PainWeek®

Hocus Pocus:
What Muscle Relaxants Do and Don't Do

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Titles & Affiliations

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Disclosures

- None

Learning Objectives

- Describe the pharmacokinetic profile of each class of anti-spasmodic medication
- Discuss pearls for selection and dosing of anti-spasmodic medications
- Choose an appropriate anti-spasmodic based on patient specific information

Pathophysiology

- Spasticity
  - "stiff' heavy, hard to move"
  - Upper motor neuron syndrome
  - Certain muscles are always contracted

- Spasm
  - Temporary
  - Sudden, involuntary tightening
  - Peripheral musculoskeletal conditions
  - Caused by dehydration, electrolyte imbalance, repetitive strain, decreased use

Common Uses

- Neck pain
- Low back pain
- Fibromyalgia
- Tension headaches
- Myofascial pain syndrome

What Does the Literature Say?

- Better than placebo, but NOT better than NSAIDs alone
  - Acute low back pain and tension headache
- Cyclobenzaprine is better than placebo, but inferior to antidepressants
  - Overall effectiveness is in the first few days
- No difference between metaxalone and placebo
- Some evidence that supports carisoprodol, cyclobenzaprine, orphenadrine and tizanidine for low back pain

What Does the Literature Say?

- Cyclobenzaprine is most studied
- Limited evidence to support use in chronic low back pain

- Overall recommendations:
  - Adjunctive therapy
  - Short term use

Class Overview

- Broken down into two categories
  - Antispasmodics
  - Spasticity (spasmolytics)
- Pharmacology
  - Mechanisms are not well elucidated
  - Often thought of as CNS depressants
  - Mechanisms will be discussed with specific agents

Class Overview

- Tolerability
  - Many “everyday” side effects
    - Dry mouth
    - Dizziness
    - Confusion
    - Somnolence
- Physical dependence and withdrawal?

