Skeletal Muscle Relaxants and Associated Medications for Nonspecific Acute Back Pain

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Educational Objectives

The reader should be able to:

- Describe pharmacological options in the treatment of nonspecific back pain.
- Review the efficacy of drugs used to treat nonspecific back pain.
- Identify the abuse potential of drugs used to treat nonspecific back pain.

Introduction

Back pain is a common public health problem, affecting between 70% and 85% of adults at some time in their lives.1 In the U.S., back pain is the second most common cause of disability in the general population and the leading cause of disability among men. Approximately 45% of adults experience back pain annually, resulting in a substantial socioeconomic impact.2 Direct medical costs result from hospitalizations, outpatient services, physician visits, and nursing-home stays; indirect costs include lost work productivity and disability compensation.

Pharmacological and non–drug-related modalities have been shown to reduce acute back pain and related symptoms, although there is less evidence of their effectiveness for chronic back pain.3 The use of pharmacotherapeutic agents is vital because they serve to increase the efficacy of non-drug modalities, allowing for earlier mobilization and rehabilitation. Although this article does not represent a systematic search of the literature, we discuss a variety of pharmacological approaches to alleviating acute back pain and elaborate upon their advantages and disadvantages.

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Etiology of Acute Back Pain

Most back pain is of nonspecific or musculoskeletal origin; the specific cause of lower back pain can be determined in only 15% of patients.3 A variety of terms are used to describe this common condition, including lumbar or cervical “sprain” or “strain” and “mechanical back pain.” The precise cause of back pain of this nature is not fully understood.

One model that has been proposed to explain the evolution and progression of back pain is the “spasm–pain–spasm” cycle. According to this theory, an initial event produces paravertebral muscle spasm (sustained muscle contraction). The spasm induces a cycle in which the resultant pain causes further muscle spasm, and the spasm increases the level of pain, establishing a self-perpetuating cycle. At a neuroanatomical level, the sustained muscle contraction (spasm), caused by an initiating event, stimulates nociceptors in the peripheral tissues that, in turn, activate afferent pain pathways, projecting to the dorsal root ganglion of the spinal cord. These neural signals (pain) are relayed to motor cells in the anterior horn cell, and activation of these motor pathways results in further muscle contraction (spasm) and further stimulation of afferent pathways.4 Whether this is a protective mechanism or a dysfunctional response to acute injury is unknown, but observations from clinical practice suggest the need to eliminate spasm to hasten the patient’s return to normal functioning.5

Most patients presenting with acute back pain have symptoms secondary to a nonspecific or musculoskeletal cause; 70% of patients recover within three weeks, and 90% recover within two months.6 However, back pain may occasionally represent a more serious underlying medical condition such as a malignancy, an aortic aneurysm, a renal stone, an infection, an epidural abscess, or another problem. Thus, an appropriate medical evaluation may be warranted, especially if the patient presents with atypical or persisting symptoms.

This article addresses only the treatment of patients with nonspecific acute back pain who have no serious underlying pathology.
**Pharmacological Therapy**

Reducing paravertebral muscle spasm is a primary objective of pharmacological therapy for musculoskeletal back pain. The term “muscle relaxant” is very broad and refers to a variety of structurally unrelated medications. Muscle relaxants can be divided into two main categories:

1. **Antispasmodic agents** (the primary topic of this article) are used to treat musculoskeletal conditions associated with spasm. The exact mechanism of action of these drugs is often poorly understood; it is not clear whether these medications actually decrease muscle spasm or whether they exert other effects.

2. **Antispasticity agents** are used to decrease spasticity (increased tone or contractions of muscles causing stiff or awkward movements as a result of an upper motor neuron lesion) in neurological disorders, such as multiple sclerosis and spinal cord injuries.

A degree of overlap exists within these two categories; some medications are used in clinical practice for the treatment of both conditions. Tizanidine (Zanaflex®, Elan) and diazepam (Valium®, Roche) are commonly prescribed for musculoskeletal spasm and are also approved for the treatment of spasticity.

