Modern Approaches to Chronic Pain
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Learning Objectives
• To introduce you to some new approaches to chronic pain that you may not be currently using
• To review the indications for buprenorphine for chronic pain therapy
• To review best practice for patients with chronic pain and an opioid use disorder
• Lightning round of pearls based on questions I often get

Learning Method
• Case-based
• Evidence-base
• Professional society guidelines
• Communication TIPS

Roadmap
Case 1

- LH is a 56yo M with obesity, schizophrenia, OUD on MMT, and chronic LBP presenting for f/u. He has a spine MRI showing lumbar DJD.
- He has tried the following:
  - PT – didn’t like it bc it caused pain
  - NSAIDs – inadequate effect, creat bumped
  - Gabapentin – caused excess sedation
- Topical agents: capsaicin cream, topical lidocaine, mentholated cream
- His perspective:
  - “This pain is killing me, doc. You’ve gotta do something for me. It goes back and forth across my lower back, and it’s horrible”

Case 1

- What would you offer this patient?
  - 1) refer for epidural spinal injection
  - 2) start oxycodone
  - 3) paraspinous lidocaine injection
  - 4) testosterone injection

Paraspinous lidocaine injection for chronic nonspecific low back pain: A randomized controlled clinical trial


Funding: None
Rationale and Research Question

- Chronic low back pain is common
- Few treatments with demonstrated effectiveness
- Trigger point injections with lidocaine commonly used for pain
  - Proposed mechanism: neuronal desensitization
  - Few data for use in chronic nonspecific low back pain
- Research question: Do paraspinous lidocaine injections improve pain and function in patients with chronic nonspecific low back pain?

Design, Setting, and Intervention

<table>
<thead>
<tr>
<th>Study Type</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time frame</td>
<td>1/2007 – 1/2013</td>
</tr>
<tr>
<td>Study Setting</td>
<td>São Paulo Medical School, Brazil</td>
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</table>

**Intervention**

- **LID-INJ:** Paraspinous lidocaine (1 inj/wk x 3 wks) + standard treatment
- **SH-INJ:** Sham lidocaine injection (1 sham inj/wk x 3 wks) + standard treatment
- **STD-TTR:** Standard treatment (tid home exercises + acetaminophen 2g/d)

**Participants**

Mean age 48, mean BMI 28, 32% male
Mean pain duration 7.25 years, mean pain score 7/10

Method
Results: Paraspinal lidocaine injections resulted in more patients with reduced pain

<table>
<thead>
<tr>
<th></th>
<th>LID-INJ (N = 126)</th>
<th>SH-INJ (N = 125)</th>
<th>STD-TTR (N = 127)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain response rate, % (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End of treatment</td>
<td>71.4 (90)</td>
<td>55.6 (70)</td>
<td>53.9 (68)</td>
<td>.004</td>
</tr>
<tr>
<td>Follow-up period (3 months)</td>
<td>56.3 (71)</td>
<td>49.6 (82)</td>
<td>40.1 (51)</td>
<td>.036</td>
</tr>
</tbody>
</table>

NNT: 5.6 (comparing LID-INJ to STD-TTR)

Discussion

- Limitations:
  - Participants not fully blinded
  - Well-documented placebo effects in pain trials
- Conclusion: In a group of patients referred for treatment of chronic nonspecific low back pain in São Paulo, Brazil, weekly paraspinal lidocaine injections resulted in pain relief for more patients than sham injections and standard treatment alone
- Bottom line: Paraspinal lidocaine injections may be one tool for managing chronic nonspecific low back pain

Results: Lidocaine injections also associated with improvements in function

Communication: "In chronic pain, your nerves are overactive. Imagine a wire that is frayed and giving off extra sparks of electricity. With the injection, I am trying to trick your nervous system into tamping down these overactive nerves."
We know that in patients with severe anatomical damages, for example, a severe bone fracture, have a higher risk of long lasting pain even when the fracture has healed. We know that heredity plays a role, meaning that some people are more prone to becoming sensitized. Furthermore, the way you cope with pain can be a risk factor for sensitization. In your case, I would like to focus on the last part to explain sensitization. Sensitization can be demonstrated in your body as follows. You told me that when you go for a walk or when you ride on your bike, you experience pain. We know that there isn’t any physical damage in your back and that walking or cycling does not lead to physical damage. Somewhere in your nervous system, a normally non-painful signal is transformed into a pain signal.