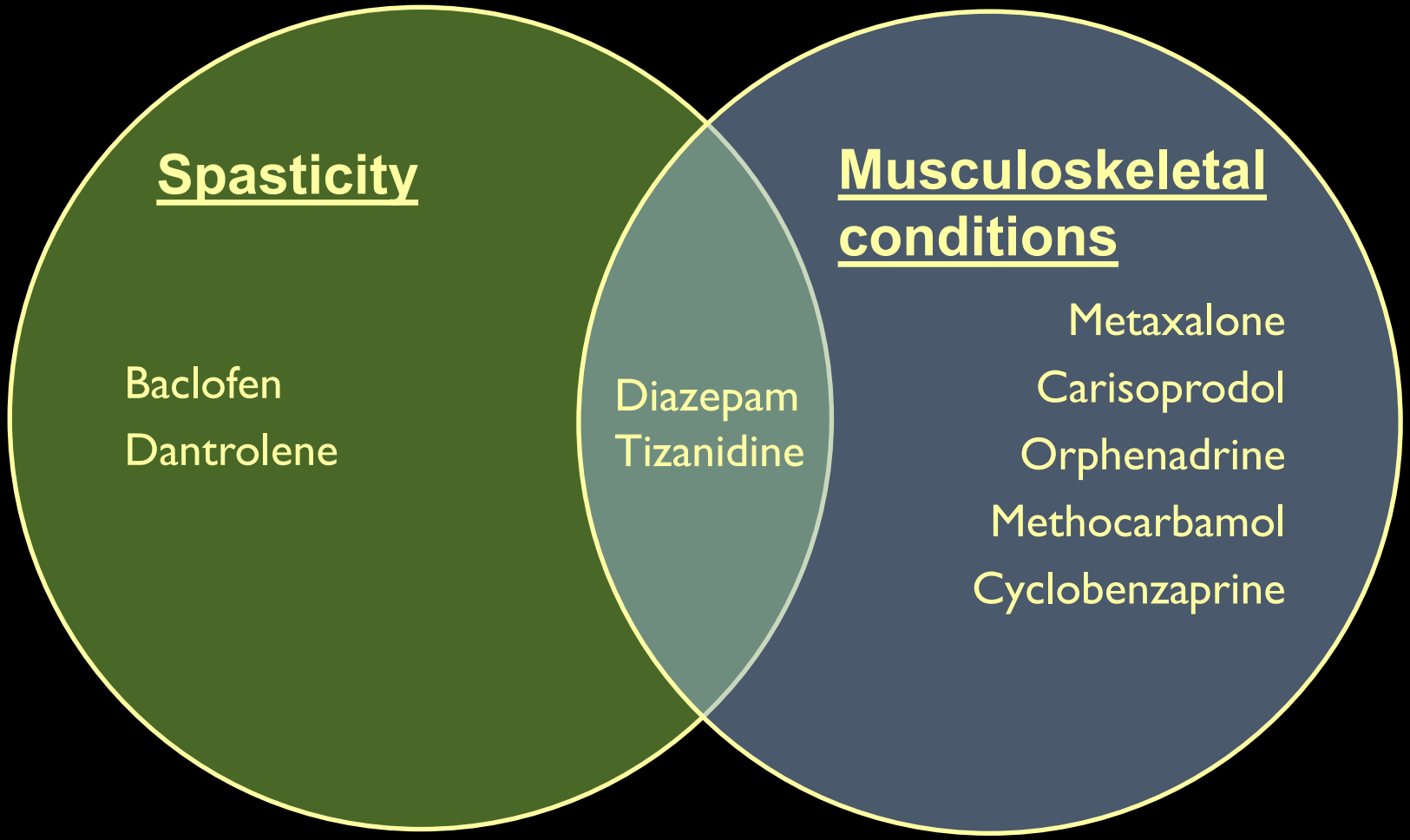
Question

- What is the most commonly prescribed muscle relaxant?
  A. Baclofen
  B. Tizanidine
  C. Methocarbamol
  D. Cyclobenzaprine

Class Overview

- Commonly prescribed...even if not by you
  - Diazepam
  - Tizanidine
  - Methocarbamol
  - Cyclobenzaprine

Medications



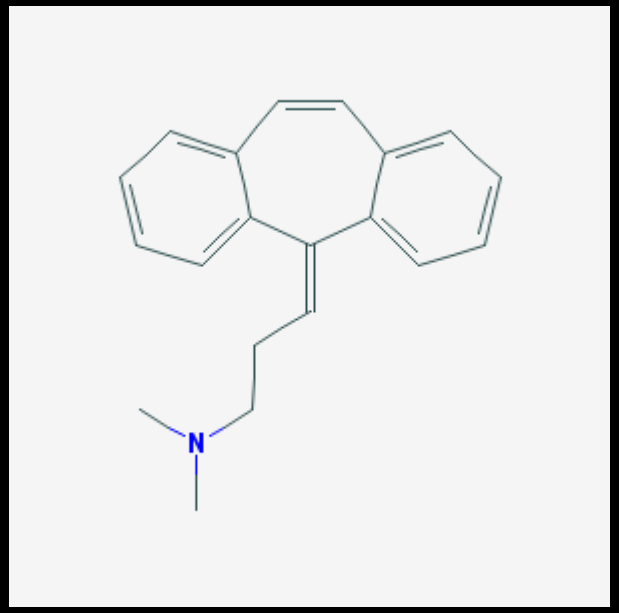
Considerations Prior to Use

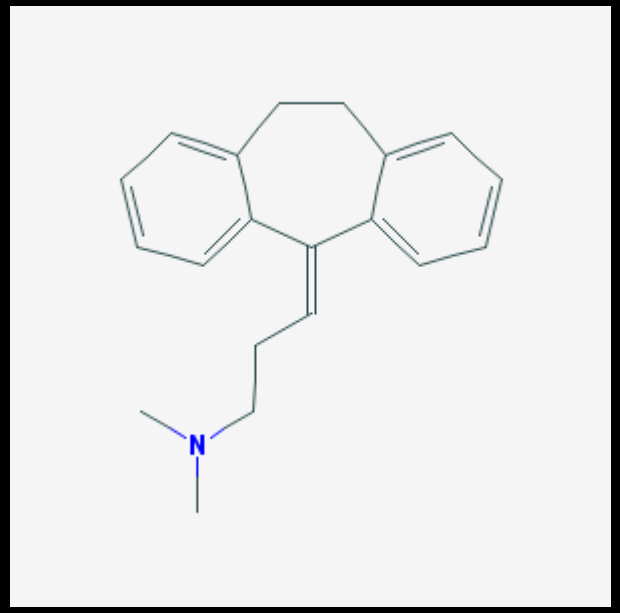
- Acute musculoskeletal pain or a chronic condition?
- Non-pharmacological considerations
- Other medication considerations
  - Acetaminophen – not likely effective or contraindication
  - NSAIDs – not likely effective or contraindication
- Recent lab work
- Drug interactions


