PAIN MANAGEMENT UPDATE 2014

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DISCLOSURE

I have no financial or other interest in any private or commercial entities which may be described, reviewed, evaluated or compared in today’s presentation.

OBJECTIVES

• To understand the difference between neuropathic and somatic pain
• To gain understanding for syndromes requiring pain management
• To review neuropathic and somatic pain medications:
  • Safe prescribing habits, indications, and monitoring
  • Mechanisms of delivery
  • Overview of technology advances
  • Trends and pipeline teaser
• To become familiar with noninvasive pain management interventions
• To gain basic understanding of more invasive interventions for pain
DEFINITION OF CHRONIC PAIN

“Chronic pain can be described as ongoing or recurrent pain, lasting beyond the usual course of acute illness or injury or more than 3 to 6 months, and which adversely affects the individual’s well-being... A simpler definition for chronic or persistent pain is pain that continues when it should not.” - International Association for the Study of Pain (IASP), 2004

There are 116 mill people with pain in the US (not including acute or peds)

This is more than heart disease, CA and DM combined!

TERMINOLOGY

1. Misuse
2. Abuse
3. Addiction
4. Pseudoaddiction

SOMATIC VS. NEUROPATHIC PAIN
SOMATIC VS. NEUROPATHIC PAIN

1. Neuropathic – resulting from disease or lesions, described as burning, cold, numb, tingling, pins & needles
   • Shingles, DPN, tic douloureux, disc

2. Somatic – nociceptive pain – direct injury
   • Stubbing toe, broken arm

3. Hyperesthesia – increased sensitivity to stimulation, r/t injury or medication

COMMON PAIN SYNDROMES

- FAILED BACK SURGERY
  • Also known as post laminectomy surgery syndrome
  • An occurrence when the outcome of surgery does not meet the expectations of the surgeon or the patient
  • Typically neuropathic in nature.
CHRONIC REGIONAL PAIN SYNDROME (CRPS)

Commonly known as RSD, chronic neurologic symptom that can occur after an initial noxious event

- **Symptoms**
  - Hyperesthesia
  - Neuropathy
  - Occasional edema
  - Sweating
  - Changes to the skin
- **Single extremity, mirror, or extension pain**
- Budapest Criteria, ISAP II
- Suicide Disease

COMMONLY SEEN ON MRI

**Spondylosis** – arthritis, chronic wear

**Spondylolisthesis** – shifting typically caused by significant arthritis
  - Retro or antero (measured in grades of 25%)

**Stenosis** – narrowing which can cause pressure on a nerve, typically a result of OA or disc
  - Central or foraminal
  - Neurogenic claudication

DISC BULGE VS. HERNIATION

**Bulge**
- Common
- Typically no pain
- Normal for age
- Large hamburger

**Herniation**
- Typically nerve pain
- Ruptured/slipped
- Localized area (pro/ext)

**Both may be incidental findings! Tears also may cause central pain**
FACET SYNDROME

- May be lumbar or cervical
- Pain is worse with extension, in the AM
- Flexion can relieve
- Can be caused by normal wear or trauma

Many times patients will have a normal MRI!

CERVICOGENIC HEADACHE

- It's not a migraine!
- Caused by inflamed nerves from facet-related issues

CARTILAGE IN THE JOINT BECOMES DAMAGED OR WORN
- OA
- Trauma
- No reason

Symptoms:
- Pain with sitting
- Prolonged walking
- Mildly radicular
- Unilateral/bilateral
- Sitting on ball or fist
- Point tenderness
- Positive Fabers

Inflammation of the sacroiliac (SI) joints

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FIBROMYALGIA

• It is real!

• Commonly diagnosed by Rheumatology

• There is no indication for narcotics in the treatment for fibromyalgia

• Treatment options: Massage therapy and/or trigger points

• There are FDA approved medications for fibro treatment.

WHO PAIN LADDER

Mild pain: 1-3  Moderate pain: 4-7  Severe pain: 8-10

NEUROPATHIC PAIN MEDICATIONS
NEURONTIN

- Antiepileptic
- MOA: unknown (Ca, Na channels), membrane stabilizer
- Peaks in 3 hrs, Half life 5-7 hours
- Renal excretion
- Drowsy, dizzy, vision changes, anxiety, Na retention
- Extended release: Gralise (PHN), Horizant (RLS)

LYRICA, PREGABALIN (SCHEDULE 5)

- Antiepileptic
- Binds to Ca channels resulting in a reduction of several neurotransmitters
- (membrane stabilizer)
- Indicated for Fibro, PHN, DPN
- Peaks in 1 hour, half life of 5-7 hours
- Renal excretion
- There have been no studies converting from gabapentin to pregabalin

