PainWeek

Relax, All Antispasmodics Are the Same…Right?

Jessica Geiger-Hayes PharmD, BCPS, CPE

Disclosure

- None

PainWeek

Learning Objectives

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

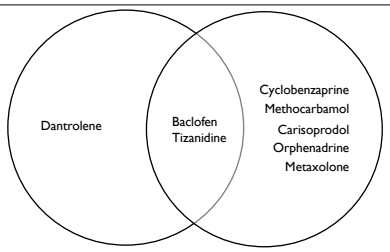
PainWeek

Pathophysiology

- Spasticity
  - Upper motor neuron syndrome
- Spasm
  - Peripheral musculoskeletal conditions

PainWeek

Medications



PainWeek

Common Uses

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

PainWeek

What does the literature say?

- Better than placebo, but NOT better than NSAIDs alone
- Cyclobenzaprine is better than placebo, but inferior to antidepressants
- No difference between metaxalone and placebo
- Some evidence that supports carisoprodol, cyclobenzaprine, orphenadrine, and tizanidine for low back pain

PainWeek

Case

JP is a 44 year old female who was in a recent automobile accident. Works full time and does not want to take medications that cause her to be too sedated, but is 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 600 mg at bedtime
Montelukast 10 mg at bedtime
Melatonin 2.5 mg at bedtime

PainWeek

Orphenadrine

PainWeek

Clinical Information

MOA	Not defined, potentially due to analgesic and euphoric effects Indirect skeletal muscle relaxant through central anticholinergic effects
Similar Structure	Diphenhydramine
Dosing	IM/IV: 60mg Q12H
Preparations	30mg/mL injection
Onset	1 hour
Brought to Market	1940s

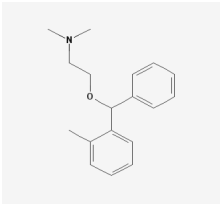
PAINWEEK

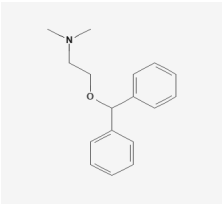
Clinical Pearls

- Caution in patients with tachycardia or arrhythmias
- Contraindicated in myasthenia gravis and glaucoma
- Potential to be very sedating

PAINWEEK

Pop Quiz





PAINWEEK

Carisoprodol

PainWeek

Clinical Information

MOA	Unclear, but likely due to CNS depression, active metabolite has anxiolytic and sedative effects
Dosing	250-350 mg TID and at bedtime for max of 2-3 weeks
Preparations	350 mg tablet
Onset	30 minutes with a peak response after 4 hours
Brought to Market	1959

PainWeek

Clinical Pearls

- Caution in patients with hx of drug abuse due to possibility of dependence
- Taper slowly after prolonged use

PainWeek

Methocarbamol

PainWeek

Clinical Information

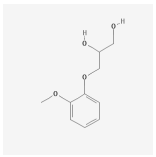
MOA	General CNS depression
Similar Structure	Derivative of guaifenesin
Dosing	1.5g PO 4 times daily for 2-3 days, then decrease to TDD of 4-4.5g 1g IM/IV Q8H, max of 3g/day
Preparations	500 mg and 750 mg tablets 100 mg/mL injection
Onset	30 minutes
Brought to Market	1960s

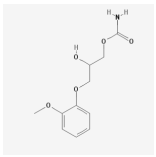
PainWeek

Clinical Pearls

- Caution in patients with a seizure disorder
- Contraindications:
  - Injectable formulation in renal impairment
- Less drowsiness than other agents

PainWeek





PainWeek

Metaxolone

PainWeek

Clinical Information

MOA	Precise mechanism has not been established; clinical effect may be associated with general depression of the nervous system; no direct effect on the contractile mechanism of striated muscle, the nerve fiber or the motor end plate
Similar Structure	N/A
Dosing	800 mg 3-4 times daily
Preparations	400 mg, 800 mg tablets
Onset	~3 hours
Brought to Market	1962

PainWeek

Clinical Pearls

- Increased bioavailability and half-life in female patients
- No dose adjustments needed
- Serum concentrations may be increased when taken with food

PainWeek

Cyclobenzaprine

PainWeek

Clinical Information

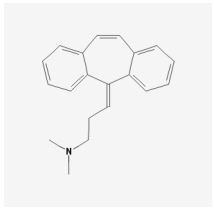
MOA	Acts at brain stem w/in CNS, decreases tonic somatic motor activity influencing both alpha and gamma motor neurons
Similar Structure	Amitriptyline
Dosing	5-10 mg TID
Preparations	5 mg and10 mg tablets
Onset	<1 hour
Brought to Market	1977