Q
A

Treatment of Acute Musculoskeletal Conditions

What Muscle Relaxant is Structurally Closely Related to Amitriptyline?





Cyclobenzaprine

Cyclobenzaprine

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Centrally acting (brainstem); affects gamma and alpha motor neurons by reducing tonic somatic motor activity	Immediate tablets and extended release capsules	- Xerostomia - Dizziness - Headache - Somnolence	Caution use: - geriatric - hepatic impairment - cardiac conditions - hyperthyroidism

Clinical Pearls

- Caution in hepatic impairment
  - Increased serum concentrations
- Potential for serotonin syndrome
  - In combination with other agents
- Contraindications:
  - Heart block
  - Cardiac conduction issues
- Use past 2-3 weeks lacks efficacy

Question

- A patient was recently started on a muscle relaxant and their urine turned green. What muscle relaxant was started?
  A. Diazepam
  B. Metaxalone
  C. Methocarbamol
  D. Chlorzoxazone

Methocarbamol

Methocarbamol

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Unknown; effects appear to be associated with general CNS depression; no direct effect on muscle	500mg and 750mg tablets 100mg/mL injection	- Flushing - Rash - Pruritus - N/V - Dizziness - HA - Vertigo - Blurred Vision - Nystagmus	- Titrate slower in pts w with renal or liver impairment - Urine may become discolored

Clinical Pearls

- Caution in patients with a seizure disorder
  - Lowers seizure threshold
- Contraindications:
  - Injectable formulation in renal impairment
    - d/t preservative (polyethylene glycol)
- Less drowsiness than other agents
- Can cause black, brown or green urine

Metaxalone

Metaxalone

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Unknown; effects appear to be associated with general CNS depression; no direct effect on muscle	400mg, 800mg tablets	- N/V - Dizziness - Headache - Somnolence	- Caution: anemia, significant hepatic/renal impairment - May cause false positive results for urine glucose tests

Clinical Pearls

- Increased bioavailability and half-life in female patients
- No dose adjustments needed
- Serum concentrations may be increased when taken with food
- Paradoxical muscle cramps
- Less dizziness and drowsiness than others
- Potential to increase opioids and other CNS depressants

Orphenadrine

Clinical Pearls

- Caution in patients with tachycardia or arrhythmias
  - Can cause tachycardia
- Contraindicated in myasthenia gravis and glaucoma
  - Due to anticholinergic side effects
- Potential to be very sedating
- Long elimination half-life (14-16 hrs.)
- Can decrease the effect of chlorpromazine and promethazine

Orphenadrine

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Exact MOA unknown; possesses analgesic and anti-cholinergic effects	30mg/mL injection ER tablet	- Syncope - N/V, Xerostomia - Dizziness - Blurred vision	Caution: - Glaucoma - Myasthenia gravis - Prostatic hypertrophy, bladder neck/ pyloric/duodenal obstruction

Chlorzoxazone

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Centrally acting; inhibits reflex arcs	Tablets – multiple strengths	- Lightheadedness - Dizziness - Somnolence - Malaise	- Caution in pts w/liver dysfunction - Urine may become discolored (red-orange)

Question

- True or False: Meprobamate was the medication utilized by the main character and her mother in The Queen's Gambit?
  A. True
  B. False

Carisoprodol

- NO, just no (Noma)

Carisoprodol

Carisoprodol

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Unclear, but likely due to CNS depression, active metabolite has anxiolytic and sedative effects	250, 350mg tablet	- Dependence - Remember – just say no	-Must be tapered after chronic use