CYMBALTA - SNRI

- Selective inhibitor of 5-HT and NE
- Central pain inhibitory actions
- Activities in descending inhibition pathways of brain and spinal cord
- Approved for Fibromyalgia and Chronic Musculoskeletal
- Side Effects: Nausea, dry mouth, dizziness, fatigue or insomnia, "jolts" / "zaps"
SAVELLA - SNRI

- Approved for Fibromyalgia
- Exact MOA is unknown
- Peak in 4-6 hours, steady state in 36-48
- Renal excretion
- Side Effects: GI, HA

ELAVIL, PAMELOR (TCA)

- Subclinical doses (10-25mg) have been shown to help with neuropathic and chronic pain syndromes, aids with sleep.
- Exact MOA is unknown
- Hypersomnia, dizziness, disorientation, orthostasis, urinary retention
- Pamelor is 2nd generation. Less SE profile. Improved orthostasis.

SOMATIC PAIN MEDICATIONS
MUSCLE RELAXANTS

SOMA:
• Indicated for acute use, 2-3 weeks
• Withdrawal/dependence have been reported
• Sedative effects
• CYP2C19 – i.e. w/ Omeprazole, one sees increase in Soma
• Poor metabolizers can have a 4-fold increase in levels
• Peaks in 1.5-2 hrs, half life of 2 hours

MUSCLE RELAXANTS

FLEXERIL
• Blocks nerve impulses sent to the brain
• Contraindicated with MAOIs, heart block, CHF, hyperthyroidism
• Side effects – weakness, dizziness, vision change
• Interactions w/: IBS meds, anticholinergics, COPD, Ultram

AMRIX
• Extended-release Flexeril, less CNS changes

MUSCLE RELAXANTS

NORFLEX
• Similar to Flexeril, may be less sedating

ZANAFLEX and BACLOFEN
• Antispasmodic due to MS or spinal cord injury

ROBAXIN
• CNS depressant, like others. Delay in renal/hep dz

SKELAXIN: Do not use with anemia, or renal/liver disease

Again, there are many from which to choose!
NONSTEROIDALS

Celebrex:
- Indicated for OA, RA, ankylosing spondylitis, acute pain
- Cox-2 inhibitor (only one)
- Dose by 50% for hepatic impairment and CYP2C9 slower
- Caution with sulfa allergy, RAD, COPD, HTN, CHF
- May interact with: ACE/ARB, lithium, fluconazole, warfarin, ASA
- Side effects: fluid retention, gastritis
- Typically approved prior to surgery (check with surgeon)

Again, many NSAIDs from which to choose –
- meloxicam, naproxyn, naprooxen, diclofenac...
- Naprelan, Duexis, Zpsor...

NONSTEROIDALS - TOPICALS

Pennsaid: Topical
- Diclofenac - reduces hormones that cause inflammation
- Uses DMSO
- Indicated for OA of the knee

Voltaren: Topical
- Diclofenac gel
- Indicated for OA of amenable joints
- Avoid showering for 1 hour

Flector: Patch
- Diclofenac transdermal
- Indicated for sprains, strains, bruising
- May be worn up to 12 hours

LIDODERM

- 5% lidocaine patch
- Inhibits ionic fluxes which initiate or conduct impulses
- Patch for provides analgesia without complete sensory block
- Indicated only for PHN
- 12 hr on and 12 hr off
- Warnings: overexposure (children/pets), non-intact skin, caine contraindications
A WORD ABOUT OPIATES

FOOD FOR THOUGHT

- U.S. News and World Report, 1997 cover:
  - “No Excuse for Pain – Doctors have a means to relieve suffering…Why aren’t they?”

- Increase in prescriptions of 149% from 1997-2007

- 2007 – Purdue Pharmaceuticals was fined $634.5 million for deceptive marketing of Oxycontin (“very little abuse potential”) They made $2.8 billion in sales that year!

- The US makes up 4.6% of the world population yet we consume 80% of the analgesics (99% of the hydrocodones)

- 6.5 billion people in the world – 4.7 do not receive adequate pain coverage. CA, 5.4 mil; surgery 8-40 mil; HIV 1 mil (WHO)

TRENDS AND CAUTIONS W/ OPIATES

- Cost of pain related conditions $200 billion/year

- Cost of abuse to the US government approximately $300 billion/year

- One person dies every 19 minutes from prescription drug overdose

- Deaths from opiates 9x higher than cocaine and 5x higher than heroin

- Diversion – unlawful channeling of regulated pharmaceuticals from legal sources to the illegal market place
WHERE ARE THE DRUGS OBTAINED?

