Depression & Chronic Pain

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New Mexico Health Resources
23rd Annual Health Provider Retreat
Taos, NM
2015
1. At the end of this talk, attendants will be able to describe the risk of developing chronic pain in people with a history of depressive illness.
2. At the end of this talk, attendants will be able to describe the risk of developing depressive illness in people with a history of chronic pain.
3. At the end of this talk, attendants will be able to describe the use of antidepressant medications in the treatment of chronic pain with and without comorbid depression present.
Not a profile, but a likelihood.

<table>
<thead>
<tr>
<th>Psychiatric Disorder</th>
<th>Current</th>
<th>Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Pain Treatment Facility</td>
<td>59%</td>
<td>77%</td>
</tr>
<tr>
<td>Community Sample</td>
<td>15%</td>
<td>34%</td>
</tr>
</tbody>
</table>

- In tertiary pain facilities in the U.S.:
  - Average age of patients: 44
  - Average duration of chronic pain: 7 years

Mayo Clinic Proc, 2010;85(3)s:42-50
Mood/Anxiety in Pain

- N = 5877, US civilian population, survey

- OR of having chronic pain, adjusted for sociodemographics

McWilliams, et al. Pain, 2003;106:127-133
Chronic Pain & Depression
Depression & Chronic Pain

- Comorbid prevalence: 40%-50%

- A reciprocal relationship:
  - Many retrospective studies support the notion that chronic pain leads to depression
  - Recent prospective studies indicate that a history of depression predicts a vulnerability to the development of chronic pain:
    - Patients with baseline depression were 2.3 times more likely to have chronic low back pain 3 years later

Dersh, et al. Spine, 2006;31:1156-1162
Reciprocal Relationship

2 ways to evaluate the relationship:

The effect of chronic pain on the risk and treatment of depression
The effect of depression on the risk and treatment of chronic pain
Depression & Chronic Pain

- Depression is associated with poor outcomes in chronic pain:
  - More pain complaints
  - More intense pain
  - Higher functional limitations, increased impairment in social functioning, increased unemployment

- Chronic pain is associated with poor outcomes in depression:
  - Lower response rates to depression treatment compared to those without chronic pain
  - Degree of functional limitation is correlated with severity of depression

Bair, Katon, et al. Archives of Internal Medicine, 2003;163:2433-2445
Effect of chronic pain on depression risk and treatment

<table>
<thead>
<tr>
<th>Setting</th>
<th>Prevalence of Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Clinic (inpatient &amp; outpatient)</td>
<td>52%</td>
</tr>
<tr>
<td>Psychiatric Clinic</td>
<td>38%</td>
</tr>
<tr>
<td>Orthopedic &amp; Rheumatology Clinic</td>
<td>56%</td>
</tr>
<tr>
<td>Dental Clinics Addressing Facial Pain</td>
<td>85%</td>
</tr>
<tr>
<td>Population-based Settings</td>
<td>18%</td>
</tr>
<tr>
<td>Primary Care Clinics</td>
<td>27%</td>
</tr>
</tbody>
</table>

Increased risk of meeting criteria for a depressive disorder:

<table>
<thead>
<tr>
<th># of pain complaints</th>
<th>2+</th>
<th>3+</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6x</td>
<td>8x</td>
</tr>
</tbody>
</table>

Bair, Katon, et al. Archives of Internal Medicine, 2003;163:2433-2445
Effect of chronic pain on depression risk and treatment

Unimproved back pain at 7 weeks, and 2 years are both associated with depressive symptoms and chronic depression compared with patients whose pain improves.

Untreated chronic pain is associated with:
- Worse depression outcomes
- More work/school absenteeism
- Higher healthcare utilization

Effect of depression on chronic pain risk and treatment

Depressive symptoms at baseline pain assessment predict future episodes of:

- Low back pain
- Neck/shoulder pain
- Musculoskeletal pain

Patients with depressive symptoms:

- 2x more likely to report low back pain

A common refrain: "I wouldn't be depressed if I wasn't in pain."

Bair, Katon, et al. Archives of Internal Medicine, 2003;163:2433-2445
Effect of depression on chronic pain risk and treatment

Active depression in patients with chronic pain is associated with:

- Worse pain prognosis
- Worse functional limitations
- More primary care backing related visits
- Treatment dropout/poor compliance

Bair, Katon, et al. Archives of Internal Medicine, 2003;163:2433-2445
Depression + Anxiety, Chronic Pain, & Disability

- 500 patients in a RCT for chronic pain assessed for depression (symptom checklist 20), anxiety (GAD-7), and pain severity & interference (BPI)

- Pain-related disability days in past 3 months:
  - Pain only: 18
  - Pain & Anxiety: 32
  - Pain & Depression: 38
  - Pain, Depression, & Anxiety: 42

Bair, et al. Psychosomatic medicine, 2008;70(8):890-897
Depression & Chronic Pain

• Relationship appears to be mediated by 2 factors:

  1. Patient's appraisals of the effects of pain on their lives

  2. Patient's appraisals of their ability to **exert any control** over their pain and their lives

Perceived Control

Drives Fear Avoidance Behaviors

- *Perceived Control*: the belief that one can exert influence on the duration, frequency, and intensity or unpleasantness of a pain stimulus

- This is distinct from control of the pain itself, rather control over how pain affects one's life

- Acceptance of the pain itself is associated with better adjustment

Maladaptive pain-related beliefs predicting poor adjustment

- Pain is a signal of damage
- Activity should be avoided when one has pain
- Pain leads to disability
- Pain is uncontrollable
- Pain is a permanent condition

The pain story.

