Muscle relaxants may be needed, including benzodiazepines such as diazepam (Valium). For increased muscle tone (spasticity) Baclofen (Lioresal?) is a useful drug.

Baclofen is a GABA-agonist, although its exact mechanism of action remains uncertain. It is known to reduce release of excitatory neurotransmitters.

Baclofen does not affect neuromuscular transmission.

It is primarily a drug used to treat spasticity (i.e. increased muscle tone) and spasm of skeletal muscles seen in neurological conditions but has also proved to be effective in the treatment of trigeminal neuralgia and has since been found useful in all types of neuropathic pain, especially if paroxysmal.

It is now widely used.

A starting dose of 5 mg once a day, increasing to two to three times per day is gradually escalated by increments of 5mg per day as tolerated to 30-90 mg per day, and possibly higher if side effects permit.

It may be helpful to time the increase of dose for the bedtime dose, to minimise the impact of side effects.

The most common adverse effects are sedation and confusion, which are due to the central nervous system depressant action of baclofen.

However, a further problem may be hypotonia (decreased muscle tone) and weakness, which can compound pre-existing weakness due to the neurological condition being treated.

Conversely, Baclofen-induced dyskinesia (abnormal movements) may occur.

Note however that sudden discontinuation of this drug must be avoided because of the high risk of seizures.

In particular, there have been warnings about abrupt discontinuation of intrathecal baclofen because of the risk of high fever, altered mental status, exaggerated rebound spasticity, and muscle rigidity, (in rare cases this has advanced to rhabdomyolysis, multiple organ-system failure and death.)

In order to avoid this, baclofen should always be discontinued by gradual dose reduction over at least 1-2 weeks. If symptoms occur, it may be necessary to prolong the gradual reduction.

Tizanidine (Zanaflex?) is a relatively new, centrally acting, alpha$_2$-adrenergic agonist that has been approved for the treatment of spasticity, such as that occurring in patients with multiple sclerosis or spinal cord injury.

This agent is believed to act like norepinephrine by inhibiting polysynaptic pathways involved in the activation of motor neurons. Chemically related to clonidine so it may cause hypotension (low blood pressure). Side effects are minimal: slight sleepiness and dry mouth.

Other anti-spasmodic drugs include:

Dantrolene (Dantrium?): acts directly on skeletal muscle and therefore has fewer central adverse effects.

Carisoprodol (Soma?)

Cyclobenzaprine (Flexeril?)

Metaxalone (Skelaxin?)

Methocarbamol (Robaxin/Robaxisal?)

Orphenadrine (Norflex/Norgesic/ Norgesic Forte?): a derivative of the antihistamine diphenydramine (Benadryl).

Quinine sulfate (Quinam?): particularly for nocturnal cramps

Diazepam: to relieve muscle spasms, dose is 2-15mg daily in divided doses up to 60mg daily if necessary.

In the context of chronic pain, drugs from this class (benzodiazepines) are quite commonly prescribed for 4 main reasons:

1. to treat anxiety/agitation secondary to chronic pain (Anxiolytic)
2. to treat sleep disturbance due to pain (Hypnotic)
3. to treat muscle spasm or spasticity (Muscle relaxant)
4. as potentiators of opiate drugs.(Adjuvant analgesic)

Clonazepam (Klonopin/Rivotril?):

(a)muscle relaxant: may be used to treat myoclonus (muscle jerks) especially nocturnal myoclonus Clonazepam has also been found to reduce involuntary muscle hyperactivity which may arise due to chronic high dose opiate therapy.([1])

(b)anticonvulsant : 1mg initially at night for 4 weeks, increased over 2-4 weeks to a maintenance dose of 4-8mg daily in divided doses. May decrease in effectiveness after months of continuous therapy.

(c) pain relief: it has been used for trigeminal neuralgia with some success

The most frequently occurring adverse effects of clonazepam are due to central nervous system depression. Drowsiness occurs in approximately 50% of patients and ataxia(drunken gait) in approximately 30%.