Source Where Respondent Obtained

- One Doctor (50.0%)
- More than One Doctor (4.4%)
- From Friend/Relative (16.6%)
- Drug Dealer/Stranger (4.6%)
- Other (5.1%)

Source Where Friend/Relative Obtained

- One Doctor (50.0%)
- More than One Doctor (4.3%)
- From Friend/Relative (10.7%)
- Drug Dealer/Stranger (4.6%)
- Other (11.1%)

Note: Totals may not sum to 100% because of rounding or because suppressed estimates are not shown.

1 The Other category includes the sources: "Written-Rule Prescription," "Sold from Doctor's Office/Chirn/Hospital Pharmacy," and "Some Other Way".

DRUG ABUSE RELATED ER VISITS

DEATH RATE PER 100,000
NUMBER OF DEATHS – RX VS TYPE

- Opioid analgesic
- Cocaine
- Heroin

Source: National Vital Statistics System

DRUG OVERDOSE BY STATE, 2007

Source: National Vital Statistics System

DRUG SCHEDULES

- I-V categorized by the DEA based on:
  1. Currently accepted use in treatment in the US
  2. Relative abuse potential
  3. Likelihood of causing dependence when abused

- December: FDA proposal for hydrocodone combinations to go schedule II

- Ultimately, it's up to the DEA to reclassify medications
**RECEPTORS**

- Opioid receptors are found in the brain, spinal cord, and digestive tract.
- Endorphins are endogenous opioids.

<table>
<thead>
<tr>
<th>RECEPTOR</th>
<th>ACTIVITY</th>
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<tbody>
<tr>
<td>Mu</td>
<td>Analgesia, euphoria, sedation, miosis, constipation, resp depression, physical dependence, hormonal changes</td>
</tr>
<tr>
<td>Kappa</td>
<td>Analgesia, drowsiness, dizziness, sedation, psychomimetic effects, resp depression, constipation</td>
</tr>
<tr>
<td>Delta</td>
<td>Analgesia, dependence, aids in mu-mediated resp depression</td>
</tr>
<tr>
<td>Nociceptin</td>
<td>Anxiety, depression, appetite changes, tolerance to mu agonists</td>
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**OPIOIDS AVAILABLE IN THE US**

<table>
<thead>
<tr>
<th>Mu receptor Agonists</th>
<th>Kappa agonist/Mu antagonist</th>
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</thead>
<tbody>
<tr>
<td>codeine</td>
<td>buprenorphine (Suboxone, Butrans)</td>
</tr>
<tr>
<td>fentanyl</td>
<td>nalbuphine (Nubain)</td>
</tr>
<tr>
<td>hydromorphone/morphone</td>
<td></td>
</tr>
<tr>
<td>oxycodone/morphone</td>
<td></td>
</tr>
<tr>
<td>methadone</td>
<td></td>
</tr>
<tr>
<td>tramadol</td>
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**SIDE EFFECTS OF OPIATES**

- Dependence
- Respiratory depression
- Itching
- Vasodilation
- CNS depression
- CONSTIPATION: Relistor – subq naltrexone
SHORT ACTING OPIATES

WHY OR WHY NOT USE THEM???

- Optimal analgesia requires steady plasma levels
- Continual flux reprograms chemicals in the brain
- Increase in addictive properties
- Dilaudid has addictive/dependency potential within 3 weeks
- OK for acute injury, palliative pain

CIII – BUTRANS

- Buprenorphine transdermal
  - Partial agonist, also viewed as agonist/antagonist
  - Patch lasts for 7 days, rotate sites, adhesive reaction
  - Avoid excess heat as temperature-dependent increases are possible
  - 5mcg, 10mcg, 15mcg, 20mcg
  - Do not increase past 20mcg due to risk of QT prolongation

CII – THE OLDIES

Oxycontin:
- Mu opioid agonist, extended release oxycodone
- Indicated for chronic pain, and opiate tolerant patients
- Metabolize multiple pathways in the liver – monitor
- Patients with Crcl <60 show plasma levels of Oxycontin 50%
- Higher addiction potential traditionally (recent reformulation)
- No generic
CII – THE OLDIES

Fentanyl:
- Opiate agonist
- Half life 17 hours after removal (prolonged in elderly and terminal)
- Contraindication in opiate naïve, RAD, obstruction, mild pain, or acute pain
- CYP3A4C – inhibitors increase Fentanyl in system
- Use only in chronic patients
- HIGH abuse potential

Methadone:
- Mu agonist, also has neuropathic component
- Half life as long as 59 hours!!!
- Extensive biotransformation – CYP3A4, CYP2B6, CYP2C19, and lesser CYP2C9 & CYP2D6
- Significant cardiac conduction affects (monitor QT!)
- Significant potential for OD with initiation and conversion
- Less than 5% of rx’s, but 33% of deaths

