

TOXICOLOGY TODAY

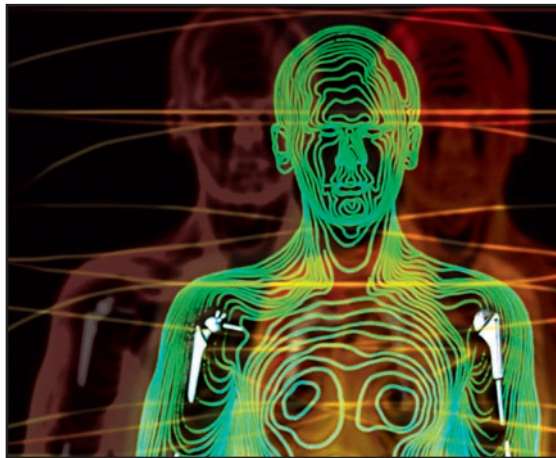


SKELETAL MUSCLE RELAXANTS

by Chad Condie, PharmD

Introduction

Skeletal muscle relaxants (SMR) are a class of drugs used in the treatment of acute musculoskeletal pain or spasms. Although these agents are grouped together, they vary in terms of their structure, pharmacology and toxicology. According to the American Association of Poison Control Centers Toxic Exposure Surveillance System (TESS) in 2004 there were 23,346 exposures to SMR reported to US poison centers; 16,822 (72%) were treated in



a health care facility, 15,031 were intentional and 61 resulted in a fatal outcome¹. This paper discusses the pharmacology and toxicology of SMR.

Pharmacology/ Pharmacokinetics

Baclofen is a derivative of gamma aminobutyric acid (GABA) and elicits pharmacologic activity through agonistic properties at the GABA_B receptor. It is structurally similar to gamma-hydroxybutyrate (GHB). It is primarily used to treat spasticity associated with spinal cord disease, and to treat pain associated with muscle spasm. Baclofen is rapidly absorbed from the gastrointestinal tract

reaching peak serum concentrations within 2 hours post-ingestion. The majority (85%) of baclofen is excreted unchanged in the urine while the remainder is metabolized in the liver to an inactive metabolite. Elimination is prolonged in patients with renal disease.²

Carisoprodol is thought to provide therapeutic benefit through its central depressant actions. It is metabolized in the liver to an active metabolite, meprobamate, as well as two inactive metabolites. Meprobamate is a sedative hypnotic and anti-anxiety agent marketed under the brand name of Miltown™.

(cont. on pg. 2)



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UPCC UPDATE

“UTOX UPDATE” BECOMES “TOXICOLOGY TODAY”

We have a new name! Effective this issue, our newsletter is Toxicology Today. You can expect the same great content in the Toxicology Today newsletter as well as new features like Poison Pearls. As always, historical copies of both health professional newsletters will continue to be available on our website at www.utahpoisoncontrol.org.

HURRY TO REGISTER FOR FUTURE ISSUES!

Utox Update/Toxicology Today is transitioning to an electronic format. Only one more issue will be printed and sent via US Postal Service. To continue to receive this newsletter, go to our website at www.utahpoisoncontrol.org/newsletters and register to receive the newsletter electronically via E-mail. Don't miss any exciting issues! If you have questions, need assistance registering or you don't have email, please feel free to call us at (801) 587-0600.

OUTREACH EDUCATION

HOW CAN YOU HELP RAISE POISON AWARENESS?

As a healthcare provider, you likely have parents and grandparents of young children as a captive audience just looking for information on health topics. Your waiting area is an ideal place to bring attention to poison prevention. Here are just a few suggestions of how you can raise poison prevention awareness.

- Setup a display or bulletin board about poisons, poison prevention tips, and the Poison Help number.
- Hand out telephone stickers and magnets at registration or checkout.
- Display poison prevention brochures in the waiting area.

The Utah Poison Control Center has brochures, stickers, and magnets available for your use. Free materials can be picked up or we can mail materials for a nominal shipping charge. Call 1-800-222-1222 and select the education office to request educational material.

Or, visit our website at: www.utahpoisoncontrol.org to download an order form that can be faxed to us.



(cont. from pg. 1)

Skeletal Muscle Relaxants

Cyclobenzaprine is a cyclic SMR structurally similar to amitriptyline. It acts primarily within the CNS to reduce somatic motor activity. Cyclobenzaprine is completely absorbed from the gut.

Metabolism is mainly hepatic through glucuronidation to inactive metabolites.

Methocarbamol acts by reducing the transmission of impulses from the spinal cord to skeletal muscle. A small portion (10-15%) is excreted unchanged in the urine and the remainder is metabolized in the liver to inactive metabolites.

