Pharmacotherapy for spine-related pain in older adults

...and a few shots too

No disclosures

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Low back/neck pain: common

- **Mainstay therapy: Multimodal approach**
  - Physical therapy
  - Patient education/time
  - **Short term analgesics**
  - Injections, epidurals, facet blocks, etc

- **Surgery: persistence or anatomy**
  - Failed radicular (symptoms/time)
  - Spinal stenosis
  - Spondylolisthesis
  - “Something must be done”
Low back and neck pain

- Common (80-90% lifetime prevalence)
  - "common LBP" (myofascial), usually resolves in weeks
- If no resolution:
  - Muscle/Myofascial: young
  - Nerve: young (herniated disc, listhesis), Older (stenosis)
  - Arthritic/facet: Laborers, Obese, Older
  - Post surgical pain syndrome
- Smoking worsens all the above (microvascular)
- Of course the above can overlap
Spine pain medication in older adults:

Muscular and arthritic complaints

Radicular/spinal stenosis/neuropathic

...Decreased renal and liver function, MMP, polypharmacy, fall/sedation risk
Spine pain medication in older adults:

Decreased metabolism vs toxicity

Common comorbidities & comedinations

…fall secondary to sedation, more risk than sedation
NSAIDs: LBP

- Understandable GI/renal/CAD caution
- More commonly used in younger patients
- Double-blind, controlled trials
  - Naproxen: CLBP benefit in 2 week, 16 week trials
    - Patients into their 80s, large cohort > 65 years
  - Many NSAIDs demonstrate efficacy in ALBP
    - Ibuprofen, diclofenac, piroxicam, etc
    - Younger patient cohorts, mean age ~ 40 years
Celecobix: CLBP

- Other Cox-2s off market, CAD
- Limit use with CAD
- Double-blind, controlled trials
  - Celecobix: CLBP >benefit over 6 weeks vs tramadol
    - Patients into their 80s, 13% of cohort > 65 years
    - Less AEs in celecobix group
  - Similar efficacy to non-selective NSAIDs for CLBP
    - Multiple studies
    - Patients into their 80s, significant cohort > 65 years
Topical NSAIDs: LBP/arthritic

- Topical creams and patches demonstrate efficacy
  - Double-blind, placebo controlled trials
  - Younger patients, < 65 years
  - Piroxicam patch and cream with benefit, LBP/arthritic
    - 8 day trial for arthritic LBP
    - Patch and cream with 42% efficacy, compared to 26% placebo
    - Included up to age 75 years, mean age 51
NSAIDs: radicular LBP

- Typically used as a **short course**

- **Double-blind, placebo controlled trials**
  - Meloxicam and diclofenac with efficacy
  - Indomethacin and piroxicam with negative studies
  - Studies mean age was ~48 years
    - Smaller cohorts > 65 years
NSAID Dosing/AEs

- Red flags: renal, GI Ulcer/bypass, severe CAD
- "caution": mild CKD*, GERD, CAD
- Rule: short course NSAID “burst therapy”
- Linear relation of GI ulcer and age with NSAID use
  - GI protection (PPI* or H2 blocker)
  - Celecobix
  - Both

Direct CAD effects, also interrupts ASA mechanism
Proper PPI use?
Topical NSAIDs first? - depends

? Sulindac
*Acetaminophen, Corticosteroids?*

- Acetaminophen less AEs, but less efficacy
  - Considered 80% as effective as celecoxib for arthritic neck and LBP
    - mean age 65 years, up to 80 years
  - Typical lower efficacy for spine pain than NSAIDS
  - Higher doses, ER formulations suggested

- Corticosteroids more AED, and less efficacy
  - Mixed evidence in older adults
  - Can have benefit radicula
  - More for true Rheumatologic d/o or bone mets

*Worth the AEs? Call someone*
Blinded clinical trials

- Better evidence: **Peripheral neuropathy**, PHN
- Mixed evidence for radicular/neuropathic LBP
  - Helpful for radicular sx, perhaps more so in younger patients
    - Great benefit when combined with a TCA (AEs though)
    - Evidence basis GBP > PGB
  - Helpful as adjuncts in spinal stenosis (with other routine care)
  - Study age means ~55-60 years, up through age 70

Poor evidence in blinded-PLACEBO CONTROLLED trials

WHY?: AEs, intention to treat analysis, dose titration
Table 3. Adverse Events Experienced by Populationa,b,c