**Antispasmodics Drugs**

Antispasmodics include medications of several different types, for example:

- antihistamines (e.g., orphenadrine [Norflex®, 3M]).
- central nervous system (CNS) depressants, such as chlorzoxazone (Parafon® Forte DSC; Paraflex®, Ortho-McNeil), methaxalone (Skelaxin®, King), methacarbamol (Robaxin®, Schwarz), and carisoprodol (Soma®, Wallace).
- central alpha-2-adrenergic agonists (e.g., tizanidine [Zanaflex®, Elan]).
- tricyclic antidepressant compounds, such as cyclobenzaprine (Flexeril®, McNeil Consumer).
- gamma-aminobutyric acid (GABA) agonists (e.g., the benzodiazepines, such as diazepam).

These medications have different indications and mechanisms of action. Consequently, drug actions and side effects may vary somewhat among the alternatives available. All antispasmodic agents can cause significant drowsiness to the extent that the manufacturers of these agents warn patients that activities requiring mental alertness (e.g., driving) may be impaired while they are taking the medication. Other potential adverse effects of this class of agents include dizziness, confusion, anorexia, nausea, vomiting, and allergic reactions.

Because these drugs undergo hepatic metabolism and renal excretion, they must be used cautiously in patients with compromised liver or kidney function. Excessive doses may result in significant toxicity with CNS depression.

An overview of the pharmacological properties of these medications for pain and spasm is presented in Table 1.

**Orphenadrine**

Orphenadrine citrate (Norflex®) is an analogue of the antihistamine diphenhydramine, which produces muscle relaxation by selectively blocking facilitatory functions of the reticular formation in the brainstem in animals. In addition, unlike other skeletal muscle relaxants, it produces some independent analgesic effects that may contribute to its efficacy in relieving painful skeletal muscle spasm.

How this agent produces analgesia is unclear. The literature suggests that the analgesic effect of some antihistamines might have more than one mechanism of action, including modulation of nociceptive responses in histaminergic and serotoninergic pathways.

In addition to the 100-mg oral tablets for twice-daily dosing, a parenteral formulation is available for intramuscular (IM) or intravenous (IV) use. Orphenadrine tablets are also produced in combination with aspirin and caffeine (Norgesic® and Norgesic® Forte, respectively). Anaphylactoid reactions have been reported following parenteral administration.

Besides the adverse effects common to antispasmodic medications in general, orphenadrine shares some of diphenhydramine’s antihistaminic and anticholinergic effects, including dry mouth, blurred vision, and urinary retention. Rare instances of aplastic anemia have been reported.

**Chlorzoxazone**

Chlorzoxazone acts primarily at the level of the spinal cord and subcortical areas of the brain, where it inhibits multisynaptic reflex arcs involved in producing and maintaining skeletal muscle spasm. The exact mode of action, although not clearly identified, may be related to the sedative properties of the drug.

Chlorzoxazone tablets are available in strengths of 250 mg (Paraflex®) and 500 mg (Parafon® Forte DSC). The recommended dose is 500 mg three or four times daily or up to 750 mg three or four times daily if needed. The side-effect profile is similar to that of other antispasmodic drugs, except for a limited number of reported cases of significant hepatotoxicity.

**Metaxalone**

The effects of metaxalone (Skelaxin®) are similar to those of other antispasmodic medications. The exact mechanism of action has not been established, but it is probably a result of CNS depression with no direct effect on the contractile mechanism of striated muscle. Metaxalone is available as 400- and 800-mg tablets. The recommended adult dosage is 800 mg three to four times daily.

Metaxalone-associated hemolytic anemia has been reported. Monitoring of liver function tests is recommended with long-term usage of the drug, although hepatotoxicity with metaxalone has not been as severe as that reported with chlorzoxazone.

**Methocarbamol**

Methocarbamol (Robaxin®) has been marketed for the treatment of musculoskeletal pain since 1957. This medication is
available in both oral tablets and parenteral formulations for IM and IV injection. A preparation containing aspirin (Robaxisal®, A. H. Robins) is also available.

