Treatments for spasticity and pain in multiple sclerosis

Treatments for spasticity and pain in multiple sclerosis: a systematic review

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Executive summary

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Background

Multiple sclerosis (MS) is one of the commonest neurological conditions of young adults in the Western world, with an estimated 58,000–63,000 people with the disease in England and Wales. Pain and spasticity are two of the commonest symptoms from which people with MS suffer. A recent survey of members by the MS Society found that 54% reported pain as a current symptom and 74% spasticity. The importance of these symptoms is not simply because of their frequency, but also because of the impact they have on daily life. As the disease progresses, so does the spasticity, resulting in muscle spasms, immobility, disturbed sleep and pain. Disability resulting from spasticity can lead to patients requiring extensive nursing care.

Pain can be caused by a variety of factors including spasticity itself, in addition to neuronal damage due to the disease process. Not uncommonly, it may be musculoskeletal in origin, arising as a result of abnormal posture following the disability caused by MS.

Methods

A systematic review was undertaken to identify what treatments are available for the management of pain and spasticity in MS and to evaluate clinical and cost effectiveness through assessment of the best available evidence. The scope of the review was limited to the consideration of drug treatments. It did not include non-drug therapy or surgical treatments. It did not consider cannabinoids, clinical trials of which were ongoing at the time of the review. Reviews of the treatment of spasticity and pain when due to other aetiologies were also sought and their conclusions were examined for consistency with the conclusions in the primary studies identified.

Results

Spasticity

Systematic searches for evidence relating to the treatment of spasticity identified 15 interventions for inclusion:

- baclofen (Lioresal)
- dantrolene (Dantrium)
- tizanidine (Zanaflex)
- diazepam
- gabapentin (Neurontin)
- botulinum toxin (BT) (Botox, Dysport)
- intrathecal baclofen (Lioresal Intrathecal)
- phenol
- threonine
- vigabatrin
- clonidine
- methylprednisone
- cyproheptadine
- magnesium
- ketazolam.

Sixty-seven papers, 41 of which were described as double-blind randomised controlled trials (RCTs), were included in the review of spasticity. Overall, the quality of the studies was poor. A wide variety of outcome measures were used. In cases where the same outcome measures were used, there were inconsistencies in the application of instruments and analysis of results across studies.

There is limited evidence of the effectiveness of four oral drugs for spasticity: baclofen, dantrolene, diazepam and tizanidine. All appear to be approximately equally effective at reducing spasticity when assessed clinically, although in no case is there any good evidence of functional benefit. Tizanidine appears to be no more effective than comparator drugs such as baclofen. Tizanidine has a slightly different side-effects profile in that the main side-effect of tizadine is a dry mouth. Despite claims that it causes less muscle weakness, there was very little evidence that tizanidine performed any better in this respect than other drugs, although it is more expensive. The findings of this review are consistent with reviews of the same treatments for spasticity derived from other aetiologies.

There is no good evidence of effectiveness for gapapentin, threonine, vigabatrin, methylprednisolone, cyprohepladine or magnesium.

There is good evidence that both BT and intrathecal baclofen are effective in reducing

spasticity, and both are associated with functional benefit. However, they are invasive, and substantially more expensive. Their use is most appropriately restricted to people with severe disabling spasticity.

Pain

Systematic searches for evidence relating to the treatment of pain identified 15 interventions:

- carbamazepine
- phenytoin
- gabapentin
- lamotrigine
- tricyclic antidepressants
- steroids
- baclofen
- intrathecal baclofen
- amantadine
- misoprostol
- octreotide
- bupivacaine
- acetazolamide
- lidocaine
- mexiletine.

Thirty-three studies were included in the review of pain. None of the studies were RCTs designed specifically to evaluate the alleviation of pain in patients with MS. The majority of papers were non-systematic reviews, small case series or individual case reports. There was no consistency regarding the use of validated outcome measures. Most papers recorded only that pain had or had not been relieved.

Cost-effectiveness and clinical effectiveness

In the absence of formal research of any quality in this area, it is not possible to draw conclusions regarding the effectiveness or otherwise of the interventions identified.

Evidence relating to the cost-effectiveness of treatments was extremely limited. In the review of spasticity, five health economic evaluations of intrathecal baclofen were identified. No studies relating to the remaining treatments were identified. The five studies suggested that although expensive, the use of intrathecal baclofen may be associated with significant savings in hospitalisation costs in relation to bed-bound patients who are at risk of developing pressure sores, thus enhancing its cost-effectiveness. No studies of cost-effectiveness were identified in the review of pain.

There is evidence, albeit limited, of the clinical effectiveness of baclofen, dantrolene, diazepam, tizanidine, intrathecal baclofen and BT and of the potential cost-effectiveness of intrathecal baclofen in the treatment of spasticity in MS. Owing to the paucity and poor quality of evidence identified in this review, no further conclusions regarding the clinical or cost-effectiveness of the remaining interventions for pain or spasticity can be drawn.

Conclusions

Many of the interventions identified are not licensed for the alleviation of pain or spasticity in MS. In addition, the lack of evidence relating to their effectiveness may militate against them being used consistently across the NHS. Lastly, the licensing and forthcoming availability of trial evidence relating to the use of cannabinoids in the alleviation of symptoms relating to MS may mean that we are in the ironic position of having better evidence of the effectiveness of new treatments than of any of the currently used drugs.

Recommendations for research

The following areas are suggested for further research:

- Double-blind RCTs, with adequate power and follow-up, of interventions used in current practice for the alleviation of pain and spasticity in MS. Outcomes should include functional benefit and impact on quality of life.
- Development and validation of outcomes measures for pain and spasticity.
- Cost–utility studies.

Publication

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