Behaviour problems have been noted in approximately 25% of patients and increased salivation in 7%. Often, the sedative side-effects subside after a time.

Alprazolam (Xanax): dosage: 0.25mg to 1.5mg daily.

A study of cancer patients([2]) found that it was helpful in relieving neuropathic pain However, it is used primarily for short-term relief of mild to moderate anxiety and nervous tension, symptoms of PMS, tinnitus and essential tremor.

Ashton ([3]) has expressed the opinion:

"Alprazolam has been widely used, particularly in the US, but is not recommended in the UK, especially for long term use."

Peter Breggin MD wrote the following in his book

"Brain-Disabling Treatments in Psychiatry: Drugs, Electroshock and the Role of the FDA" in 1997 ([4])

"Studies of Xanax show that most patients develop withdrawal symptoms during routine treatment lasting only 8 weeks."

Within 2-4 weeks tolerance can develop to the sedative effect of minor tranquillisers taken at night for sleep.

Short-acting BZDs can produce especially severe withdrawal symptoms (this includes Xanax, Halcion, Ativan, Restoril and Serax).

Note:

Benzodiazepine use carries a high risk of addiction and tolerance which can develop rapidly within a couple of weeks of starting treatment; however, withdrawal symptoms tend to occur only in about 50% of people. There is a wide range of symptoms.

Withdrawal symptoms after stopping a long-acting BZD may not develop for up to 3 weeks after last dose, whereas with short-acting they occur within a few hours (hence the possibility of inter-dose withdrawal symptoms.)

CLONIDINE

Clonidine is an alpha-2 adrenergic agonist that has been used for many years as an antihypertensive drug (treating high blood pressure) It has also been found to have analgesic effects in migraine, post-operative pain, post-herpetic neuralgia and diabetic neuropathy.

Spaulding et al ([5])noted that it can potentiate morphine analgesia. The transdermal preparation has been reported anecdotally([6]) to decrease the pain of CRPS (Reflex sympathetic dystrophy) if applied to the affected extremity.

Clonidine is often administered via the epidural route in conjunction with other analgesia.

In the cancer population, a trial of oral or transdermal clonidine may be considered in the management of persistent neuropathic pain refractory to opioids and other adjuvants.

Clonidine is available in 0.1 mg tablets, but the Catapres? patch (0.1 mg and 0.2mg) is designed to deliver the specified dose daily and must be changed every seven days.

A trial should commence with very low doses e.g. start at 0.1mg at bedtime and increase gradually. Side effects include sedation (the major side effect) bradycardia(slow pulse), hypotension(low blood pressure), dry mouth, constipation, dizziness and depression. Postural hypotension (drop in blood pressure on standing up) is a common adverse effect which may limit the dose that can be tolerated.

NIFEDIPINE

Nifedipine is a calcium channel blocker usually used to relieve angina pain and to reduce mild to moderate hypertension (raised blood pressure).

However, it has also been found to be helpful in neuropathic pain such as that in CRPS (Complex Regional Pain Syndrome, also known as RSD Reflex Sympathetic Dystrophy).

Ohta et al([7]) reported that a case of RSD responded favourably to sublingual nifedipine. A testing dose of 10mg gave relief of pain in 10 minutes, lasting 6 hours. Regular dose of 30-60mg daily was successful in reducing symptoms , which had markedly improved within 4 weeks.

At 3 months, there was complete resolution of pain and although it has recurred from time to time, nifedipine has successfully reduced it again each time.

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[4] Breggin PR Review of Behavioral Effects of Benzodiazepines With an Appendix on Drawing Scientific Conclusions from the FDA's Spontaneous Reporting System (MedWatch). Excerpted from "Brain-Disabling Treatments in Psychiatry: Drugs, Electroshock and the role of the FDA", Pub. Springer, 1997.

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[7] Ohta S, Tanahashi T, Iida H, Asano T, Ueda N, Tani T, Suzuki A, Uematsu H, Yamamoto M *Masui* 1989 May;38(5):679-83[A case report of reflex sympathetic dystrophy treated with

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