The drug’s mechanism of action probably involves general CNS depression. Methocarbamol has no direct effect on the contractile mechanism of striated muscle.

This agent is available as 500- and 750-mg tablets. The recommended dosage ranges from 4,000 to 4,500 mg daily in divided doses. For severe conditions, doses as high as 6,000 to 8,000 mg may be given for the first 48 to 72 hours.

### Table 1: Medications for Musculoskeletal Pain and Paravertebral Muscle Spasm

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trade Name/ Manufacturer</th>
<th>How Supplied</th>
<th>Dosage</th>
<th>Onset of Action</th>
<th>Duration of Action</th>
<th>Comment/Possible ADEs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orphenadrine*</td>
<td>Norflex® (3M)</td>
<td>100-mg tablets; 30 mg/ml injection</td>
<td>100 mg b.i.d.</td>
<td>1 hour</td>
<td>4–6 hours</td>
<td>Has some analgesic effect; has anticholinergic and antihistaminic effects; aplastic anemia (rare)</td>
</tr>
<tr>
<td>Chloroxazone†</td>
<td>Parafon® Forte DSC, Paraflex® (Ortho-McNeil)</td>
<td>500-mg tablets</td>
<td>Up to 750 mg t.i.d. or q.i.d.</td>
<td>1 hour</td>
<td>3–4 hours</td>
<td>Hepatotoxicity (rare)</td>
</tr>
<tr>
<td>Metaxalone</td>
<td>Skelaxin® (King)</td>
<td>400- and 800-mg tablets</td>
<td>800 mg t.i.d. or q.i.d.</td>
<td>1 hour</td>
<td>4–6 hours</td>
<td>Liver functions should be monitored; drug may cause hemolytic anemia</td>
</tr>
<tr>
<td>Methocarbamol‡</td>
<td>Robaxin® (Schwarz Pharma)</td>
<td>500- and 750-mg tablets; 100-mg/ml injection</td>
<td>4,000–4,500 mg/day in divided doses</td>
<td>1 hour</td>
<td>Not reported</td>
<td>Drowsiness; IV injection may cause hypotension or convulsions</td>
</tr>
<tr>
<td>Carisoprodol</td>
<td>Soma® (Wallace)</td>
<td>350-mg tablets</td>
<td>350 mg t.i.d. and 350 mg at bedtime</td>
<td>30 minutes</td>
<td>4–6 hours</td>
<td>Metabolized to meprobamate; risk for abuse; contraindicated with acute intermittent porphyria</td>
</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>Flexeril® (McNeil Consumer)</td>
<td>5- and 10-mg tablets</td>
<td>10 mg t.i.d., range 20–40 mg/day in divided doses</td>
<td>1 hour</td>
<td>12–24 hours</td>
<td>Anticholinergic properties; sedation may limit dosage; not to be used in patients with arrhythmias, congestive heart failure, or hyperthyroidism or following myocardial infarction</td>
</tr>
<tr>
<td>Tizanidine</td>
<td>Zanaflex® (Elan)</td>
<td>2- and 4-mg tablets</td>
<td>See text</td>
<td>1 hour</td>
<td>3–6 hours</td>
<td>Possible interaction with antihypertensives; dose-related hypotension; liver function should be monitored; safety of long-term use at high doses not established</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Valium® (Roche)</td>
<td>2-, 5-, and 10-mg tablets; 5-mg/ml injection</td>
<td>2–10 mg t.i.d. to q.i.d. (PO)</td>
<td>30 minutes</td>
<td>Variable</td>
<td>Controlled substance with abuse potential; antiepileptic, anxiolytic, hypnotic properties; may cause withdrawal syndrome</td>
</tr>
</tbody>
</table>

ADE = adverse drug event; b.i.d. = twice daily; IV = intravenous; mg = milligram; PO = orally; q.i.d. = four times daily; t.i.d. = three times daily.

* Orphenadrine is also available as Norgesic® (containing orphenadrine 25 mg, aspirin 385 mg, and caffeine 30 mg) and Norgesic® Forte (exactly twice the strength of Norgesic®).

