Pharmacology Refresher for Home Health Therapists & Nurses

Session 4:
Medications for Musculoskeletal Pain and Inflammation

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Learning Objectives

- At the end of this presentation the participant should be able to:

1. Explain the general step-wise approach to the treatment of pain.
2. Given a patient case, identify which medications are primarily being used to treat pain or inflammation.
3. Identify basic therapeutic effects and common adverse effects for the medications used to treat musculoskeletal pain and inflammation
4. Explain the rationale for the use of two or more pain medications together in combination.

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Skeletal Muscle Relaxants

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Skeletal Muscle Relaxants

- Agents used to decrease muscle excitation and contraction
  - Used for spasm and spasticity
- Produce effects at various levels
- Higher doses associated with sedation and weakness

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Anti-spasticity drugs: Baclofen (Lioresal)

- Binds to GABA receptors and inhibits alpha-motor neuron activity
  - Especially useful in spinal cord injury and associated spasticity
  - Administered PO or via Intrathecal (IT) pump
  - Equally effective to diazepam with less sedation
- ADRs: weakness, sedation, ataxia, nausea, impaired cognition, orthostatic hypotension
- Withdrawal symptoms possible with abrupt discontinuation

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Anti-spasticity drugs: Dantrolene Sodium (Dantrium)

- Acts directly on skeletal muscle to attenuate muscle contraction
- ADRs:
  - generalized muscle weakness
  - dose-dependent risk of liver toxicity

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Anti-spasticity / Anti-spasmodic drugs: Tizanidine (Zanaflex)

- Decrease release of excitatory neurotransmitters in CNS → decreased input to alpha-motor neurons → decreased spasticity and spasm.
- Efficacy comparable to diazepam, baclofen
- ADRs: drowsiness, dry mouth, some generalized weakness, possible liver toxicity, hypotension possible

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Anti-spasticity / Anti-spasmodic drugs: Benzodiazepines

- Increases central and peripheral GABA activity causing relaxation
- Primary ADR: generalized sedation
- With chronic use- associated with development of tolerance and dependence
- E.g., diazepam (Valium), clonazepam (Klonopin)

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Anti-spasmodic drugs: Central Muscle Relaxants

- Polysynaptic Inhibitors
- Central Muscle Relaxants
  - Carisoprodol (Soma)
  - Cyclobenzaprine (Flexeril)
  - Chlorzaxazone (Paraflex)
  - Metaxalone (Skelaxin)
  - Methocarbamol (Robaxin)
  - Orphenadrine citrate (Norflex)
- Often formulated with other analgesics
- ADRs: drowsiness, dizziness. Long term use discouraged

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Botulinum Toxin: Type A (Botox, Dysport) or B (Myobloc)

- Binds strongly to pre-synaptic acetycholine vesicles
  - Neurons become unable to release acetylcholine → Causing reversible partial flaccid paralysis
- Administered via local injection into affected muscle
- Relaxation occurs within few days to 1 week, effects last 3-6 months
- ADRs: local pain, bruising
- Black box warning : Toxin may spread beyond initial site of injection, immediate action needed if respiratory, speech or swallowing difficulties appear

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Use of Skeletal Muscle Relaxants

- Used commonly with rehab interventions
  - Can make interventions more effective
- Try to discontinue drugs ASAP
- May need to support patients who have adapted increased muscle tone for activities or support those with muscle weakness
- May need to accommodate sedation and ADRs in sessions

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Pain Management

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General Principles of Pain Management

- Use step-wise approach
  - Nonpharmacologic Therapy
  - Acetaminophen
  - NSAIDs (including aspirin)
  - Combinations of opioid and non-opioid agents
  - Opioid agents
  - Add adjuvant agents when needed
- The same drugs are used to relieve somatic or visceral pain from various causes
- Consider a 'round the clock' treatment schedule with PRN available for breakthrough pain.

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Acetaminophen (Tylenol, generic brands)

- Efficacy and Use
  - Effective for mild, non-inflammatory pain
  - Anti-pyretic activity
  - No anti-inflammatory activity
- Notable adverse Effects
  - Does not generally cause GI irritation
  - Hepatic toxicity: Avoid alcohol
  - Little bleeding effect
    - Better option for patients at risk of bleeding

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NSAIDs (Non-Steroidal Anti-Inflammatory Drugs)

- Mechanism and Clinical Effects:
  - Analgesic properties
  - Anti-inflammatory properties at higher doses
  - Antipyretic effects
  - Anti-thrombotic effects
- Efficacy and Use
  - Overall, agents are therapeutically equivalent
  - Effective for mild-moderate pain
  - Many formulations available
  - Most agents have similar adverse reaction profiles

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Example NSAIDs

- Aspirin (Bayer Aspirin, others)
- Celecoxib (Celebrex)
- Diclofenac (Voltaren, others)
- Ibuprofen (Motrin, others)
- Indomethacin (Indocin)
- Nambutone (Relafen)
- Naproxen (Naprosyn, others)
- Naproxen sodium (Aleve, others)

