



Cherry Blossoms-Botanical Gardens, Birmingham, EN

## PIC QUESTION OF THE WEEK: 4/27/09

Q: What is the role of sodium thiosulfate in the treatment of calciphylaxis?

A: Calciphylaxis or calcific uremic arteriopathy (CUA) is a rare, but potentially life-threatening complication that typically occurs in individuals with chronic kidney disease (CKD) and secondary hyperparathyroidism. It develops in approximately 1% of dialysis patients and is associated with a mortality rate of nearly 80%. Rarely, the condition develops in patients with normal renal function. CUA is characterized by calcification of small arteries resulting in dermal necrosis, ulceration, and painful subcutaneous deposits of calcium. Previous therapeutic options have included hyperbaric oxygen, vitamin D analogs, parathyroidectomy, intensified dialysis regimens, and calcium-based phosphate binders. Each of these treatments was only modestly successful. Bisphosphonates may be of some benefit, while cinacalcet (a calcium receptor stimulating agent) has shown considerable promise for managing the condition. Sodium thiosulfate (in combination with sodium nitrite) has been used for several years as an antidote in cyanide poisoning. It was suggested as a possible therapy for CUA because of its generally effective use in related diseases such as nephrocalcinosis, recurrent calcium urolithiasis, and tumoral calcinosis. When employed for CUA, the drug has most commonly been administered in a dose of 25 g infused over 60 minutes three times weekly. Sodium thiosulfate is probably removed by hemodialysis and thus should be administered *after* the procedure. On occasion, it has been combined with cinacalcet. Pain relief is generally noted in several days, while resolution of ulceration may require months of therapy. Treatment has extended from 6 weeks to 34 months. Sodium thiosulfate is believed to exert its benefit in CUA because of its ability to chelate cations such as calcium, thus converting previously insoluble tissue calcium deposits to hydrophilic and soluble *calcium thiosulfate*. This salt is 250 to 100,000 times more soluble than other calcium salts and stimulates resorption, then elimination of calcium from subcutaneous and arterial sites. The antioxidant effects of sodium thiosulfate enhance endothelial function resulting in arteriole vasodilation and a subsequent reduction in pain. Adverse effects are limited to mild nausea, CNS effects, blood pressure changes, and possible anion gap metabolic acidosis. Sodium thiosulfate holds promise as an effective therapy for calciphylaxis, a potentially fatal complication of severe renal disease.

### References:

- Raymond C, Wazny L. Sodium thiosulfate, bisphosphonates and cinacalcet for treatment of calciphylaxis. *Am J Health Syst Pharm* 2008;65:1419-29
- Messner M, Bauer R. Sodium thiosulphate as promising therapeutic option to treat calciphylaxis. *Dermatology* 2006;212:373-6
- Rogers N, Teubner D. Calcific uremic arteriopathy: advances in pathogenesis and treatment. *Semin Dial* 2007; 20:150-157

Photo by: Heaven's Gate (John), used under Creative Commons License, <http://www.flickr.com/photos/59303791@-N00/3426161276/> (Accessed April 21, 2009)

Autumn Tami and Ryan Hancher, Pharm.D. Candidates

**The PIC Question of the Week is a publication of the Pharmaceutical Information Center, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA 15282 (412.396.4600).**