Co-morbidities in Low Back Pain Patients

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Personal Disclosure
- None

Learning Objectives
- Understanding the common co-morbid conditions found in patients with low back pain
- Understanding the limitations and side effect profiles of medications used in patients with low back pain
- Understanding adverse events associated with treatment of low back pain

Outline
- Incidence & Prevalence
- Comorbid conditions
- Medications
- Procedures
- Therapies

Low Back Pain
- Point prevalence 15-30%
- Lifetime prevalence 60-85%
- % Population perm. disabled = 1.0%
- % Population temp. disabled = 1.0%
- Functionally limiting LBP
  - Age < 60 years = 8.5%
  - Age > 60 years = 5.0%

Low Back Pain
- Leading cause of expenditures for workers comp
- Financial cost = $100 Billion per year
- Male = Female
- Younger patients tend to be male
- Older patients ( > 60 years) tend to be female
Low Back Pain

- Incidence increases with age
- Genetic cause postulated
- Highest incidence of LBP
  - in manual labor
  - decreased job satisfaction
  - poor workplace social support

Incidence in the first month, only 15% will have an identifiable source of pain:

- 5% disk herniations
- 5% spinal stenosis
- 4% vertebral compression fracture
- 1% primary metastasis or osteomyelitis
- <1% AAA, renal, gyn, or visceral pain

Deyo, RA, JAMA 1992

National Low Back Pain Study

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herniated disc</td>
<td>36.7%</td>
</tr>
<tr>
<td>Myofascial pain</td>
<td>19.6%</td>
</tr>
<tr>
<td>Spinal Stenosis</td>
<td>14.0%</td>
</tr>
<tr>
<td>Lumbar Spondylosis</td>
<td>12.2%</td>
</tr>
<tr>
<td>Degenerative Disc Dz.</td>
<td>8.7%</td>
</tr>
</tbody>
</table>

Risk Factors

- Obesity
- Tobacco
- Decreased physical activity
- Decreased strength
- Decreased flexibility
- ??? Height
- Family history

Low Back Pain

- Mechanical
- Myofascial
- Neuropathic
NSAIDS

Prevalence
- 17 Million Americans use NSAIDs daily
- 60 Million prescriptions written in the US per year
- 300 Million patients use NSAIDs worldwide
- The elderly use NSAIDs 3.6x more often than their younger counterparts

NSAID Indications
- Analgesic
- Anti-inflammatory
- Anti-pyretic
- Anti-platelet effect
- Anti-neoplastic

NSAID Uses
- Reduce pain
- Decrease stiffness
- Improves function
  - Common uses include:
    - Osteoarthritis/RA
    - Musculoskeletal strain
    - Headache
    - Dysmenorrhea
    - Postoperative pain

NSAID Categories
- Acetic Acids
- Carboxylic Acids
- COX 2 Inhibitors
- Enolic Acids
- Fenamates
- Naphthikanones
- Propionic Acids
**Classification**

<table>
<thead>
<tr>
<th>NSAID Classification</th>
<th>Brand Name</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Excedrin</td>
<td>2-8 pills/day, (up to 2,000 mg/day aspirin, 2,000 mg/day acetaminophen, and 520 mg/day caffeine)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Motrin IB</td>
<td>1-6 pills/day, (up to 1,200 mg/day)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Nuprin</td>
<td>1-6 pills/day, (up to 1,200 mg/day)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Orudis KT</td>
<td>1-6 pills/day, (up to 75 mg/day)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Bayer</td>
<td>1-12 pills/day, (up to 4,000 mg/day)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Ecotrin</td>
<td>1-12 pills/day, (up to 4,000 mg/day)</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Actron</td>
<td>1-6 pills/day, (up to 75 mg/day)</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Orudis KT</td>
<td>1-6 pills/day, (up to 75 mg/day)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Aleve</td>
<td>1-3 pills/day*, (up to 660 mg/day)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Motrin IB</td>
<td>1-6 pills/day, (up to 1,200 mg/day)</td>
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</tr>
<tr>
<td><strong>Total Dose</strong></td>
<td></td>
<td>upto 80g/day</td>
</tr>
</tbody>
</table>