† Paraflex® contains 250 mg of chloroxazone, Parafon® Forte DSC® 500 mg.

‡ Methocarbamol is also available in an injectable form containing 100 mg/ml and as Robaxisal® (containing 400 mg of methocarbamol and 325 mg of aspirin).
Parenteral use has been associated with sloughing of the skin at the injection site. Rapid IV injection has been associated with syncope, hypotension, and convulsions. Parenteral use of the drug is not recommended for patients with epilepsy.9

Carisoprodol
Carisoprodol (Visoprylmeprobamate, Soma®) is a carbamate derivative that was first introduced in the late 1950s. It inhibits interneuronal transmission in the descending reticular formation and spinal cord and is thought to act via sedation rather than by direct skeletal muscle relaxation.

Carisoprodol is available as 350-mg tablets. The recommended dosage is one tablet three times daily and one tablet at bedtime. It is also available combined with aspirin (Soma® Compound) and with aspirin and codeine (Soma® Compound with Codeine). The onset of action is rapid (within 30 minutes), and the duration of action is four to six hours.

Carisoprodol is metabolized in the liver to hydroxycarisoprodol, hydroxymeprobamate, and meprobamate, which are excreted by the kidneys.11 The pharmacologically active metabolite, meprobamate, has a half-life of 11.3 hours, or up to 48 hours with chronic use.12 Because meprobamate is a controlled substance with a known potential for abuse, many clinicians have expressed concern about the potential of abuse of carisoprodol (see “Risks of Abuse” later).13–21

Adverse events are consistent with those considered to be typical for this drug class and mainly involve the CNS (e.g., drowsiness, dizziness, vertigo, ataxia, tremor, irritability, and headache).

Cyclobenzaprine
Cyclobenzaprine (Flexeril®) is structurally and pharmacologically related to the tricyclic antidepressants and produces its effects within the CNS, primarily at the brainstem level. Tablets are available in strengths of 5 and 10 mg. The recommended dose is 10 mg three times per day, with a range of 20 to 40 mg daily in divided doses. However, sedation may limit the dosage level in some patients.

Like the tricyclic antidepressants, cyclobenzaprine has anticholinergic properties and may cause dry mouth, blurred vision, increased intraocular pressure, urinary retention, and constipation. It should not be used in patients with cardiac arrhythmias, conduction disturbance, or congestive heart failure or after myocardial infarction. Potentially dangerous interactions may occur with monoamine oxidase inhibitors. As with some antidepressants, withdrawal symptoms consisting of nausea, headache, and malaise have been reported following abrupt cessation of cyclobenzaprine after prolonged use.9

Drugs Used as Both Antispasmodic and Antispasticity Agents
Tizanidine
Tizanidine (Zanaflex®) is approved for the treatment of spasticity, and it is also used clinically to treat pain and spasm associated with musculoskeletal conditions. It is an agonist at alpha2-adrenergic receptor sites and presumably reduces spasticity by increasing presynaptic inhibition of the motor neurons without directly affecting skeletal muscle, the neuromuscular junction, or the monosynaptic spinal reflexes. Its effects are greatest on the polysynaptic pathways, and the overall effect of these actions is thought to reduce the facilitation of spinal motor neurons, resulting in muscle relaxation.

At least five studies have demonstrated the usefulness of tizanidine for patients with musculoskeletal back pain and paravertebral muscle spasm.22–27 Side effects are similar to those seen with other skeletal muscle relaxants. Drowsiness was the most common reason for discontinuing the medication. Tizanidine has been associated with hepatic amino-transaminase elevations that are usually asymptomatic and reversible with cessation of therapy.22

The imidazoline structure of tizanidine is related to that of the antihypertensive drug clonidine and other alpha2-adrenergic agonists, but tizanidine has one-tenth or less of the potency of clonidine in lowering blood pressure. However, a case of hypotension caused by an interaction between the angiotensin-converting enzyme–inhibitor lisinopril (e.g., Zestril®, Astra-Zeneca; Prinivil®, Merck) and tizanidine has been documented,28 suggesting that caution might be advisable for patients using tizanidine and an antihypertensive medication simultaneously.

