCTs have been done on CBD-only products for pain management!
- ▶ Most supporting data come from mouse studies
- ▶ Small studies maybe with some evidence in favor? But to be honest, there are no major convincing data thus far
- ▶ What is the biggest risk of CBD or cannabis?

Dronabinol

- ▶ FDA-approved medication which is a form of THC
- ▶ Does not contain CBD, or most of the isomers of THC (just one specifically)
- ▶ FDA-approved for HIV-induced anorexia and chemotherapy-induced nausea and vomiting
- ▶ In practice, can be used for appetite stimulation, weight gain (?), nausea.
- ▶ No significant proven pain management properties
- ▶ Takes an hour to reach full systemic effect (as opposed to seconds or minutes for smoked cannabis), which is why it's not much of a threat to cannabis sales

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“Pain could be killed. Sadness could not, but the drugs did shut its mouth for a time.”

--Colson Whitehead

“The great art of life is sensation, to feel that we exist, even in pain.”

--Lord Byron