**Dosing**

**AMERICAN COLLEGE OF GASTROENTEROLOGY**

- **Actron® ketoprofen**: 1-6 pills/day, (up to 75 mg/day)
- **Advil® ibuprofen**: 1-6 pills/day, (up to 1,200 mg/day)
- **Aleve® naproxen sodium**: 1-3 pills/day*, (up to 660 mg/day)
- **Bayer® aspirin**: 1-12 pills/day, (up to 4,000 mg/day)
- **Ecotrin® aspirin**: 1-12 pills/day, (up to 4,000 mg/day)
- **Excedrin® aspirin, acetaminophen and caffeine**: 2-8 pills/day, (up to 2,000 mg/day aspirin, 2,000 mg/day acetaminophen, and 520 mg/day caffeine)
- **Motrin IB® ibuprofen**: 1-6 pills/day, (up to 1,200 mg/day)
- **Nuprin® ibuprofen**: 1-6 pills/day, (up to 1,200 mg/day)
- **Orudis KT® ketoprofen**: 1-6 pills/day, (up to 75 mg/day)*

*2-pill limit for patients over age 65

**Mechanism of Action**

- Cyclooxygenases are enzymes involved in arachidonic acid metabolism
- Cyclooxygenases convert arachidonic acid into prostaglandins, thromboxanes, prostacyclin, and malondialdehyde
- Cyclooxygenase 1 and 2 are involved in this process

**Function of Prostaglandins**

- **PHYSIOLOGIC**
  - Thermoregulation
  - Bronchial tone
  - Intestinal mobility
  - Myometrial tone
  - Cytoprotection
  - Semen viability

- **PATHOLOGIC**
  - Fever
  - Asthma
  - Ulcers
  - Diarrhea
  - Dysmenorrhea
  - Pain
  - Inflammation
  - Bone erosion

**Function of Prostaglandins**

- **PGE2 and PG2**
  - Vasodilatation
  - Bronchodilatation
  - Inhibit plt. aggregation

- **TXA2**
  - Promotes plt. aggregation
Function of Cyclooxygenase

**COX 1**
- Constitutive
- Housekeeping
- Stomach
- Intestine
- Kidney
- Platelet
- Endothelium

**COX 2**
- Regulated
- Pathologic
- Inflammatory
- Pain
- Proliferation (deregulated)
- Brain
- Physiologic
- Uterus
- Vas deferens
- Bone
- Kidney (development)

Pharmacology of NSAIDs

- Weak organic acids – highly protein bound
- Hepatic metabolism – CYP 2C9 isoform
- Absorbed well
- Enterohepatic and renal excretion
- Variable half-life
  - Some NSAIDs are "pro-drugs" such as Sulindac and Nabumetone

Pharmacology

**SHORT HALF LIFE**
- Rapid Effect
- Rapid Clearance
- Less ADRs (+/-)
  - Ibuprofen
  - Diclofenac
  - Indomethacin

**LONG HALF LIFE**
- Slow Onset
- Slow Clearance
- More ADRs (+/-)
  - Naprosyn (+/-)
  - Celocoxib
  - Rofecoxib
  - Nabumetone
  - Piroxicam

Pharmacology

- Balancing side effects may also mean trying to use more cox-2 selective drugs?

Toxicity

- Gastrointestinal
- Hematologic/Cardiac
- Renal
- Hepatic
- Allergic
- Skin
### Toxicity

<table>
<thead>
<tr>
<th>FREQUENCY</th>
<th>ADVERSE EVENT</th>
</tr>
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<tbody>
<tr>
<td>&gt; 10%</td>
<td>Dyspepsia</td>
</tr>
<tr>
<td>1-10%</td>
<td>Gastric bleeding/ulcer</td>
</tr>
<tr>
<td>&lt;1%</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td></td>
<td>CNS – confusion</td>
</tr>
<tr>
<td></td>
<td>Pulmonary</td>
</tr>
<tr>
<td></td>
<td>Hepatic</td>
</tr>
<tr>
<td></td>
<td>Hematologic</td>
</tr>
<tr>
<td></td>
<td>Rash</td>
</tr>
</tbody>
</table>

### Gastrointestinal AEs

- **GI symptoms**
  - Dyspepsia, nausea, vomiting, abdominal pain, heartburn
- Mucosal lesions (endoscopy/x-ray)
  - Gastroduodenal erosions and ulcers
- **Serious GI complications**
  - Bleeding, perforation, or obstruction

### Gastrointestinal AEs

- **Patient Risk Factors**
  - Age > 65
  - Concomitant disease
  - History of PUD, GIB, esophagitis
  - Family history
  - Tobacco/ETOH
  - H. pylori co-infection

- **Iatrogenic Risk Factors**
  - Corticosteroid use
  - Anticoagulant use
  - Prolonged NSAID use
  - NSAIDs with long T1/2
  - NSAIDs at high dosages
    - Endoscopic ulcers: Gastric 15-30%, Duodenal 10% (no symptoms)
    - 4 of 5 patients who develop a serious GI complication are asymptomatic before event

