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LONG-TERM MODIFICATION OF SPASTICITY

Anthony B. Ward

From the Rehabilitation Centre, North Staffordshire Hospital, Stoke-on-Trent, Staffordshire, UK

This review of the long-term management of spasticity addresses some of the clinical dilemmas in the management of patients with chronic disability. As it is important for clinicians to have clear objectives in patient treatment, the available treatment strategies are set out. Why is it important to treat spastic patients and what treatment does one use? When should one consider a change in the strategy and why is it necessary to have a clear discharge policy from the service to avoid serious logistic problems? The review reiterates the role of physical treatment in the management and thereafter the maintenance of patients with spasticity. There are now a number of good papers on the use of botulinum toxin in spasticity, but this review sets out their context in clinical management and briefly mentions the use of phenol nerve blockade and intrathecal baclofen in clinical practice. Finally, how does one justify the use of an agent regarded as expensive? It is important to use outcome measures that are valid and sensitive to change, and an example is given of ways of demonstrating benefit.

Key words: spasticity, long-term management, pharmacological treatments, outcomes.

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Correspondence address: Anthony B Ward, Rehabilitation Centre, North Staffordshire Hospital, The Haywood, High Lane, Burslem Stoke-on-Trent, Staffordshire, ST6 7AG, UK. E-mail: anthony@bward2.freeserve.co.uk

INTRODUCTION

Spasticity occurs as part of the response to an upper motor neurone injury. Several things can occur, depending on the size, age and location of the lesion, and it is necessary to understand this before successful treatment can be instituted. Classically, spasticity appears several weeks after an acute insult to the brain or spinal cord, but acute muscle changes are also seen, often in the presence of muscle weakness. Therefore, different patterns are commoner in different situations and the experience of a clinician in acute care may be quite different from one in a rehabilitation unit.

WHY IS IT IMPORTANT TO TREAT SPASTICITY?

There is good evidence that spasticity may increase disability in people following brain and spinal cord injury (1). The evidence for treating, however, is less clear in terms of functional gain, but many studies point to benefit. Most of these do not indicate the relative treatment value, i.e. how much treatment is required to make a critical difference in terms of e.g. cost effectiveness, but better evidence appears to be forthcoming. Firstly not all spasticity requires treatment – stroke patients may utilise spasticity in a limb to allow standing when the underlying weakness would not otherwise allow it. Reducing the tone may render them more disabled and would not be beneficial. So, the prime indication for active pharmacological intervention is harmful spasticity.

Left untreated, spasticity gives rise to many problems, such as pain, spasms, limb contracture and deformity. As a result, loss of mobility and dexterity, hygiene/self-care and care problems and an inability to wear orthoses occur, which can lead to decreased functioning and participation and poor self-esteem and body image.

Having said this, treatment may not be beneficial in the long term. Spasticity is a consequence of an upper motor neurone injury and shortens overactive muscles. Rheological changes occur within them to stiffen the limb, which contributes to biomechanical changes in the tendon and soft tissues (2). This in turn leads to contractures and limb deformity. Therefore, treating spasticity involves managing both the neurogenic and biomechanical aspects of limb stiffness and this is one of the main reasons why spasticity is so difficult to measure and treatment so difficult to evaluate. Patients may present with an array of clinical examples of the upper motor neurone syndrome. Those with residual neuromuscular function have more of a motor control problem, e.g. an inability to release flexor patterns or associated reactions, whereas those with dense hemiplegia may produce a spastic dystonic picture with problems of hygiene, ill-fitting orthoses and painful spasms. Neurological functioning demands a sensory input and those with altered or lost sensation (somatic or special senses) or a cognitive disturbance will be less likely to benefit from treatment. Therefore careful selection of patients is necessary. There is always something that can be done for someone with spasticity, but the overall usefulness or value need to be considered.

Type IV evidence suggests that multi-disciplinary assessment and management is superior to a clinician working on his or her own in this field (3). There is evidence that botulinum toxin (BTX) followed by physical treatment can prolong the clinical effect of the drug (4). Firstly, any concomitant provocative factors have to be removed before pharmacological treatment should be commenced. The latter is adjunctive to good nursing care, physiotherapy or casting/splinting and nurses or therapists will often advise the doctor of the need for pharmacological intervention, when they feel they cannot adequately control the situation physically.