First of all, your concern about what causes this pain, your own experience of back pain, gives you the belief something must be physically wrong, although the neurologist and the physicians told you that nothing is wrong. This contradiction causes more stress that will have a negative effect on your pain. Second, you told me that moving your back is thought to cause further damage and more pain. This makes your muscles very tense and your back is stiff. You are continually running not to make any sudden movements. I think this fear of movements and muscle tension is part of why the alarm bells go off. Finally, an important factor is the stress you feel about your work. You would like to go back to work, but on the other hand you told me you are afraid this might cause more pain.

As I illustrated with the example of the burglar alarm, the underlying mechanism of acute pain is different from chronic pain. In the first case, there is a danger causing the alarm to go off. In the latter case the alarm isn’t overreactive. This means that your pain is not imaginary, in fact, your pain is just as real as the pain that is caused by a burglar.

When it comes to therapy of acute pain, triggering down and getting rid of the burglar is sufficient. With chronic pain, matters are a bit more complicated, because there is no burglar. This does not mean that nothing can be done to alleviate chronic pain. We know that stress, muscle tension, inactivity, worries and negative thoughts are able to influence the degree of sensitization and that these factors are capable of aggravating pain. With a specific multidisciplinary program, we can try to reduce the influence of these factors.

**TENS Unit**
- **What**: electrical massager, decrease central sensitization
- **Where**: Covered by Medical, or Purchasable OTC (~$20)
- **Instructions on Use**:
  - YouTube Videos
- **Evidence base**: Cochrane review with poor quality evidence (2017)

**Case 2**
- JM is a 63yo F with OUD on bupe-nal, scoliosis, chronic low back pain, COPD on chronic oxygen, uses a walker for ambulation complaining of ongoing back pain
- Non-focal neuro exam and MRI stable
- Prescribed the following:
  - Acetaminophen
  - Intermittent NSAIDs
  - Lacrosse massage ball
  - PT
- She asks: “what about a muscle relaxant?”

**Question**
- Which of the following is true about muscle relaxants in chronic pain?
  - A) Tizanidine is dosed 1 mg q day
  - B) Evidence suggests a benefit only with short term use
  - C) Use is associated with QTC prolongation
  - D) Adding them to an NSAID confers no additional benefit
Case 2: Muscle relaxants in back pain

- Commonly used muscle relaxants in the US:
  - Cyclobenzaprine
  - Tizanidine
  - Baclofen
  - (carisoprodol and BZDs) – discouraged given abuse liability

- Evidence-based:
  - Meta-analyses of muscle relaxants: 5 high quality trials (496 participants)
  - Clinically significant pain relief in the SHORT TERM for acute flares of low back pain
  - No data on long term use in chronic pain


Head-to-head trials of muscle relaxants

Case 3

- GM is 43 and has hx of cocaine UD, low back pain, nicotine use disorder and depression.
- He is complaining of chronic pain and requesting oxy-APAP as he says this works the best for him?
- You’re wondering if you can just give him buprenorphine and call it a day.

Question

- Which of the following is true of buprenorphine for chronic pain?
  - A) It is covered by Medical
  - B) It is inferior to full agonists for control of chronic pain
  - C) The half life for analgesia of buprenorphine is 12 hours
  - D) It has no abuse liability
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Buprenorphine and Chronic Pain

• FDA approved in the US for use in moderate-severe chronic pain
  • Transdermal buprenorphine 5, 10, 15, 20 mcg/hr (max 20mcg/week)
  • Buccal buprenorphine
• Widely used in Europe
  • Dose range: 0.1-3.2mg/day
  • Formulations patch up to 700mcg/hr and have 2000mcg SL tab
• Effectiveness:
  • Decrease mean pain scores **2.3/10 points**
  • Patch equivalent to 51 buprenorphine

Buprenorphine and OUD

• Formulations
  • Sublingual film (Suboxone)
  • Sublingual tab (bup-naloxone, Zubsolv)
  • SC injection (Sublocade; 4 weeks)
• DOSAGES ARE HIGHER
  • Standard dose for a patient with OUD: 8-24mg/day
• Strength of buprenorphine
  • 30x stronger than morphing (estimate)

Back to our patient

• GM is 43 and has hx of cocaine UD, low back pain, nicotine use disorder and depression.
• What does this history tell us? Is he at risk for having problems with COT?
  • ORT
  • DIRE
  • COMM
  • Provider assessment
Risk Assessment Tool