### Gastrointestinal prophylaxis

- PPI
- H2 blocker
- Prostaglandin analogue
- Sucralfate (No benefit)
- Cox 2 selective inhibitors

### Cox 2 selective inhibitors

- Celebrex marketed for OA, RA, FAP (approved by the FDA on December 31, 1998)
- Vioxx marketed for acute pain, OA, and primary dysmenorrhea (approved by FDA in May 1999)
CLASS and VIGOR trials

- Both studies showed fewer GI ulcers and ulcer complications compared with traditional NSAIDs
- When baby eASA was added to Vioxx, it had the same risk as Ibuprofen 800mg TID for ulcer
- MI rates for COX-2 inhibitors in the VIGOR trial were significantly higher than placebo

Cardiac toxicity

- Vioxx vs. Naprosyn – 2.38 times the cardiac risk
- Solomon (Pennsylvania Medicare Data) showed:
  - High increase in risk of AMI at >25 mg/day
  - Still increased risk of AMI at <25 mg/day
  - Still increased risk of AMI in first 90 days/use
  - No increased risk of AMI with Celebrex

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- Aleve (naprosyn)
  - Alzheimer's Prevention Trial
    - 2500 patients
    - Study stopped after 3 years
    - Patients on 220mg bid had 50% increase in cardiac events (no events in Celebrex group)
  - BOTTOM LINE – all NSAIDs may increase cardiac risk!!!

Cardiac toxicity

- 1671 patients post CABG
- 3 days Parecoxib and 7 days Valdecoxib vs. Placebo
  - 3.7x increased risk with COX-2 inhibitor for MI, sudden death, stroke and PE

Nussmeier, et al. NEJM, February 15, 2005

Hematologic AEs

- NSAID effect on platelet:
  - Depends on the half-life of the NSAID
  - Inhibition of the COX-1 enzyme in platelet
    - Leads to prolonged bleeding time secondary to impaired platelet aggregation
  - Need to hold ASA, which has an irreversible effect, at least 7 days prior to surgery
  - Need to hold conventional NSAIDs a minimum of 24 hours, but often 3-4 days
  - No need to hold NSAIDs prior to epidural
Renal toxicity

- Prostaglandins and prostacyclins are important for maintenance of intrarenal blood flow and tubular transport
- All NSAIDs, except the nonacetylated salicylates, have the potential to induce reversible impairment of GFR

- Cox 2 in the kidney is constitutive
- Both Cox 1 and 2 inhibit PGE2 and PGI2
  - PGE2 decreases Na+ absorption at the ascending loop of Henle
  - PGI2 increases K+ secretion with renin and aldosterone
  - PGI2 is a potent vasodilator in hypovolemia and hypoperfusion

Risk factors:
- Age > 65
- Heart disease
- CHF
- Cirrhosis
- CRI
- SLE
- Gout

NSAID side effects:
- Fluid retention
- Nephrotic syndrome: Interstitial nephritis
- Papillary necrosis
- Stones
- Electrolyte imbalance (K+)
- Renal insufficiency

Hepatic toxicity

- Elevated transaminases (often in JRA or SLE)
  - Elevations may exceed 2-3x normal level
  - May cause drop in serum albumin
  - May alter prothrombin time
  - Overt liver failure reported with:
    - Sulindac, Diclofenac, and Flurbiprofen
    - Sulindac causes highest incidence of cholestasis
    - Patients with liver disease should be monitored again after 8 – 12 weeks

Allergic reactions

- Urticaria
- Anaphalaxis
- Bronchospasm
- Nasal polyps, Asthma
Skin

- Stevens-Johnson can occur as an idiopathic reaction related to Valdecoxib and was one reason for FDA removal of this drug.

Acetaminophen

- Most commonly used analgesic in the world.
- Most commonly used anti-pyretic in the world.