<table>
<thead>
<tr>
<th>Description</th>
<th>Prevalence, No. (%)</th>
<th>Population With Adverse Event, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregabalin (n = 31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea, vomiting, headache</td>
<td>7 (22.6)</td>
<td>39</td>
</tr>
<tr>
<td>Bowel disturbance</td>
<td>5 (16.1)</td>
<td>28</td>
</tr>
<tr>
<td>Diplopia, dysarthria</td>
<td>5 (16.1)</td>
<td>28</td>
</tr>
<tr>
<td>Dizziness, vertigo</td>
<td>4 (12.9)</td>
<td>23</td>
</tr>
<tr>
<td>Drowsy, sedation</td>
<td>3 (9.7)</td>
<td>17</td>
</tr>
<tr>
<td>Lethargy, numbness</td>
<td>2 (6.5)</td>
<td>11</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>1 (3.2)</td>
<td>6</td>
</tr>
<tr>
<td>Alertness</td>
<td>1 (3.2)</td>
<td>6</td>
</tr>
<tr>
<td>Weight gain</td>
<td>1 (3.2)</td>
<td>6</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>1 (3.2)</td>
<td>6</td>
</tr>
<tr>
<td>Psychiatric disturbance</td>
<td>1 (3.2)</td>
<td>6</td>
</tr>
<tr>
<td>Gabapentin (n = 7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drowsy, sedation</td>
<td>3 (42.9)</td>
<td>17</td>
</tr>
<tr>
<td>Dizziness, vertigo</td>
<td>2 (28.6)</td>
<td>11</td>
</tr>
<tr>
<td>Nausea, vomiting, headache</td>
<td>1 (14.3)</td>
<td>6</td>
</tr>
<tr>
<td>Alertness</td>
<td>1 (14.3)</td>
<td>6</td>
</tr>
</tbody>
</table>

a Frequency and severity measured on a scale of 1 to 10 with 10 being the worst possible score.

b The same participant may have experienced multiple adverse events of different descriptions.

c Gabapentin count was 7, and pregabalin count was 31 (P = .002).
GBP, PGB Dosing/AEs

- Lowest possible dose, that “could” be effective
- Adjust for creatine clearance, then titrate
- Dizziness/somnolence -> gait?

- Substance abuse, respiratory suppression:
  - Takes effort, fairly dramatic polypharmacy/substance

- Sexual problems, often not discussed
In short: Avoid antispasmodics
- carisoprodol, chlorzoxazone, cyclobenzaprine*, metaxalone, methocarbamol*, and orphenadrine
  Antichol, sedation, fall....

Use more often, but with caution: Antispastics
- Baclofen and tizanidine >> dantrolene
- Tizanidine with benefit in blinded clinical trials, ALBP
  - Multiple studies demonstrate tizanidine benefit
  - Younger patients, mean age ~42 years, up through age 70
- Baclofen, one blinded, placebo-controlled trial, ALBP
  - Younger patients, mean age ~42 years, up through age 74
Muscle relaxants: AEs

- Anticholinergic AEs limit antispasmodics use
  - Associated with fall, retrospective case-control study
  - Cyclobenzaprine with some TCA activity (5HT caution)

- Antispastic AEs sedation/cognitive impairment
  - Associated with fall, opinion papers only
  - Tizanidine (use 1-2mg) associated with urinary retention and **hepatotoxicity**, check LFTs
  - Higher dose baclofen: **withdraw**/seizure if stop abruptly
    - Renal adjust (5mg, not 10mg)
  - Dantrolene potentially fatal hepatotoxicity (black box)
*Radicular Pain: A clinical approach*

**Table 1 Attributes and demographics**

<table>
<thead>
<tr>
<th></th>
<th>Classic presentation</th>
<th>Common level</th>
<th>Common age</th>
<th>Gender</th>
<th>Risk factors</th>
<th>Mimicker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical radicular pain</td>
<td>Typically no inciting event, “woke up with pain”(^1,13)</td>
<td>C7 &gt; C6(^{13,19})</td>
<td>40–60(^{13})</td>
<td>Variable with</td>
<td>Spurling’s(^{14,19})</td>
<td>Shoulder pathology, carpal tunnel syndrome, ulnar neuropathy(^{14,19})</td>
</tr>
<tr>
<td>Lumbar radicular pain</td>
<td>May be associated with physical exertion, or not(^2,7)</td>
<td>L4–L5(^{13,19})</td>
<td></td>
<td>Smoking, heavy labor, obesity(^5,6)</td>
<td>+ Straight leg raise(^2,7)</td>
<td>Piriformis syndrome, peripheral neuropathy, spinal stenosis(^2,7)</td>
</tr>
<tr>
<td>Lumbar spinal stenosis</td>
<td>((L4–L5) and related factors (sitting)(^{10,12})</td>
<td>L4–5(^{40})</td>
<td>&gt;50, peak 60s(^{46})</td>
<td>M &gt; F(^{46})</td>
<td>+ Shopping cart sign (relief with lumbar flexion)(^{11,12})</td>
<td>Vascular claudication, arthropathies, peripheral neuropathy(^{10})</td>
</tr>
</tbody>
</table>

IMAGING? NO, YES, IT DEPENDS
Tricyclic antidepressants, TCAs & 5HT-norepi reuptake inhibitors, SNRIs

- Standard of care in neuropathic and chronic pain
  - Often coupled to GBP/PGB (neuropathy, neuralgia)
  - Indicated for radicular or neuropathic spine pain

..........It depends, complex.