- Opioid Risk Tool (ORT)
  - 5-item initial risk assessment
  - Stratifies risk into low (6%), moderate (28%) and high (91%)
  - Family History
  - Personal History
  - Age
  - Preadolescent sexual abuse
  - Past or current psychological disease
- Available at: https://www.drugabuse.gov/sites/default/files/files/OpioidRiskTool.pdf
- Several alternative options: DIRE, SOAPP, others

This patient

- GM is 43 and has hx of cocaine UD, low back pain, nicotine use disorder and depression.
- Management
  - Opioids not 1st line
  - Non-pharm. and non-opioid tx are preferred
  - Treat/stabilize mental health and SUD prior to any initiation of opioids
  - If non-pharmacologic and non-opioid treatments not effective, consider opioids trial with close monitoring

Communication:

Let me get this right: you’ve overcome cocaine addiction and you want me to give you another addictive substance?

What about people on COT switching to buprenorphine?

- Reasons to switch
  - Most common: co-occurring OUD
    - Patient is voluntarily tapering and then you discover the OUD
  - Safety
  - Lack of benefit from full agonist and provider doesn’t want to increase dose
  - Patient preference

VA Experience: Co-occurring disorders clinic

<table>
<thead>
<tr>
<th>Patients</th>
<th>APS change</th>
<th>% (retail)</th>
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<tbody>
<tr>
<td>Preferred opioid</td>
<td>Heroin</td>
<td>16</td>
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<tr>
<td>Methyl</td>
<td>Methadone</td>
<td>23</td>
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<tr>
<td></td>
<td>Oral</td>
<td>Oxycodeine</td>
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<td></td>
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<tr>
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<tr>
<td></td>
<td>Oral</td>
<td>Morphine</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>Oxycodone</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>Hydromorphone</td>
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</tbody>
</table>

Age group:

- 21-40 y: 25 -1.1 (15%)
- 41-50 y: 81 -0.7 (54%)
- 51-60 y: 37 -0.27 (72%)
Case 4

- KD is a 40yo F with a hx of chronic ileocolonic Crohn's disease s/p ileal resection c/b perforation s/p ileostomy and R hemicolectomy with subsequent takedown, immunosuppression, s/p chole, depression, fibromyalgia, and chronic abdominal pain presenting for nausea, vomiting and abdominal pain. Due to nutritional failure, she had a GI tube placed for supplemental nutrition.
- She has had multiple trips to the hospital and emergency department for similar complaints (>6 visits in the past 3 months). She is on vedolizumab with good response (repeat colonoscopies demonstrating no active disease). During her multiple admissions, she has had normal inflammatory markers and no evidence of infection. Her last admission included starting TPN for nutritional support because any trial of PO/TF nutrition led to pain.

Case continued

- The patient expressed concern over her continued health problems. She says that she is frustrated that she is continually in the hospital. She said that she tried to stay at home, but could not tolerate the pain.
- When asked how things are going with the pain medication, she says that she has wanted to not be on the medicine, but whenever she tries to not take it, she feels worse. Several months ago she voluntarily decreased the dose of her opioids with her primary care provider. She feels like her life revolves around her health conditions and pain. She wishes she could "be normal again." Her pain & health needs creates problems w/her mom and dad (and her) because they don’t understand why she’s still so bad off. She has a degree in psychology, but hasn’t worked for several years.
Question

- Which of the following would be your next step in her management?
  - A) Increase oxycodone
  - B) Decrease oxycodone
  - C) Stop oxycodone
  - D) opioid rotation

Does this patient have an opioid use disorder?

- 4Rs
  - Risk of bodily harm
  - Relationship trouble
  - Role Failure
  - Repeated attempts to cut back

- 4Cs
  - Loss of Control
  - Consequences**
  - Compulsion
  - Craving

Tolerance**
Withdrawal

DSM-5 Criteria for Substance Use Disorders

Case continued

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- She has a degree in psychology, but hasn’t worked for several years.
Language & Communication is Everything

- How are things going with your opioid medicine(s)?
  - That sounds really hard to feel like you’re only getting partial relief.
  - Have you ever wished you never started the meds? Have you ever wished you were off of them?
  - That's impressive that you've even contemplated a world with out pills.
- Do you ever think the meds might be in control of you? Like you can't do the things you want or be the person you want to be because you're dealing with your pain meds?
  - You're obviously someone who has suffered a lot and overcome a huge amount.