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NSAIDs- Adverse Reactions

- GI Effects
  - Minor: nausea, dyspepsia, abdominal pain
  - Major: GI bleeding
    - Chemical structure is acidic and irritating
    - Impairs gastroprotective prostaglandin production
- Renal toxicity
- CNS depression possible
- Bleeding risk:
  - Aspirin- irreversible (up to 7 days after last dose)
  - Others- reversible (up to 3 days after last dose)
  - Use caution in patients at risk of bleeding or before surgery
- CV risk

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NSAIDs

- Onset
  - Analgesia onsets within 1-2 doses
  - Anti-inflammatory effects onset over 1-3 weeks
- Patient response is variable
  - Ensure adequate time and dose before d/c
  - Reasonable to try another NSAID
- Avoid combination with other NSAIDs or acetaminophen
  - Sometimes used in combination with opiates

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"Weak" Opioids

- Used for moderate to severe pain
- ADRs limit dose titration to treat severe pain
- Potential for abuse. Chronic use may lead to development of dependence and tolerance
- Controlled substances, but less regulation that stronger opiates
- Propoxephene removed from market

Example Agents:
- Tramadol (Ultram, Ryzolt)
- Codeine
- Propoxephene (Darvon, Darvocet-N with acetaminophen)

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"Strong" Opioid Agents

- Tolerated at higher doses for treatment of severe pain
- Selection depends on time to onset, duration, patient response
- Various dosing regimens, can be individualized to patient needs
  - Can titrate up to max doses as needed until limited by ADRs – no "official" max doses for opiates

Example Agents:
- Morphine (MS Contin)
- Fentanyl (Duragesic, Actiq)
- Hydromorphone (Dilaudid)
- Oxycodone (Oxycontin)
- Meperidine (Demerol)
- Methadone (Dolophine)

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Opioid Agents – Adverse Effects

Therapeutic and toxic effects are dose related
- May change agents to see if adverse effects improve

- CNS
  - Somnolence, sedation
  - Mood changes (euphoria and dysphoria)
  - Respiratory depression
  - Dependence / Tolerance
- GI
  - Decreased GI motility (leading to constipation)
  - Nausea, vomiting
- Histamine release

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Using Opioid Agents

- Schedule therapy when drugs are at peak effectiveness for best pain control (risk greatest ADRs as well)
- Watch for sedation, decreased respiratory rate
  - ADRs may be problematic, but analgesia should allow more vigorous physical activity
  - Respiratory response to exercise may be blunted
- Opioid withdrawal can lead to diffuse muscle aches and pains

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Combinations of Analgesics

- Opioids + NSAIDs or acetaminophen:
  - Treat pain by two mechanisms
  - Allows for lower doses of each
  - Better adverse effect profile
  - Beware of too much acetaminophen or NSAID when using combo
- Long acting agents + short acting agents:
  - Use long acting around the clock with short acting as needed for breakthrough pain

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Regional (Local) Anesthetics

- Inhibit conduction of action potential to interrupt pain signal transmission
- Metabolized quickly, short term use or continuous administration needed
- If systemic circulation, may have CNS or CV effects

Example Agents:
- Procaine (Novocain)
- Benzocaine
- Bupivacaine
- Lidocaine (eg Lidoderm Patch)

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Neuropathic Pain

- Results from nerve damage
- Described many ways:
  - Burning
  - Tingling
  - Electric
  - Shooting
- Non-opioid analgesics usually not effective

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Neuropathic Pain

First line agents:
- Tricyclic Antidepressants
- Antiepileptic Drugs
- SNRIs
- Lidocaine patch

Second line:
- Tramadol
- Opioids

Third line:
- Topical Capsaicin

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Capsaicin

- Topical anesthetic derived from pungent substance in hot peppers
- Depletes substance P from neurons so pain signals are not transmitted to CNS
- Applied to affected area 3-4 times daily
- Associated with local skin irritation, burning and stinging
- Available in high potency 8% Rx patch (Qutenza) or low potency (less than 0.15%) OTC products

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General Anti-Inflammatory Agents

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Other General Anti-Inflammatory Agents

- NSAIDs are most commonly used
- Glucocorticoids
  - Possess anti-inflammatory and immunosuppressive properties
- Used in continuous low-doses or occasionally in high-dose bursts to control inflammation or immune response

Example Agents
- Prednisone
- Methylprednisolone
- Dexamethasone
- Hydrocortisone
- Cortisone
- Triamcinolone

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Glucocorticoids

- Adverse Effects are dose related
  - Adrenal suppression
  - Immunosuppression (with increased susceptibility to infection)
  - Musculoskeletal effects: catabolic agents
    - Muscle wasting, pain, weakness
    - Atrophy of bone → osteoporosis
    - Risk of tendon rupture
  - Hyperglycemia / decreased glucose tolerance
  - CNS
    - Euphoria, insomnia, mood swings, psychoses possible

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Glucocorticoids

- Onset can take up to several weeks
- Used for many diseases
- May be used to 'bridge' patients until other therapy is effective
- Local therapy used to minimize adverse effects
  - Intra-articular
  - Topical
  - Inhaled
  - Nasal

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Questions?

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