CII – NEW KIDS ON THE BLOCK

Opana ER/IR: Oxymorphone
- Mu agonist with high level of functioning
- Indicated for opioid naïve and tolerant patients
- Use caution with hepatic impairment 1.6 increase in Opana, renal impairment increases Opana bioavailability 57-65%
- Best absorbed on an empty stomach, may take with food
CII – NEW KIDS ON THE BLOCK

Nucynta ER/IR: Tapentadol

• Mu agonist, high level of functioning
• Has some SNRI component – neuropathic
• Caution for serotonin syndrome with associated meds
• No dose adjustment is needed for mild renal/hepatic impairment
• No affect on QT

Exalgo:

• 24 hour extended release Hydromorphone
• For use in opiate tolerant patients with chronic severe pain
• 1 mg = 60 mg oxycodone
• Caution with age >65, renal/hepatic/cardiac disease

HORMONES AND PAIN?

Depending on the axis, stimulate or inhibit, affect a milieu of hormones!

HPA (hypothalamic-pituitary-adrenal) axis –

Decrease cortisol and increase ACTH
Increased interest, temp intolerance (make sure no other cause)

HPG (hypothalamic-pituitary-gonadal) axis –

Decreases in LH, FSH, estrogen, and testosterone THAT...
Libido, amenorrhea

Check free and total testosterone!

Low testosterone – well being, increase in CV risk, bone loss, etc.
Males – supplement
Females – Over 60 to 1 yr on opiates have 2x risk of fracture! Ca and D. Estrogen too risky
MONITORING PATIENTS ON OPIATES

Contracts are a **MUST**
Misuse, abuse, and diversion should be addressed on three fronts:

1. Drug monitoring programs
   - DHEC
   - 38 states participating - differences in manner & frequency

2. Screening tools
   - UDS, pill counts, SOAPP, COMM, etc.

3. Development of Abuse Deterrent Formulations (ADF)

SOAPP-R

1. How often do you have mood swings?
2. How often do you smoke a cigarette within an hour after you wake up?
3. How often have any of your close friends, including parents and grandparents, had a problem with alcohol or drugs?
4. How often have you taken medication other than the way that it was prescribed?
5. How often have others suggested that you have a drug or alcohol problem?
6. How often have you attended an AA or NA meeting?

DEVELOPMENT OF ADFS

- Targinique – Purdue, Oxycontin with naloxone in a 2:1 ratio
- Oxycodone ER – at least 3 different pharmaceutical companies working on this drug
- Hydroxodone ER – at least 3 different pharmaceutical companies working on this drug
- Novel compounds
- Who’s going to pay for them?
DOCUMENTATION:

- History and Physical Exam
- Diagnostic, therapeutic, and laboratory results
- Treatment objectives
  - Discussions of risks, benefits, and limitations of treatments
  - Details: date, type, dosage, and quantity
  - Instructions given
  - Review of outcomes, functional status (validated tools)
- Current and accessible – for colleagues as well as authorities

PROTECTING YOURSELF AND YOUR PATIENTS

- No blank scripts – Midlevels lose their licenses this way!
- Overdose comparable to deaths with MVA
- Start low and go slow
  - HAVE AN EXIT STRATEGY!
- Monitor for aberrant behaviors
- After 90 days on opiates, there is an 80% chance they’ll still be on it in 5 years!
- Remember: Pain is a bio-psycho-social disease!

WATCH FOR THE COCKTAIL…

- Short acting opioid
- Benzodiazepine (Typically Xanax)
- Soma
- Phenergan
NONINVASIVE INTERVENTIONS

- Pain psychology
- Physical therapy
- Chiropractic
- Medical Massage Therapy
- Back brace/low back garment

NONINVASIVE INTERVENTIONS

- Cervical traction
- TENS – transcutaneous electrical nerve stimulation
  - CMS no longer approves as of 2012
  - Muscle stimulator – think atrophy
  - Knee stimulator – OA of knee
  - Knee brace – unloader
INVASIVE INTERVENTIONS

- Trigger point injections
- Ilioinguinal injections
- Bursa injections
- Meralgia Paresthetica
- Sacroiliac joint injections
INVASIVE INTERVENTIONS

• Cervical ESI

• Caudal injection

• PRP (platelet rich plasma)

INTERVENTIONS

INTERLAMINAR LESI

TRANSFORAMINAL LESI

INVASIVE INTERVENTIONS

• Stellate ganglion block – C6

• Lumbar sympathetic nerve block – L2-L3

• Ganglion impar – sacral

• All are locations for sympathetic chains. Most common uses are RSD, PHN, and perineal pain.
INVASIVE INTERVENTIONS

Facet injection vs. Medial branch block

RHIZOTOMY (RFA)

CERVICAL RFA LUMBAR RFA

NEUROSTIMULATION

An option for those who have failed conservative therapy
Stimulation trial lead placed over T8 seen under fluoroscopy.
THANK YOU