Tizanidine is available as 2- and 4-mg tablets. Dosing begins at 4 mg, which can be repeated at six- to eight-hour intervals. The doses can be gradually increased in 2- to 4-mg steps to optimal effect. Experience with single doses greater than 8 mg and with daily doses exceeding 24 mg is limited.

Benzodiazepines
Diazepam (Valium®) is also approved for the treatment of spasticity and is the most frequently prescribed benzodiazepine used for patients with paravertebral muscle spasm and musculoskeletal pain. Other available benzodiazepines have not proved superior to diazepam for this indication.7

The muscle-relaxant effects of this drug are thought to result from enhancement of GABA-mediated presynaptic inhibition at spinal and supraspinal sites. Diazepam also has antiepileptic, anxiolytic, and hypnotic properties.

Studies comparing diazepam with placebo and other skeletal muscle relaxants have yielded inconsistent results. In general, diazepam has been found to be superior to placebo but not consistently superior to other skeletal muscle relaxants for the relief of muscle spasm and pain;22 however, it is more effective than other skeletal muscle relaxants that are approved for the treatment of musculoskeletal conditions when it is used to treat spasticity associated with CNS disorders (cerebral palsy and spinal cord injury). Its efficacy is similar to that of baclofen (Libras®; Novartis), tizanidine, and dantrolene sodium (Dantrium®, Procter & Gamble) for this problem.29

Diazepam is available as 2-, 5-, and 10-mg tablets and as 5-mg/ml parenteral preparations for IM or IV usage. For musculoskeletal conditions, the recommended oral dosage is 2 to 10 mg three to four times daily; the IM dose is 5 to 10 mg every three to four hours as needed. The drug is highly lipid-
solute and easily crosses the blood–brain barrier with a rapid onset of action.

CNS depressant activity may cause sedation, cognitive dysfunction, or behavioral changes. Diazepam is a controlled substance whose use, like that of any benzodiazepine, is limited by the potential for abuse and dependency. Withdrawal symptoms similar to those of barbiturate or alcohol withdrawal may occur upon abrupt cessation.

**Antispasticity Medications**

Diazepam, tizanidine, baclofen, and dantrolene are approved for use in patients with spasticity. The latter two medications are not usually prescribed for paravertebral muscle spasm or musculoskeletal pain. However, because medications used to treat spasticity are also referred to as skeletal muscle relaxants, we briefly mention them here.

**Baclofen**

Baclofen (Lioresal) is a chemical analogue of GABA (an inhibitory neurotransmitter) that acts primarily by inhibiting synaptic transmission in the spinal cord and, probably, in the supraspinal regions. It is used mainly in the management of spasticity secondary to CNS lesions, such as multiple sclerosis and spinal cord lesions. Baclofen is equivalent to tizanidine, diazepam, and dantrolene in reducing spasticity. It causes less sedation than diazepam or tizanidine, but it may be associated with more weakness. It is not associated with the serious hepatotoxic side effects of dantrolene. Baclofen is not generally used as therapy for acute paravertebral muscle spasm.

**Dantrolene**

Dantrolene (Dantrium) is a peripherally acting skeletal muscle relaxant that produces its effect by interfering with the release of calcium from the sarcoplasmic reticulum. It is used to decrease spasticity associated with upper motor neuron disorders and to treat malignant hyperthermia by reducing the hypermetabolic processes associated with this disorder. It has been associated with serious hepatotoxic side effects of dantrolene. Dantrolene is not indicated for the treatment of other painful musculoskeletal conditions.

**Medications for Musculoskeletal Spasm**

With the many medications available for the treatment of muscle spasm, the question of which ones are the better options invariably arises. Numerous clinical trials have been conducted over the years. Several studies that were performed more than 20 years ago lack the rigid methodology that would generally be required today.