Metaxalone is thought to act therapeutically through its depressant actions on the CNS. It is metabolized in the liver to inactive metabolites.

Tizanidine is the newest SMR. It is a central alpha-2 receptor and imidazoline receptor agonist, similar to clonidine. Tizanidine inhibits the release of excitatory amino acids from spinal interneurons. It is extensively metabolized by the liver and has no known active metabolites.

Adverse Effects

Adverse and toxic effects seen within this class of medications are primarily an extension of the pharmacologic properties of the individual drugs.

Clinical Toxicology

All of the SMRs are associated with varying degrees of CNS depression. Baclofen overdose is associated with profound CNS depression including hypotonic, hyporeflexia, hypothermia and respiratory depression.³⁻⁵ Toxicity is usually evident within 2-6 hours following an oral overdose. Seizures and hallucinations have also been reported. Bradycardia, tachycardia, hypotension and hypertension have all been reported. Cardiac dysrhythmias have also been reported. The duration of effects can be prolonged and mechanical ventilation was required for up to 61 hours in a series of adolescents who ingested baclofen to get high.³ Pupillary changes are not consistent. Baclofen is also administered intrathecally. Profound CNS depression can occur with inadvertent intrathecal administration. In addition, a withdrawal syndrome following intrathecal administration includes hypotension,

altered mental status, rebound spasticity, rhabdomyolysis and multiple organ failure.

Carisoprodol and its active metabolite are both CNS depressants. Due to the presence of an active metabolite, CNS depression may be prolonged. Carisoprodol has been associated with tachycardia, myoclonic jerking and other signs/symptoms that might be attributed to a serotonin excess.^{6,7} Meprobamate is a central nervous system depressant that has been associated with hypotension.

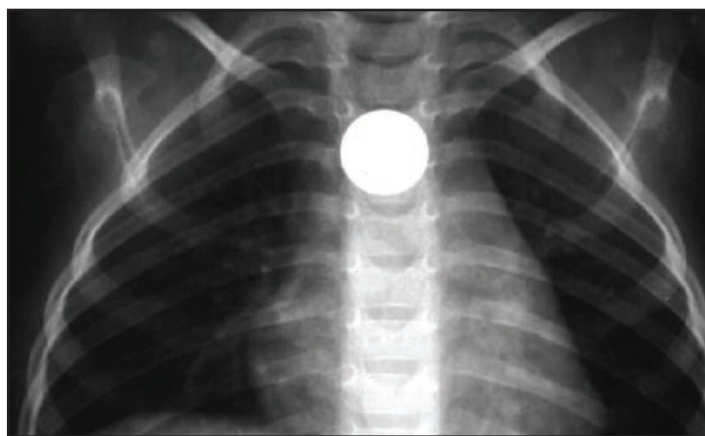
Cyclobenzaprine produces CNS depression and anticholinergic toxicity in an overdose.^{8,9} Although structurally related to amitriptyline, toxicity does not generally mimic tricyclic antidepressants. In a series of 402 cyclobenzaprine overdoses reported to poison centers, all cases with a known time of ingestion were symptomatic within 4 hours.⁹

Tizanidine is a unique SMR and produces toxic effects similar to clonidine. Acute overdose is associated with hypotension, bradycardia and coma.¹⁰ Clonidine sometimes is associated with initial tachycardia and hypertension. This may be less likely with tizanidine because it is much less potent than clonidine. (cont. on pg. 3)

PEDIATRIC COIN INGESTIONS

Problem

Between January 2005 and March 2006, the Utah Poison Control Center (UPCC) was involved in the care of 7 children, ages 8 months – 7 years, who swallowed a coin, were initially asymptomatic and subsequently were found to have the coin lodged in their esophagus. This represents a rate of “asymptomatic” esophageal coins of 7%!



University of Hawaii School of Medicine

Scope of the Problem

Coins are a common foreign body ingested by children. Coins were involved in 260 (1%) of all exposures reported to the UPCC in children less than 6 years of age in 2005. While the majority of children who swallow coins pass them without problem, a few children who are asymptomatic are eventually found to have the coin lodged in the esophagus. Delayed removal of an esophageal coin entails the risk of anesthesia and perforation.

Solution

All symptomatic pediatric coin ingestions are currently referred immediately to the closest emergency department for evaluation. All asymptomatic pediatric coin ingestions are referred to an emergency clinic or emergency department for localization of the coin within 12-24 hours of the ingestion. Coins in the stomach generally pass without problems. No further follow-up from the UPCC will be performed in children who have coins localized in the stomach.

