EM Pharmacy Mythbusting

Stephen Rolfe, Pharm.D., BCPS
Joleen Bierlein, Pharm.D., BCPS
Maine Medical Center Departments of Pharmacy and Emergency Medicine

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Myth: Physostigmine should not be used in the treatment of anticholinergic toxicity due to severe adverse effects

Physostigmine, an acetylcholinesterase inhibitor, can be used as an antidote for patients presenting with anticholinergic toxicity. Historically there have been concerns regarding its adverse effect profile due to cholinergic excess, as well as published case reports causing asystole with physostigmine in tricyclic antidepressant overdoses.[1] A 10-year retrospective review from the California Poison Control Systems suggests that physostigmine is safe in the treatment of anticholinergic toxicity with 95.3% of patients experiencing no side effects.[2] When treating patients with anticholinergic toxicity, consult with your local poison center and consider physostigmine in doses of 0.5-1 mg every 10-15 minutes.

References:

1. Pentel P, Peterson C. Asystole complicating physostigmine treatment of tricyclic antidepressant overdose. Ann Emerg Med. 1980;9(11):588-90.
2. Arens AM, Shah K, Al-Abri S, et al. Safety and effectiveness of physostigmine: a 10-year retrospective review. Clin Toxicol (Phila). 2018 Feb;56(2):101-7.

Additional Resources:

1. Nguyen TT, Armengol C, Wilhoite G, et al. Adverse events from physostigmine: An observational study. Am J Emerg Med. 2018 Jan;36(1):141-2
2. Watkins JW, Schwarz ES, Arroyo-Plasencia AM, et al. The use of physostigmine by toxicologists in anticholinergic toxicity. J Med Toxicol. 2015 Jun;11(2):179-84.
3. Burns MJ, Linden CH, Graudins A, et al. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. Ann Emerg Med. 2000 Apr;35(4):374-81.

Myth: Trimethoprim-Sulfamethoxazole (TMP-SMX) is not effective against *Streptococcus species*

Combination therapy with TMP-SMX and an oral beta lactam is frequently used in the treatment of mild cellulitis. TMP-SMX is used due to the increasing rates of community acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA), and the beta lactam agent is added to target *Streptococcus species* as it is believed that TMP-SMX does not cover it. Both TMP and SMX disrupt folate synthesis, causing defective thymidine. Sources of exogenous thymidine in test media will circumvent the inhibition by TMP-SMX and render it ineffective *in vitro*, though thymidine concentrations in test media are now regulated.[1-3]

Some clinical data suggests TMP-SMX has activity against *Streptococcus species.* A randomized, controlled, non-inferiority trial compared benzylpenicillin to TMP-SMX for the treatment of impetigo in children. 90% of patients cultured positive for *S. pyogenes* prior to treatment, and TMP-SMX was found to be non-inferior to benzylpenicillin.[4] The results of this clinical study suggests TMP-SMX has activity against *Streptococcus species*. Another study was conducted comparing clindamycin to TMP-SMX for patients with cellulitis, abscesses, or both. Despite only 6% of patient with positive cultures for *Streptococcus*, there were no differences in outcomes, suggesting TMP-SMX monotherapy is effective for cellulitis, abscess, or a combination of both.[5]

References:

1. Proctor RA. Role of folate antagonists in the treatment of methicillin-resistant *Staphylococcus aureus* infection. Clin Infect Dis. 2008 Feb 15;46(4):584-93.
2. Bushby SR. Trimethoprim-sulfamethoxazole: in vitro microbiological aspects. J Infect Dis. 1973 Nov;128:S442-62.
3. Coll PF, Ausina VR, Vernis JV, et al. Exogenous thymidine and reversal of the inhibitory effect of sulfamethoxazole-trimethoprim on streptococci. Eur J Clin MIcrobiol. 1984 Oct;3(5):424-6.
4. Bowen AC, Tong SY, Andrews RM, et al. Short-course oral co-trimoxazole versus intramuscular benzathine benzylpenicillin for impetigo in a highly endemic region: an open-label, randomized, controlled, non-inferiority trial. Lancet. 2014 Dec 13;384(9960):2131-40.
5. Miller LG, Daum RS, Creech CB, et al. Clindamycin versus trimethoprim-sulfamethoxazole for uncomplicated skin infections. N Engl J Med. 2015;372:1093-103.

Additional Resources:

1. Bowen AC, Carapetis JR, Currie BJ, et al. Sulfamethoxazole-trimethoprim (Cotrimoxazole) for skin and soft tissue infections including impetigo, cellulitis, and abscess. Open Forum Infect Dis. 2017 Nov 2;4(4):ofx232

Myth: Sodium Polystyrene Sulfonate (SPS) significantly reduces serum potassium levels in patients with acute hyperkalemia

Sodium polystyrene sulfonate is a cation-exchange resin that is frequently used in the treatment of acute hyperkalemia. It has been available for use since 1958, which was prior to legislation requiring medications to be proven both safe and effective.[1] High quality data supporting its use are limited. Two small, non-randomized studies from 1961 suggest SPS is effective in decreasing serum potassium by 1.0 mEq/L after 24-48 hours.[2,3] One prospective study of 6 chronic renal failure patients found no difference in potassium reduction when compared to placebo.[4] Dosing and effect of SPS was evaluated in a retrospective study of 118 patients who received 15-, 30-, or 60 grams of SPS. The largest reduction in potassium (mean 0.91 mEq/L) was seen in the 60 gram group. Furthermore, the weak data to support efficacy is coupled with well-documented safety concerns regarding colonic necrosis with a near 33% mortality rate.[6] The FDA has updated the drug labeling to include warnings for these adverse

events and drug-drug interactions.[1] For the acute treatment of hyperkalemia, consider alternative treatments and the judicious use of SPS.

References:

1. FDA website
2. Flinn RB, Merrill JP, Welzant WR. Treatment of the oliguric patient with a new sodium-exchange resin and sorbitol. New Engl J Med. 1961;264:111-5.
3. Scherr L, Ogden DA, Mead AW, et al. Management of hyperkalemia with a cation-exchange resin. New Engl J Med. 1961;264:115.
4. Gruy-Kapral C, Emmett M, Santa Ana CA, et al. Impact of single dose resin-cathartic therapy on serum potassium concentration in patients with end-stage renal disease. J Am Soc Nephrol. 1998;9:1924-30.
5. Mistry M, Shea A, Giguere P, Nguyen M. Evaluation of sodium polystyrene sulfonate dosing strategies in the inpatient management of hyperkalemia. Ann Pharmacother. 2016:50(6):455-62.
6. Harel Z, Harel S, Shah PS, et al. Gastrointestinal adverse events with sodium polystyrene sulfonate (Kayexalate) use: a systematic review. Am J Med 2013;126(3):264.e9-24.

Additional Resources:

1. Mahoney BA, Smith WAD, Lo D, et al. Emergency interventions for hyperkalemia (Review). Cochrane Database of Syst Rev. 2005 apr 18;(2):CD003235