- Mechanism unknown
- Maximum analgesic effect, 650mg - 1300mg
- Toxic ≥ 4 grams in 24 hours
- Cautious use in post-op patients – fever
- Cautious use in patients with acute hepatitis

Muscle Relaxants

- Baclofen –
  - anti-spasmodic effect
  - may have intrinsic analgesic efficacy
  - avoid with seizure disorder or renal problems
  - starting dose 5 mg TID - up to 80mg/day
  - avoid abrupt discontinuation – may be used long-term

- Flexeril –
  - local muscle spasms
  - not for CNS disease
  - starting dose 5 mg BID/TID
  - Stop in 2-3 weeks

Anti-convulsants

- Gabapentin
- Anti-convulsant – alpha (2) delta Ca++ channel antagonist.
- Major uses: peripheral neuropathy, radiculopathy
- Dosage
  - 100-300mg QHS → Max 3600 mg/day (TID/QID doses)
- Typically well tolerated > first choice neuropathic pain
Anti-convulsants
- Gabapentin
- Interactions and side effects:
  - Fatigue
  - Somnolence
  - Dizziness
  - Edema
  - Decrease in those with renal compromise

Anti-depressants - TCA
- Indicated for chronic neuropathic pain
- Avoid in patients with cardiac problems
- Baseline EKG (prolonged QTc?)
- Nortriptiline least ASE
- APS discourages use of Elavil with elderly
- Starting dose 5 mg
- ASE: sedation, dizziness – usually lessen with time

Opioids
- Opioids
  - Tolerance is common
  - Partial agonist or mixed agonist/antagonist can precipitate withdrawal symptoms when given with full agonist
  - Incomplete cross tolerance

Topical Agents
- EMLA (Eutectic Mixture of Local Anesthetics)
  - Myofascial pain
  - Neuropathic pain
- Lidoderm Patch (5%)
  - Post herpetic neuritis
- Capsaicin Cream
  - Depletes Substance P/C-fiber activity
  - Not for acute pain
  - Takes up to 4 weeks work
- Methyl-Salicylate Cream
  - Essentially topical aspirin

Physical Therapy
- Modalities
  - Heat
  - Cold
  - Ionto
  - Diathermy
Physical Therapy

- **TENS**
  - Contraindications include
    - Gravid Uterus
    - Malignancy
    - Skin disorder
    - Pacemaker
    - Carotid/Vertebrals

Physical Therapy

- **Cardiac**
- **Pulmonary**

Procedures

- **Epidural Steroid Injections**
- **Medial Branch Block + RFA**
- **Sacroiliac Joint Block + RFA**
- **Spinal Cord Stimulation**
- **Intrathecal Medication Pump**

Epidural Steroid Injections

- **Indications**
  - Low back and radicular pain symptoms
  - Spinal Stenosis

- **Insomnia (39%), facial erythema (20%), nausea (20%), rash/pruritis (8%)**

- **Temperature <100F, euphoria, depression, mood swings, pain flare, fluid retention, headache, hyperglycemia, hypertension, gastritis, menstrual irregularities**

- **No persistent complaints noted after 14 days**

(Andrade, MD's Newsletter 1993)
Epidural Steroid Injections

- True Cushingoid effect (facial edema, bruising, fat pad development) very rare and resolves within several weeks (Abram, Reg Anesthesia, 1996)
- Suppression of plasma cortisol can occur for usually 2 and up to 3 weeks (Jacobs, Anesthesia, 1983 and Burn, Am J Phys Med, 1974)

- Retrospective review of 322 TF ESIs
- 9.6% incidence of minor self limiting SEs including transient non-positional headache, increased back pain, increased leg pain, facial flushing, vasovagal reaction, increased BG, one case of intra-operative HTN
- No dural punctures or hospitalizations (Botwin KP: Arch Phys Med Rehabil; 81 (8): 1045, 2000)

- Vasovagal most common
- Allergic and anaphylactic reactions
- Direct NR or cord trauma should not occur
- Spinal headache – “wet tap”
- Compression of spinal NRs or cord by epidural hematoma/abscess

- Nerve root ischemia
- Case reports of infarct occurring in the territory of the anterior spinal artery
- Durocutaneous fistulas rare
- Prospective study found no short or long term complications in over 350 consecutive transforaminal epidurals (Huston: Arch Phys Med Rehabil; 77:937, 1996)

Medial Branch Block

- Increased pain
- Bleeding
- Infection
- Nerve injury

Sacroiliac Joint Block

- Increased pain
- Bleeding
- Infection
- Nerve damage
Spinal Cord Stimulation
- Cannot MRI a SCS
- Lead migration or fracture
- Dural puncture with spinal headache
- Infection
- Spinal cord compression
- Hematoma formation
- Stimulation of ligamentum flavum
- Increased pain

Intrathecal Medication Pump
- MRI compatible up to 1.5 T magnets
- Infection
- Catheter fracture or migration
- Pump failure with overdose/withdrawal
- Intrathecal mass/granuloma
- Seroma
- Spinal fluid leak – persistent

Summary
- All medications have some chance of causing side effects
- The treatment plan should minimize further damage to the patient
- All procedures have the potential to increase damage and pain
- Therapies should be tailored to the limitations of each patient