Risk of radiograph?

The risk of a single chest x-ray is minimal. The amount of natural radiation we are exposed to in a year is equivalent to approximately 10 chest x-rays.

(cont. from pg. 2)

Skeletal Muscle Relaxants

Treatment

The primary treatment for all of the SMRs is good supportive care. Profound respiratory depression requiring mechanical ventilation is most likely to be seen with baclofen but could occur with any of the SMRs. Decontamination with activated charcoal is appropriate if the patient presents within 1-2 hours after an overdose, and possibly longer with cyclobenzaprine. Atropine has been used successfully to treat bradycardia associated with baclofen. There are anecdotal reports of the use of flumazenil to reverse CNS depression associated with carisoprodol and physostigmine to reverse anticholinergic effects associated with cyclobenzaprine. The use of these two antidotes is not routinely recommended. Please feel free to contact the Utah Poison Control Center (UPCC) to consult on the use of these medications in a SMR overdose.

Serum concentrations of the SMR are not routinely available and are not likely to be of benefit in managing an acute overdose. Likewise, none of these medications are

routinely detected on commonly available urine or blood toxicology screens.

Conclusion

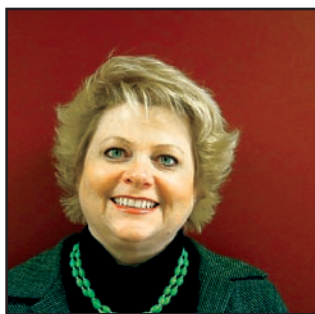
Skeletal muscle relaxants commonly produce CNS depression in an overdose and responds to good supportive care. Baclofen may be

mechanical ventilation and tizanidine may be more likely to cause hypotension and bradycardia. Toxicity of a large carisoprodol overdose can mimic serotonin syndrome. For additional information or for assistance in managing an acute SMR overdose, please contact the UPCC.

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MEET THE UPCC STAFF



SANDEE OLIVER

is a registered nurse, having received a BSN in Nursing from the University of Utah in 1979. She has worked in a variety of nursing specialties including; labor and delivery, intensive care, emergent care, public health,

and healthcare informatics. She has been a specialist in poison information at the Utah Poison Control Center since 2004. She loves a challenging poisoning call, but cherishes the break that a non-toxic silica gel brings to a hectic shift. She is the proud mother of two grown children, Erik and Katie, which she believes to be her greatest accomplishment in life. Now that they are out of the home, she spoils a couple of hairy little beasts, her two cats and two dogs. In her spare time she runs a darling gift boutique, Two Dancing Cats.

EMPLOYMENT

The UPCC has one position available: A Specialist in Poison Information-Pharmacist. You can find out more about this position on our website at www.utahpoisoncontrol.org/employment or apply on the University of Utah Human Resource page at <http://www.hr.utah.edu/joblist> (Use keyword "poison" to easily find the job postings.)

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TELECOMMUNICATIONS AND THE UPCC

All "emergency" calls to the UPCC are recorded. The digital recording becomes part of the patient's medical record. Digital recordings are valuable in training new employees and are an integral part of our continuous quality improvement program.

UTAH POISON CONTROL CENTER STAFF

Director

Barbara Insley Crouch,
PharmD, MSPH

Medical Director

E. Martin Caravati, MD, MPH

Associate Medical Director

Douglas E. Rollins, MD, PhD

Assistant Director

Heather Bennett, MPA

Administrative Assistant

Julie Gerstner

Specialists in Poison Information

Kathleen T. Anderson, PharmD, CSPI*

Bradley D. Dahl, PharmD, CSPI*

Su Bryner-Brown, RN, BSN

Michael L. Donnelly, RN, BSN

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Ed Moltz, RN, BSN, CSPI*

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Cathie Smith, RN, BSN

John Stromness, BS Pharm, RPh, CSPI*

Mary Towns, BSN, MS, APRN, CSPI*

Outreach Education Provider

Marty C. Malheiro, MS, CHES

Intern, Community Outreach

Joel Arvizo

Editors

E. Martin Caravati, MD, MPH

Barbara Insley Crouch, PharmD, MSPH

Publisher

Heather Bennett, MPA

Please send comments and suggestions for future articles to the editor of Toxicology Today at:

**585 Komas Dr., Suite 200
Salt Lake City, Utah 84108**

Or send e-mail to

poison@hsc.utah.edu

*CSPI denotes Certified Specialist in Poison Information.



THANK YOU

The Utah Poison Control Center expresses its sincere thanks to McNeil Consumer & Specialty Pharmaceuticals for their generous contribution that allows us to produce and distribute this newsletter.



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