Clinical Pearls

- Metabolized into meprobamate
- Caution in patients with hx of drug abuse due to possibility of dependence
  - Meprobamate
    - Affects GABA, thalamus and limbic system, inhibition of spinal reflexes
- Taper slowly after prolonged use (1-2 weeks)
  - Too fast = anxiety, anorexia and insomnia

Treatment of Spasticity

Tizanidine

Tizanidine

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Centrally acting α_2-agonist – decreases release of excitatory amino acids in spinal interneurons	2mg, 4mg tablets 2 mg, 4 mg, 6 mg capsules	- Drowsiness - Insomnia - Dry mouth - Dizziness - Hypotension	- Does not alter muscle strength or improve functional measures -- Use cautiously with anti-hypertensive medications

Clinical Pearls

- Reduce dose in CrCl < 25mL/min
- Dose reduce in hepatic impairment
  - Monitor LFTs at 0, 1, 3, and 6 months
- Contraindications:
  - Use with ciprofloxacin or fluvoxamine
    - d/t CYP1A2 inhibition
- Can cause hypotension
  - Dose related
- Taper recommended
  - Withdrawal effects include rebound HTN, tachycardia and anxiety

Dantrolene

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Decreases Ca^{2+} release from skeletal muscle interfering with excitation-contraction of skeletal muscles		- Hepatotoxicity - Weakness - Drowsiness - Malaise - Diarrhea	- Can cause clinically meaningful weakness

Baclofen

Baclofen

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
GABA analogue – binds to GABAB receptors causing: Decreased neurotransmitter release and decreased sensory neuron response	5mg, 10mg tablets Injectable	- Weakness - Sedation - Fatigue - Dizziness - Nausea	- Abrupt cessation may cause seizures and hallucinations - Doses > 80 mg/day have been used - May also be used for hiccups

Clinical Pearls

- Black Box Warning: Avoid abrupt discontinuation, use a slow taper
- Dose reduction required in CrCl < 80mL/min
  - Renal elimination
- Potential to cause acute urinary retention
- Caution in patients with GI disorders

Benzodiazepines

Diazepam

Mechanism of Action	Dosage Forms	Adverse effects	Helpful information
Binds to GABAA receptors – enhances endogenous GABA receptor binding leading to increased inhibition	Tablets Parenteral Rectal gel Nasal solution	- Sedation - Cognitive impairment - Depression	- Abrupt cessation associated with withdrawal syndrome - Sedating - Gradually increase doses, caution as a first line agent

Clinical Comparison

Medication	Onset (hours)	Half-life	Active metabolite?	Equivalent Dose	Comments
Alprazolam	1-2	12-15	Yes	1mg	
Clonazepam	1-4	10-46	Yes	0.5mg	Avoid in hepatic impairment
Diazepam	0.25-2.5	>100	Yes	10mg	Avoid in hepatic impairment
Lorazepam	2	10-20	No	2mg	Preferred agent in hepatic and renal failure

Clinical Pearls

- Taper recommended with chronic use
- Half-life
  - Clonazepam>diazepam>lorazepam>alprazolam
- Sedating

Take Aways

- Short term use
- Review side effect profile
- STOP if ineffective
- Start low
- Not meant to be monotherapy

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JP is a 44 year old female that was in a recent automobile accident. Works full time and does not want to take medications that cause her to be too sedated, but us also unable to sleep at night.

CC: “Every time I stand up I am in so much pain, feels like my back is tightening up whenever I try to move”

PMH: Old herniated disks at L4/L5 and L5/S1

NKDA

Current medication list:

Gabapentin 600mg at bedtime

Montelukast 10mg at bedtime

Melatonin 2.5mg at bedtime

MN is an 80 year old male

CC: “My whole body hurts, my legs feel tight”

PMH: Epilepsy, a fib, stroke 5 years ago, fibromyalgia

NKDA

Current medication list:

Lisinopril 10mg daily

Metoprolol tartrate 12.5mg BID

Acetaminophen 500mg Q4H prn pain

Pregabalin 75mg BID