Systematic reviews of many of these investigations have been conducted. Chou and colleagues, assessing 101 randomized trials of non-benzodiazepine agents, found fair evidence that cyclobenzaprine, carisoprodol, orphenadrine, and tizanidine were more effective than placebo in patients with musculoskeletal disorders. Cyclobenzaprine was evaluated in the highest number of clinical trials and was consistently found to be effective. The authors found limited or inconsistent data supporting the effectiveness of metaxalone, methocarbamol, chloroxazone, baclofen, and dantrolene. They concluded that no one agent was superior for musculoskeletal conditions but suggested that practitioners might avoid those with limited evidence of effectiveness.

Van Tulder and associates analyzed a series of studies that included the benzodiazepines. The authors found strong evidence that all of the muscle relaxants were more effective than placebo for patients with acute low back pain for short-term pain relief, but they concluded that they should be used with caution because of the associated adverse events. Consequently, many questions remain unanswered regarding the use of these medications.

**Analgesics**

Paravertebral muscle spasm may initiate a pain–spasm–pain cycle that leads to more pain and, as a result, to increased spasm. Treating pain and inflammation may thus be an important aspect of treating paravertebral spasm.

Several agents may be beneficial, including acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and possibly cyclooxygenase-2 (COX-2) inhibitors—although recent concerns may limit use of this family of drugs. Studies have not been completed to indicate which agents would be more effective.

Narcotics also provide pain relief, but they carry the obvious risks of abuse and addiction. Trials are still needed to evaluate whether analgesics or NSAIDs are more effective than muscle relaxants for the treatment of musculoskeletal disorders accompanied by painful muscle spasm. Systematic reviews of the use of these agents for back pain are available from other sources.

**Nonpharmacological Treatment Options**

Treatment of acute back pain should not be limited to pharmacotherapy alone; it should incorporate other treatment approaches. A number of options are available, but reviews of randomized controlled trials have not yielded definite conclusions as to the efficacy or superiority of other methods. In acute, severe cases, bed rest or at least some restriction of activities for a short period of time is often recommended. However, there is now evidence that bed rest might not be effective for acute low back pain, and prolonged bed rest can lead to progressive inactivity and avoidance of movement.

Physiotherapists may suggest several types of physical therapies, including modalities such as ultrasound, electric muscle stimulation, traction, heat and ice, and manual therapy. Isotonic exercises that strengthen the muscles surrounding the spine are widely used, and “back schools” to educate and train patients are popular internationally; however, these modalities are no more effective than other conservative treatment approaches.

Many believe that manipulative therapy can be helpful for back pain. Steps include alleviating restriction of range of motion in the cervical, thoracic, and lumbar spinal areas.
through osteopathic and chiropractic manipulation. The preponderance of evidence from numerous clinical trials of spinal manipulation indicate that this treatment has proven, but modest, benefits for both acute and chronic back pain.35

Initial studies have found massage to have positive effects, especially on patient function.36 The effectiveness of acupuncture remains unclear.

Large clinical trials are still needed to determine the relative effectiveness and best applications of some of these modalities. These treatment options are detailed in other sources.34,35

### Risks of Medication Abuse

As controlled substances, diazepam and other benzodiazepines pose well-known risks for drug abuse. The potential for abuse of other skeletal muscle relaxants has been a concern of some physicians for decades. In recent years, this concern has grown as more evidence has come to light.

The skeletal muscle relaxant with the highest abuse potential seems to be carisoprodol because it is metabolized to meprobamate, a Schedule IV controlled substance at the federal level. Carisoprodol was introduced to the market in the late 1950s. By 1978, there had been a report of its abuse,14 and by the 1990s, the drug began to be recognized as having abuse potential.

Case reports described the following scenarios:

1. A patient tried to obtain prescriptions for the drug from multiple physicians.20
2. A group of four patients regularly obtained quantities of carisoprodol and then used it in excessive amounts to achieve mind-altering effects.5
3. A group of patients in India attempted to use carisoprodol as a substitute for opiates.16
4. A patient abused the drug after obtaining it through a veterinary mail-order service.17
5. A patient forged prescriptions for carisoprodol.18
6. In a series of three cases, one patient used carisoprodol to calm himself after using cocaine, a woman used carisoprodol as a substitute for illicit drugs, and another patient became dependent on the drug as a sleep aid.19

