

Muscle Relaxants

The muscle relaxants included in this chapter are used in the management of musculoskeletal and neuromuscular disorders. There are 2 main types:

- **centrally acting relaxants**—these generally have a selective action on the CNS and are principally used for relieving painful muscle spasms or spasticity occurring in musculoskeletal and neuromuscular disorders. Their mechanism of action may be due to their CNS-depressant activity. Baclofen and tizanidine are two examples.
- **directly acting relaxants**—dantrolene is a drug that has a direct action on skeletal muscle and is used for the relief of spasticity associated with a variety of conditions.

Also included in this chapter are **botulinum toxins A and B**, which inhibit the release of acetylcholine at the motor nerve terminals.

Some benzodiazepines are also used in the treatment of muscle spasms; further details may be found under Diazepam, p.986.

Other drugs that block transmission at the neuromuscular junction and are used as adjuncts to general anaesthesia are discussed in the chapter on Neuromuscular Blockers, p.1900.

Drugs used to relax *smooth muscle* include the various antispasmodics (p.1692) used for their antimuscarinic or direct smooth-muscle relaxant effects in the management of gastrointestinal disorders, as well as some other drugs such as papaverine (p.2191).

Muscle spasm

Spasm is a painful involuntary contraction of muscle that can cause involuntary movement, interfere with function, and cause distortion. It is a symptom of many muscular and other types of disorders and treatment should primarily be aimed at the underlying cause. Centrally acting muscle relaxants and benzodiazepines are used to treat muscle spasms such as *splinting* that occur in response to local trauma or musculoskeletal and joint disorders. Splinting is a reflex muscular spasm that produces muscular rigidity and acts as a protective mechanism to prevent movement and further damage of the affected part. Short courses of muscle relaxants may be considered in the management of acute low back pain (p.7).

Cramps are muscle spasms of abrupt onset that occur at rest and usually last for a few seconds or minutes. They are often precipitated by dehydration and hyponatraemia produced by vigorous exercise, excessive sweating, diarrhoea, and vomiting, or may be associated with drug therapy or haemodialysis (see Haemodialysis-induced Cramp, p.1671). Pregnant women, the elderly, and those with peripheral vascular disease, appear to be particularly susceptible to night cramps of the feet or legs, the cause of which is not well understood.

The management of muscle cramps has been reviewed.^{1,2} Quinine has traditionally been used for *nocturnal cramps* but there has been concern over its efficacy and potential for adverse effects, especially in the elderly. Meta-analyses^{3,4} have indicated that although quinine was modestly effective in the treatment of nocturnal cramps in ambulatory patients the risk of serious adverse effects should be borne in mind; patients should be closely monitored over a period of at least 4 weeks while the efficacy of quinine was assessed. In the UK, it is recommended that treatment should be stopped every 3 months to see whether it is still needed.⁵ In the USA, the FDA has ruled that quinine products should no longer be used for the management of nocturnal cramps.^{6,7} There is little convincing evidence to support the use of other drugs.^{1,2,6}

A systematic review⁸ concluded that magnesium (as the lactate and citrate) is modestly effective in the treatment of *leg cramps in pregnancy*; calcium salts were ineffective, and although early evidence suggested benefit with sodi-

um chloride, high doses were required with their attendant cardiovascular risks.

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Spasticity

The term spasticity has been loosely applied to various disorders of motor control resulting from CNS disease and marked by effects such as increased muscle tone, exaggerated stretch reflexes, impaired voluntary movement, weakness, loss of dexterity, abnormal posture, and often disturbed gait. In some patients muscle spasm and pain may be more distressing than impaired movement. Other complications may include contractures, pressure sores, and infection. Spasticity is a feature of neurological conditions such as multiple sclerosis, cerebral palsy, head injury, and stroke, particularly if there are spinal lesions.

Spasticity is disabling and difficult to treat when severe, but mild or moderate forms may be effectively managed by conservative treatment. Some patients may even use spasticity to provide a means of posture control and care should be taken that treatment does not lead to increased disability.

Various discussions on the management of spasticity have been published.^{1–10} The mainstay of management is physiotherapy with antispastic drugs, although the evidence for the latter is rather scanty.^{9,11,12} Baclofen, dantrolene, diazepam, and tizanidine are the drugs most often used. These 4 drugs act via different mechanisms, which are not fully understood.

Baclofen is thought to act at the spinal cord level but may also have supraspinal sites of action. It is a powerful neuronal depressant and may exert its inhibitory effects by acting as an agonist at GABA (gamma aminobutyric acid) receptors. *Diazepam* is also thought to act centrally by enhancing the response to GABA. In contrast, *dantrolene* acts directly on muscles, possibly by interfering with the release of calcium from muscular sarcoplasmic reticulum needed for contraction. *Tizanidine* is a centrally acting relaxant and α -adrenergic agonist; it is thought to act at spinal and supraspinal levels by inhibiting the presynaptic activity of excitatory interneurons.⁷ It can produce additive effects with baclofen, allowing a reduction in the dosage of both drugs; use with benzodiazepines is not recommended because of the potential for interactions. All these are usually given by mouth but baclofen may also be given intrathecally in severe chronic spasticity.^{10,13,14} Injection directly into the spinal subarachnoid space allows immediate delivery to the site of action in the spinal cord and the use of considerably lower doses than those given orally. It has been reported¹⁵ that some patients receiving long-term intrathecal baclofen treatment have been able to stop their therapy without symptoms of spasticity re-appearing, and that others have been able to reduce the dosage required.

Other drugs that may produce some benefit or are being studied in spasticity include *other benzodiazepines*, *clonidine*, *gabapentin*, and *mementine*.

Alternative approaches to treatment include nerve blocks using *local anaesthetics*; they should generally only be used when further muscle relaxation would not increase disability. *Chemical neurolysis* using alcohol or phenol is only considered when there is intractable continuous pain. Local injections of *botulinum A toxin* have produced some encouraging results in the management of limb spasticity in post-stroke or spinal injury patients and in children with

cerebral palsy;^{16–18} its temporary effect may be an advantage over chemical neurolysis but the need for regular injections may limit acceptability in children.¹⁶ Systematic reviews^{19,20} have found insufficient evidence to support or refute such use in children with cerebral palsy.

Nondrug treatments have included electrical stimulation techniques such as transcutaneous nerve stimulation and dorsal column stimulation; vibration applied to agonist spastic muscles to improve voluntary movement; cooling to decrease afferent inputs from peripheral receptors; and orthopaedic surgery or neurosurgery.

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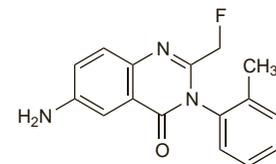
Afloqualone (†INN)

Afloqualone; Afloqualonum; HQ-495. 6-Amino-2-fluoromethyl-3-o-tolylquinazolin-4(3H)-one.

АФЛОКВАЛОН

C₁₆H₁₄FN₃O = 283.3.

CAS — 56287-74-2.



Pharmacopoeias. In *Jpn*.

Profile

Afloqualone is a centrally acting skeletal muscle relaxant that has been given orally for the treatment of muscle spasm associated with musculoskeletal conditions. Photosensitivity reactions have been reported.

References

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