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Table I. *Functional risk factors for development of chronic spasticity*

Dense weakness	
Brain stem lesions	Midbrain, e.g. pons & medulla oblongata are especially prone to develop spasticity.
Sensory loss	Proprioception Light touch Visual impairment
Cognitive loss	Memory Perception Neglect

The development of chronic spasticity in some individuals and not in others is still not clearly understood. It is not entirely dependent on the localisation of the lesion, but brain stem lesions do have a positive correlation (5). It is also noteworthy to identify the risk factors that are likely to contribute to chronic spasticity (Table I).

Of similar interest is why some patients following early severe brain injury develop acute muscle shortening and others do not. Whether or not this is spasticity is debatable, but the patient still ends up with marked limb and truncal contractures, which may require prolonged serial casting and surgery. It is believed that prevention of deformity is possible with a combination of casting and focal anti-spastic treatment, and a study of the prevention of talipes equino-varus deformity is shortly to be completed. In it, patients placed in a lower leg cast for twelve weeks and given an injection of placebo into the posterior calf muscles are compared to those placed in a similar cast and injected with botulinum toxin type A. Both groups are compared to a control group of current standard treatment with physiotherapy alone and an interim analysis of the first twenty-two patients highlighted some interesting facts, which are worth sharing (Table II).

The impression of the interim analysis is that casting is beneficial to patients, but botulinum toxin provides additional benefits and the number of treatment failures is significantly reduced. The study also identified a sub-group of patients, for whom botulinum toxin is possibly justified as a prophylactic in terms of value-added costs. These are those patients, who have had a very severe injury (Glasgow Coma Score (GCS) A6) and who develop four-limb spasticity (by our definition) within two weeks of their injury. 56% and 84% of patients developed sufficient muscle shortening to cause limb deformity within two weeks and twenty days respectively, which signifies that preventative rehabilitation should start in the intensive therapy unit[1]. The study has therefore been educational in:

i) educating intensive care staff in rehabilitation principles and in allowing them to identify long-term patient outcomes for perhaps the first time;
ii) demonstrating to health service managers the true impact of spasticity in this patient group.

[1] Personal communication: Verplancke D, Snape S, Salisbury C, Ward AB. The management of spasticity in adults following severe brain injury.

Table II. *Interim data from prevention study in early severe brain injury (See further in the text.)*

Condition	Features
Early brain injury	18% of those admitted Those with GCS <6 & four-limb spasticity require active treatment Appears in 56% patients in 2 weeks Appears in 84% patients in 20 days
Stroke	16% of all new strokes 1/3 require botulinum toxin
Post neurosurgery	16% of patients

GCS: Glasgow Coma Score.

MANAGEMENT PRINCIPLES

The principle of management, therefore, is to diminish the impact of the neurogenic component of the problem by reducing harmful inputs, in particular nociceptive stimuli, to maintain a stretch on a complex of limb and trunk muscles and through anti-spastic medication (6). At the same time, the biomechanical aspects need to be dealt with. The role of the multi-disciplinary team in the management of spasticity has been well-described and good nursing care, optimal posture and physical therapy underlie the basic principles of treatment. This article will discuss the long-term situation for spasticity management.

The essential treatment for spasticity is physical and this must be provided before, during and after any pharmacological intervention. The individual treatments will not be discussed here, as there are already a number of good reviews of physical management by clinicians and researchers with greater expertise than myself.