One patient experienced a withdrawal syndrome, consisting of anxiety, tremors, muscle twitching, insomnia, auditory and visual hallucinations, and bizarre behavior, after taking up to 30 carisoprodol tablets (10,500 mg) per day when he abruptly stopped taking the drug.21 These symptoms closely parallel those described after abrupt cessation of meprobamate when taken in doses larger than those clinically indicated.36

Other literature has described the use of carisoprodol by substance abusers to modify the effects of other drugs, for instance, augmenting the effect of alcohol, extending the effect of alprazolam (Xanax®, Pfizer), and reducing jitteriness after cocaine usage.37,38

Carisoprodol has also been abused by individuals who took it with tramadol (Ultram®, Ortho-McNeil) to produce feelings of euphoria and sedation, using the combination as an easier-to-obtain substitute for controlled substances.39

In a retrospective study of deaths conducted at the Jefferson County (Alabama) Coroner’s Office from January 1, 1986 to October 31, 1997, carisoprodol was found to be present in 24 of the cases. The reviewers concluded that the drug was probably partly responsible for the deaths.40 Despite these facts, many physicians remain unaware of the potential of carisoprodol for abuse and its metabolism to meprobamate.41 However, this situation may be changing, now that carisoprodol has been declared a controlled substance in Oregon, Oklahoma, and Alabama.40

There may be abuse potential with other skeletal muscle relaxants, but reports are scantier. Two studies suggested that methocarbamol may produce short-term effects similar to those of lorazepam (Ativan®, Wyeth).42,43 Baclofen has been described as causing “a buzz” at high doses,44 and orphenadrine may produce “mood enhancement and pleasant disperceptions.”45 Cyclobenzaprine and chlorzoxazone have also been reported to be misused.46

Better data, such as that from large pharmacoepidemiological studies, would probably produce a better sense of the abuse risk of different skeletal muscle relaxants, particularly carisoprodol.

### Conclusion

Although skeletal muscle relaxants are an important modality for the treatment of acute musculoskeletal pain and spasm, a number of concerns about their use remain unresolved. No one single agent has proved superior to another.7 Clinical trials have yet to be performed to determine whether skeletal muscle relaxants or analgesics are more efficacious for treating paravertebral spasm or whether the best approach would be to use these medications simultaneously to combat both components of the pain–spasm–pain cycle.7

Because it is not yet clear as to which agent is best, it has been suggested that preference be given to the non-benzodiazepines with more evidence to support their efficacy (e.g., cyclobenzaprine, carisoprodol, orphenadrine, tizanidine).22 Without a clearly superior agent, side-effect profiles become a significant consideration in the selection of medications to be prescribed in individual cases. Cost difference is not a significant factor. All of these agents are available as generic preparations.

The abuse potential of skeletal muscle relaxants appears to be poorly recognized in the medical community. Clinicians may feel comfortable prescribing these agents because they are not controlled substances at the federal level, but carisoprodol is thought to carry an important risk for abuse because of its metabolism to meprobamate.

A final question to consider is how long these agents should be used. Nearly all clinical trials of skeletal muscle relaxants have involved their short-term use.22 The possible role of these medications in the treatment of chronic back pain is a more complex issue.
References


38. Chop WM. Should carisoprodol be a controlled substance (letter)? Arch Fam Med 1993;2:911.


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Continuing Education Questions for Physicians and Pharmacists

**TOPIC: Skeletal Muscle Relaxants and Associated Medications for Nonspecific Acute Back Pain**

ACPE Program # 079-999-05-021-H01

**CE Evaluation:** Select the one best answer to each of the following questions, and record your response on the examination answer sheet. Complete the additional requested information. Forward the answer sheet, with appropriate payment, to the Department of Health Policy, Thomas Jefferson University Hospital, at the address indicated. A certificate of completion will be mailed within six to eight weeks of receipt of your exam/payment. (A minimum test score of 70% is required.)

**Multiple Choice**

Select the one correct answer.