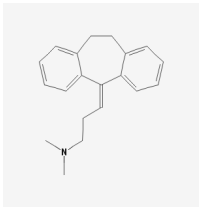
PainWeek

Clinical Pearls

- Caution in hepatic impairment
- Potential for serotonin syndrome
- Contraindications:
  - Heart block
  - Cardiac conduction issues
- Use past 2-3 weeks lacks efficacy

PainWeek





PainWeek

Baclofen

PainWeek

Clinical Information

MOA	Acts on spinal end of upper motor neurons to cause muscle relaxation, general CNS depressant
Similar Structure	Derivative of the GABA neurotransmitter
Dosing	5 mg TID, max of 80 mg/day
Preparations	5 mg, 10 mg tablets Injectable
Onset	3-4 days
Brought to Market	1992

PainWeek

Clinical Pearls

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

PainWeek

Tizanidine

PainWeek

Clinical Information

MOA	Alpha-2 adrenergic agonist
Similar Structure	Clonidine
Dosing	2 mg TID, can titrate up to a max of 36 mg/day
Preparations	2 mg, 4 mg tablets
Onset	1-2 hours
Brought to Market	1996

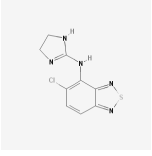
PAINWEEK

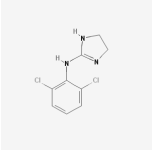
Clinical Pearls

- Reduce dose in CrCl < 25 mL/min
- Dose reduce in hepatic impairment
- Contraindications:
  - Use with ciprofloxacin or fluvoxamine
- Can cause hypotension
- Taper recommended

PAINWEEK

Pop Quiz





PAINWEEK

Benzodiazepines

PainWeek

Clinical Information

MOA	Act at GABA synapse, leading to increased affinity of receptors to GABA and skeletal muscle relaxation. (GABA is major inhibitory neurotransmitter)
Similar Structure	N/A
Dosing	Medication dependent
Preparations	Medication dependent
Onset	Medication dependent

PainWeek

Clinical Pearls

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

PainWeek

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	0.5 mg	Avoid in hepatic impairment
Diazepam	0.25-2.5	>100	Yes	10 mg	Avoid in hepatic impairment
Lorazepam	2	10-20	No	2 mg	Preferred agent in hepatic and renal failure

PainWeek

Case

MN is an 80 year old male

CC: "My whole body hurts, my legs feel tight"

PMH: Epilepsy, afib, stroke 5 years ago, fibromyalgia
NKDA

Current medication list:
Lisinopril 10 mg daily

Metoprolol tartrate 12.5 mg BID

Acetaminophen 500 mg Q4H prn pain
Pregabalin 75 mg BID

PainWeek

References

1. Lexicomp
2. See S, Ginzburg R. Choosing a skeletal muscle relaxant. *Am fam physician*. 2008;78(3):365-370
3. Witenko C, Moorman-Li R, Motycka C, et. al. Considerations for the appropriate use of skeletal muscle relaxants for the management of acute low back pain. *P&T*. 2014;39(3):427-435.
4. Chou R, Peterson K, Hefland M. Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review. J Pain Symptom Manag. 2004;28(2): 140-175.
5. Nicol AL, Hurley RW, Benzon HT. Alternatives to opioids in the pharmacologic management of chronic pain syndromes: A narrative review of randomized, controlled, and blinded clinical trials. Anesth Analg. 2017;125(5):1682-1703.

PainWeek

References (cont'd)

6. Tick H, Nielson A, Pelletier KR. Evidence-based nonpharmacologic strategies for comprehensive pain care: The consortium pain task force white paper. Explore. 2018;14:177-211.
7. Uhl RL, Roberts TT, Papaliodis DN. Management of chronic musculoskeletal pain. J Am Acad Orthop Surg. 2014;22(2):101-110.
8. See S, Ginzburg R. Choosing a skeletal muscle relaxant. Am Fam Physician. 2008;78(3):365-370.
9. Cyclobenzaprine [package insert] North Wales, PA: Teva Pharmaceuticals; 2013.

painweek

References (cont'd)

10. Methocarbamol [package insert] Malvern, PA: Endo Pharmaceuticals; 2016.
11. Carisoprodol [package insert] Somerset, NJ: Meda pharmaceuticals; 2009.
12. Orphenidrine [package insert] Northridge, CA: 3M Pharmaceuticals; 2006.
13. Baclofen [package insert] St Paul, MN: CNS Therapeutics; 2010.
14. Tizanidine [package insert] Ardsley NY: Acorda Therapeutics; 2013.
15. Metaxolone [package insert] Middlesex, NJ: CorePharma LLC; 2015.

painweek