- ACT-UP is a guide for a psychosocial assessment of the patient living with chronic pain.

<table>
<thead>
<tr>
<th>TABLE 1. Brief Psychosocial Screening: ACT-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Activities: How is your pain affecting your life (i.e., sleep, appetite, physical activities, relationships)?</td>
</tr>
<tr>
<td>2. Coping: How do you deal/cope with your pain (what makes it better/worse)?</td>
</tr>
<tr>
<td>3. Thinking: Do you think your pain will ever get better?</td>
</tr>
<tr>
<td>4. Upset: Have you been feeling worried (anxious)/depressed (down, blue)?</td>
</tr>
<tr>
<td>5. People: How do people respond when you have pain?</td>
</tr>
</tbody>
</table>

### Suicide Risk
In the last 12 months in U.S.

<table>
<thead>
<tr>
<th></th>
<th>Chronic Headache</th>
<th>Chronic Body Pain</th>
<th>Comorbid Substance Use Disorder</th>
<th>Comorbid Anxiety Disorder</th>
<th>Comorbid Mood Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N=5692</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Suicidality</strong></td>
<td>4.3 x</td>
<td>2.1x</td>
<td>OR 2.7</td>
<td>OR 4.1</td>
<td>OR 6.9</td>
</tr>
<tr>
<td><strong>Plan</strong></td>
<td>4.6 x</td>
<td>2.6x</td>
<td>OR 7.1</td>
<td>OR 12.2</td>
<td></td>
</tr>
<tr>
<td><strong>Attempt</strong></td>
<td>6.5 x</td>
<td>4.4x</td>
<td>OR 5.3</td>
<td>OR 7.8</td>
<td></td>
</tr>
</tbody>
</table>

Migraine & Suicidality

• In a study of 1186 subjects:

• Risk of suicide increased 17% for every 1 point increase on a 1-10 pain intensity scale

Don't screen; assess.

- Diagnose Major Depressive Disorder:
  - 5 criteria, at least one must be #1 or #2
  - 5 point decrease in score: partial response
  - Decrease of 50%: response
  - Absolute score <5: remission

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**PHQ-9**

### Nine Symptom Checklist

Over the last 2 weeks, how often have you been bothered by any of the following problems?

<table>
<thead>
<tr>
<th>Problem</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things..........................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<tr>
<td>2. Feeling down, depressed, or hopeless......................................</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much..............</td>
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<td>6. Feeling bad about yourself - or that you are a failure or have let yourself or your family down.......</td>
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<td>7. Trouble concentrating on things, such as reading the newspaper or watching television.................</td>
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<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual..........</td>
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(For office coding: Total Score ___ = ___ + ___ + ___)

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all
- Somewhat difficult
- Very difficult
- Extremely difficult

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From the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MD PHQ). The PHQ was developed by Drs. Robert L. Spitzer, Janet R.W. Williams, Kurt Kroenke and colleagues. For research information, contact Dr. Spitzer at niah@columbia.edu. PRIME-MD® is a trademark of Pfizer Inc. Copyright © 1999 Pfizer Inc. All rights reserved. Reproduced with permission.

Kroenke K & Spitzer R, Psychiatric Annals, 2002;32(9)
Treat to remission

- 76% of treatment compliant depressed patients with lingering symptoms of depression relapse within 10 months

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**Nine Symptom Checklist**

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Nonpharmacological Treatment

- Behavioral Activation (with pacing)
- Stretching with normalization of body sensations
Behavioral Activation vs. Back Surgery

Study #1

- RCT of lumbar spinal fusion vs. CBT in 64 patients with documented disc pathology at L4/L5 and/or L5/S1

- Inclusion criteria: spondylosis, pain greater than 1 year, ages 25-60

Behavioral Activation vs. Back Surgery

Study #1

- CBT intervention: 1 week in clinic, 2 weeks at home, then 2 more weeks in clinic (average 25 hours per week)

- Content:
  1) a lecture on pain receptors in the discs, facet joints and muscles; reflexive interplay between structures; ability to suppress and reinforce peripheral stimuli; an explanation that the disc/back can not be harmed by performing normal ADLs; instructions to use and bend their backs, and not be overly careful;
  2) fear of exercise and activity was challenged daily;
  3) lessons in lifting ergonomics;
  4) individualized exercise regimen and individualized rehabilitation goals defined;
  5) 3 workouts daily (aerobics, water gymnastics, individual work out);
  6) group and peer discussions

Behavioral Activation vs. Back Surgery

• Surgical intervention: posterolateral fusion with transpedicular screws at L4/L5 and/or L5/S1

Behavioral Activation vs. Back Surgery

- Pre-study belief that surgery was better than non-surgery: twice as likely in both groups.