1. **Back pain affects approximately what proportion of adults at some point in their lives?**
   a. 10%–25%
   b. 40%–60%
   c. 70%–85%
   d. 90%–95%

2. **All of the following are examples of antispasmodics except:**
   a. CNS depressants (chlorzoxazone, metaxalone)
   b. central alpha2-adrenergic agonists (tizanidine)
   c. gamma-aminobutyric acid (GABA) agonists (benzodiazepines)
   d. xanthine oxidase inhibitors (allopurinol)

3. **Although the exact mode of action is unknown, what is the most probable mechanism of chlorzoxazone?**
   a. modulation of nociceptive responses in histaminergic and serotoninergic pathways
   b. inhibition of multisynaptic reflex arcs involved in producing and maintaining skeletal muscle spasm
   c. selective inhibition of facilitatory functions of the reticular formation in the brainstem
   d. interference with the release of calcium from the sarcoplasmic reticulum

4. **Which of the following agents may be associated with dose-related hypotension and should be used with caution in patients taking antihypertensive medications?**
   a. tizanidine
   b. orphenadrine
   c. metaxalone
   d. carisoprodol

5. **Which of the following agents has been associated with aplastic anemia?**
   a. cyclobenzaprine
   b. diazepam
   c. methocarbamol
   d. orphenadrine

6. **When delivered parenterally, this agent has been associated with sloughing of the skin at the injection site:**
   a. carisoprodol
   b. methocarbamol
   c. cyclobenzaprine
   d. tizanidine

7. **All of the following statements are true regarding carisoprodol except:**
   a. The drug is thought to act by direct skeletal muscle relaxation rather than by causing sedation.
   b. The pharmacologically active metabolite is a controlled substance with known abuse potential.
   c. The drug is metabolized in the liver to hydroxycarisoprodol, hydroxymeprobamate, and meprobamate.
   d. It is also available in combination with aspirin and with aspirin and codeine.

8. **Which of the following medications should not be used in patients with cardiac arrhythmias, conduction disturbance, or congestive heart failure or after a myocardial infarction?**
   a. tizanidine
   b. cyclobenzaprine
   c. orphenadrine
   d. metaxalone

9. **Which of the following statements regarding baclofen is false?**
   a. It is a chemical analogue of GABA.
   b. It is used mainly in the management of spasticity secondary to CNS lesions.
   c. It causes more sedation than diazepam or tizanidine.
   d. It is equivalent to tizanidine, diazepam, and dantrolene for reducing spasticity.

10. **All of the following are appropriate management therapies for acute back pain except:**
    a. strict bed rest.
    b. physical therapies.
    c. exercise therapy.
    d. manipulative therapy.
CE Registration and Evaluation Form

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Answer Sheet

Please fill in the box next to the letter corresponding to the correct answer

1. a □ b □ c □ d □ 6. a □ b □ c □ d □
2. a □ b □ c □ d □ 7. a □ b □ c □ d □
3. a □ b □ c □ d □ 8. a □ b □ c □ d □
4. a □ b □ c □ d □ 9. a □ b □ c □ d □
5. a □ b □ c □ d □ 10. a □ b □ c □ d □

Evaluation

Rate the extent to which: 

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<th>Very High</th>
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<th>Low</th>
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<td>1. Objectives of this activity were met</td>
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<td>2. You were satisfied with the overall quality of this activity</td>
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<td>3. Content was relevant to your practice needs</td>
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<td>4. Participation in this activity changed your knowledge/attitudes</td>
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<td>5. You will make a change in your practice as a result of participation in this activity</td>
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<td>6. This activity presented scientifically rigorous, unbiased, and balanced information</td>
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<td>7. Individual presentations were free of commercial bias</td>
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<td>□ This program will not change my behavior because my current practice is consistent with what was taught.</td>
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<td>□ This activity will not change my behavior because I do not agree with the information presented.</td>
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<td>□ I need more information before I can change my practice behavior.</td>
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<td>□ I will immediately implement the information into my practice.</td>
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<td>10. Will you take any of the following actions as a result of participating in this educational activity (check all that apply)</td>
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<td>□ Discuss new information with other professionals</td>
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