SKELETAL MUSCLE RELAXANTS
by Chad Condle, 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 intentional and 61 resulted in a fatal outcome. 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 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.

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.

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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. 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. 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. Meprobamate is a central nervous system depressant that has been associated with hypotension.

Cyclobenzaprine produces CNS depression and anticholinergic toxicity in an overdose. 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.

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

ACCESS TO NEW EMPLOYEES 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.

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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 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.

References

TOXICOLOGY TODAY
**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, emergency 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.

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*CSPI denotes Certified Specialist in Poison Information.

**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.)

**FYI**

**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.

**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.