- At 3 mo, 6 mo, and 1 year: no differences between groups in pain, medication use, or employment.

- CBT group has significantly less fear-avoidance behaviors.

Behavioral Activation vs. Back Surgery

Study # 2

• RCT of lumbar spinal fusion vs. CBT in patients with a prior history of surgical repair of disc herniation

• CBT and surgical intervention identical to study #1

• Only subject difference between studies is the history of prior surgery

Wait: Why do they need another surgery?

- Adjacent Segment Degeneration

Narrowed disc space, osteophyte complex, anterior spondylolisthesis

Behavioral Activation vs. Back Surgery

Outcome variables included: overall function, fear-avoidance with physical activity and work, back pain, emotional distress, medication use, lower limb pain, full-time employment, fingertip-floor distance

- CBT group: improved in all areas except pain, emotional distress, employment
- Surgical group: improved only in back pain

Behavioral Activation vs. Back Surgery

Study #2

<table>
<thead>
<tr>
<th>Independent observer overall rating by the Prolo scale for functional status</th>
<th>Lumbar fusion ($n = 28)^a$</th>
<th>Cognitive/exercises ($n = 29)^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete recovery</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Recurrent pain</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Mild pain</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Unchanged</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Worse</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Proportion with success at 1-year</td>
<td>15/28</td>
<td>18/29</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient overall rating by the Global Disability Question</th>
<th>Lumbar fusion ($n = 28)^a$</th>
<th>Cognitive/exercises ($n = 29)^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Good</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Fair</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Poor</td>
<td>12</td>
<td>15 $^*$</td>
</tr>
<tr>
<td>Worse</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Proportion with success at 1 year</td>
<td>14/28</td>
<td>14/29</td>
</tr>
</tbody>
</table>

Data are number of patients. Odds ratio (95% CI) for success (excellent, good, or fair) of surgery at 1-year: 1.1 (0.4–3.0), $p = 0.91$ (Pearson’s $\chi^2$ test).

*2 subjects in this group had back surgery in the 1 year of follow up.

Pharmacological Treatment

Antidepressants with analgesic effects:
- Tricyclic Antidepressants (TCAs)
- Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

Antidepressants without analgesic effects:
- Selective Serotonin Reuptake Inhibitors (SSRIs)
Tricyclic Antidepressants

- Cardiovascular Side effects:
  - Orthostatic hypotension (imipramine>nortriptyline)
    - 2-3 fold increase in risk of hip fracture
  - HEART BLOCK
    - Chance of 1st degree progressing
    - BBB carries 10 fold increased risk in developing 2:1 AV Block
  - PVCs may improve (TCAs are quinidine-like antidysrhythmics)
    - May need to modify dose of other antidysrhythmics to avoid bradycardia
  - Baseline ECG on all patients over 40

TCA dose < 100mg daily does not increase risk of sudden cardiac death; Higher doses increase risk 2-3 times

TCA serum level does not predict analgesia

Presence of depression did not affect efficacy of TCAs in reducing pain. Fluoxetine associated with decreased pain more than placebo if depression was present at baseline.

# Tricyclic Antidepressants for depression

<table>
<thead>
<tr>
<th>Plasma Concentrations</th>
<th>Concentration (ng/mL)</th>
<th>Response Rate (in/out of range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (Ami + Nor)</td>
<td>93-140</td>
<td>50%/30%</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>58-148</td>
<td>66%/26%</td>
</tr>
<tr>
<td>Imipramine (Imi + Des)</td>
<td>175-350</td>
<td>67%/39%</td>
</tr>
<tr>
<td>Desipramine</td>
<td>&gt;115</td>
<td>51%/15%</td>
</tr>
</tbody>
</table>

Serotonin Norepinephrine Reuptake Inhibitors

Duloxetine:
Analgesic dose: 60 mg
Antidepressant dose: 60-120 mg
FDA indications:
- Major Depressive Disorder
- Generalized Anxiety Disorder
- Neuropathic Pain, Diabetic
- Fibromyalgia
- Musculoskeletal Pain, Chronic

Need to monitor transaminases

Venlafaxine:
Neuropathic Analgesic dose: 225 mg
Migraine Prophylaxis dose: 150 mg
Antidepressant dose: 75-225 mg
FDA indications:
- Major Depressive Disorder
- Generalized Anxiety Disorder
- Social Anxiety Disorder
- Panic Disorder

Need to monitor blood pressure
Thank you.