Question

- Which of the following would be your next step in her management (in the hospital)?
  - A) Increase oxycodone
  - B) Decrease oxycodone
  - C) Stop oxycodone
  - D) Opioid rotation

Case Continued

- After checking labs and urine drug screen, we stopped the patient’s long-acting and short-acting opioids. She developed symptoms of withdrawal.
- We informed her in advance she would have to go 12-16 hours without the oxycodone.
- We gave her medication to help with her symptoms:
  - Ondansetron 4mg PO q6hrs PRN nausea
  - Diphenhydramine 25-50mg PO q8hrs PRN insomnia/anxiety
  - Clonidine 0.1-0.3mg PO q6hrs PRN agitation from w/d
  - Others (see SHOUT guide)
- We calculated a CDWS score

Case Continued

- After 16 hours, she got her first dose of 4mg and did not develop worsening withdrawal symptoms.
  - She got another 4mg after 1hr
  - She got another 4mg after 1hr
  - 4 hrs later she got one more 4mg dose
  - Total 16mg on the first day
- The next day she got 8mg in the morning, and 8mg at night
- We gave her A LOT of praise for undergoing the induction
Case Continued

• The patient ultimately required 24mg daily of buprenorphine-naloxone, split TID
• She was discharged back to follow-up with her primary care providers
  • Unfortunately her PCP did not have an x-license, so she had to be seen by another provider
• The new provider didn’t think the patient had an OUD and prescribed the buprenorphine mono product (instead of bupe-nall). This required a prior authorization for Medical. The dose was also reduced to 4mg TID (instead of 8mg TID)
• The prior authorization was not approved the same day and the patient had returned to the emergency department.

Lightning Round

• “If I take my patients off opioids, can I just put them on tramadol?”

Tramadol

• Schedule 4 (not schedule 2; max 5 refills/6mo), happened in 2014
• MOA:
  • Mu opioid receptor agonist
  • NE and SHT reuptake inhibitor (avoid with MAOIs and TCAs) – can cause serotonin syndrome
  • PK: has active metabolite (M1, CYP 2D6) with higher affinity for mu receptors: T1/2 3hr, 9hr (M1)
• Medicare requests you trial this before bupe
• Abuse liability?

Abuse Liability of Tramadol

• Surgical literature (Mayo)
  • 444,764 patients post-op, analgspod claims data
  • 357,884 filled rx for opioids (50% HC, ~40% oxy, 4% tramadol/post-op
    • 7% had at least 1 REFILL 90-180 days after surgery (additional use)
    • 1% refilled 180-270 days (persistent use)
    • 0.5% 10 or more rx (long-term use)
    • All 3 of these groups were more likely to have received tramadol (~40% increase risk for persistent/chronic use)
• Observation studies in countries with rx not required
  • Egypt – ~10% with OUD; ~60% using tramadol
  • Iran – survey of customers – 60% reporting addiction sx
• BOTTOM LINE: tramadol is not without risk; follow same practices as schedule 2 substances

Lightning Round

• “What do you do for a positive urine toxicology for marijuana on opioids?”

Pearls

• Marijuana in urine toxicology screens
  • Notoriously poor for detecting recent cannabis use
  • Can have positive tests, then negative, then positive tests during periods of abstinence!
  • Excretion delayed with increased BMI because THC deposits in body fat due to its lipophilicity
  • Window of test positivity extends to 30 days post-abstinence
• Marijuana will not “solve” the opioid epidemic
  • Original data showing dec opioid OD in states with legalization → recent study showing the OPPOSITE (cannabis 23% inc mortality)

My practice

• + marijuana
  • Expect it: ~18-25% of patients using it on CDT
  • Evidence Base:
    • Some studies show better pain control w/THC; others do not
    • Marijuana positivity is risk for future aberrant drug related behaviors
  • So...
    • “Let’s talk about the role marijuana plays in your life?”
    • Monitor: inquire about side effects (sedation, function impairment); increase utox frequency; establish conditions for ongoing prescribing (i.e., if fail to detect CDT, this means we will discontinue your opioids)
  • Marijuana use disorder → taper opioids

References

• Education about pain sensitization: Van Wilgen and Kelzer, Pain Management Nursing 2012