- Older drugs (amitriptyline) often have:
  - More evidence (for efficacy)
  - More AEs
Tricyclic antidepressants, TCAs

- **Amitriptyline**
  - Multiple blinded trials: efficacy for CLBP and neck pain
    - Improvements in pain and disability, some mixed results
    - Study age means ~50 years, up through age 75
  
  Efficacy in neuropathic pain: Nortrip = Amitrip, but less AEs

- **Nortriptyline**
  - Few blinded trials: mixed efficacy LBP & radicular
    - Younger patients only, no over 65 years

- **Desipramine**: similar
Duloxetine: LBP +/- Depression

- Good efficacy: Multiple Blinded, placebo controlled trials
  - Many studies including older patients, but mean age ~41
- Older adult focused trial: LBP, depression *(Am J Psych 2007)*
  - Mean age 72.6 years, up to age 90, n=311 patients
  - Very good LBP VAS pain reduction (~ 5 points)
  - Very good benefit in multiple depression scales
  - Need 3-4 weeks to see benefit
  - Lack of efficacy; dulox 2.9% versus placebo 9.6%
  - Left study: due to AEs; dulox 9.7% versus placebo 8.7%

Other Older adult CLBP studies

- Benefit when longer(14 weeks) or neuropathic aspect
- Mean age 60, with patients up to 80s

Some similar efficacy for venlafaxine, much less evidence
TCAs & SNRIs AEs

- **TCAs**
  - Duloxetine/Venlafaxine are safe/good, but slow
  - TCAs: It's Ok, start low, warn patient
  - Rule of 3: CNS agents

- **SNRIs**
  - Nausea, insomnia, sexual side effects *(TCAs too)*
  - 5HTT syndrome
Tramadol IR, ER

- AGS: caution with tramadol, but OK
  - Tapentadol/Nucynta, strong potency- reserved use
  - When other therapies fail, tramadol is a reasonable trial
    - GI/CNS AEs possible (classic opioid), but usually mild
    - Very little abuse or diversion potential
  - Trial Tramadol 25-50mg, prior to XR formulation
  - Do not use with seizure PMH, 5HT problems very rare

- Efficacy:
  - CLBP: 4, 14 weeks studies, tramadol ER (200-300mg)
    - Mean age ~48, with patients up to 80 years
  - Similar studies with dose response, ER v IR Tramadol IR, ER
  - Tramadol-Acetaminophen
    - CLBP Efficacy: 4, 14 weeks studies, 37.5mg/325mg
    - ALBP Efficacy: 2.5 days, ER 75/650
    - Mean age ~60 chronic, 42 acute, patients up to 80 years
On Opioids...

- OutPt: All else fails, moderate-severe pain
  - Respiratory/overdose/death risk, also diversion
- InPt/ED: Go ahead
  - CNS effects, constipation
- Blinded trials, chronic neck and LBP/acute flairs

Opioid related death/abuse, young patients highest risk but older patients are fastest group on the rise

- Dosing in the hands of MD, close watch
- Combos with naltrexone did not catch on
Then, if 6–12 weeks of continued moderate–severe pain....
Summary: Diagnostically driven

Older adult spine pain

- Axial v radic, acute v chronic, severe v moderate

- Acute/exacerbation
  - NSAIDs burst/cox2 > 1/celecoxib/Tylenol ES/ER (1g/1.3g)

- Acute axial/myofascial/facet
  - Same NSAIDs, + smart antispastic (baclofen, tizanidine)
  - Severe -> tramadol

- Acute radicular
  - Same NSAIDs, GBP/PBG, tramadol
  - Severe -> telephone -> ESI
  - Surgery? -> red flags only
Summary: Diagnostically driven Older adult spine pain

- Axial v radic, acute v chronic, severe v moderate

- Chronic axial/myofascial/facet
  - Same NSAIDs, bursts only, chronic smart antispastic
  - Severe-> tramadol (limit #)
  - PT, LMBB/facet block -> RFA

- Chronic radicular
  - Same NSAIDs, bursts, duloxetine > TCAs (but can use)
  - GBP/PBG, tramadol (limit #), PT course
  - Pain clinic follow, ESI, etc
  - Surgery?-> Elective works well (not for axial)
Thank you

- **Presented material:** Fu JL, Perloff MD. Pharmacotherapy for spine-related pain in older adults. Drugs Aging. 2022 Jul;39(7):523-550

- **QUESTIONS?**
Neck/LBP myofascial: triggers
ESI for focal disc/foramen
LESI for spinal stenosis
CESI for focal disc/foramen, and “+”
Epiduralysis: postsurgical radicular
Spinal cord stimulator: the big gun

- Big step, but....
- Excellent benefit for **neuropathic** pain that:
  - Has failed everything
  - Pt is mentally stable
- Proven benefit:
  - FBSS
  - CRPS (RSD)
  - Severe peripheral neuropathy
  - IC, Angina!
  - Anything-
- $30K, so.....
LBP: Joint arthropathy