A management algorithm is useful to follow (Fig. 1), which demonstrates the relationship between the patient, carer and members of the treating team (7). At some point in assessment and management, the question of pharmacological intervention may

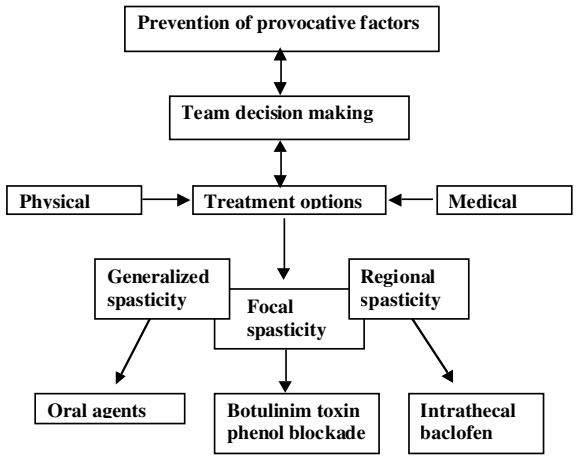

Fig. 1. Spasticity management strategy.

be raised and adherence to a clinical pathway will bring to clinicians a consistent approach. Clinicians will be able to contribute to the whole of the management pathway and not be restricted to their own professional work. In this way, important issues do not get overlooked and the interdisciplinary approach can cover all aspects of care.

PHARMACOLOGICAL TREATMENT

All pharmacological treatments are adjunctive to good physical management. This article discusses some of the available treatments and particularly addresses the combined use of botulinum toxin and phenol. The latter has been available for many years, but has been discredited by its indiscriminate use in the past. However, in safe hands, it is a valuable agent and has seen a revival as an adjunct to botulinum toxin. Although clinicians are using larger doses of botulinum toxin, this combined usage can allow more muscles to be treated while at the same time remaining within the current safe dose of both agents.

Botulinum toxin

Botulinum Toxin is the pharmacological treatment of first choice for focal spasticity and a number of publications have demonstrated its effectiveness in reducing tone and pain and in improving range of movement. Its effect on changing function has also now been shown in a recent publication (8). One of the problems in the management of spasticity is the lack of adequate measures of the impairment (9). Furthermore, the demonstration of functional change in the management of focal spasticity has been blighted by inadequate measures, which has led to difficulties in botulinum toxin in obtaining a licence for use in spasticity (see below). A new and useful measure is now described, which observes pre- and post-treatment changes in four domains in upper limb functioning: pain, dressing, hygiene and limb position. It is based on a four-point score, and for the purposes of Brashear's study, the patient and physician separately chose the principal therapeutic target as the most relevant to their situation. Very significant and significant changes were seen at six and twelve weeks post botulinum toxin, respectively, and this is the first study to have truly demonstrated a functional benefit. Furthermore, physiotherapy was not included in the study methodology in order to make a direct comparison between the active and placebo treatments and there is, therefore, the possibility of greater and more prolonged benefits in normal clinical practice according to previous observation (10) and anecdotal clinical impression. These findings reflect clinical practice and the measure is therefore valuable as a clinical as well as a research tool.

Clinical impressions of benefit should thus not be discarded and clinicians should be aware of the treatment process, when they are defining the goals for treatment. If the team is clear about the expected outcome of treatment, the measurement becomes straightforward. Nonetheless, functional benefits may occur from reducing impairments, e.g. reducing adductor spasticity, while improving the range of thigh abduction may allow better ambulation (walking speed, stride length, etc.), relief of adductor spasms and stiffness and reduce carer burden for hygiene and dressing.

Phenol

6% phenol in aqueous solution acts by local chemodenervation, and multiple injections in the peri-neural area result in this (11). It has an immediate local anaesthetic effect and, when acting, has a selective effect, as do many other local anaesthetics, which block the influx of sodium ions through ionic pores, thereby causing depolarisation. The magnitude of the effect is determined by the ratio of the surface area of the nerve and the concentration of the agent. Consequently gamma fibres, which have a greater relative surface area, are most easily paralysed, whereas alpha motor neurones are less susceptible. The nerve or motor point is located by electrical stimulation and 1–2.5 ml is injected at multiple points, producing decreased motor unit activity in target muscles lasting for about 16–24 weeks. The clinical effect starts after about ten days and denervation can be confirmed neurophysiologically at 17–21 days. Studies to date have also confirmed a reduction in Ashworth scores comparable to those of botulinum toxin. The relevant outcomes are as for botulinum toxin and will be discussed under that heading. The effect is reversible, but with every injection, some permanent denervation occurs, allowing for a progressive reduction in motor unit activity.

Phenol is inexpensive, but its correct placement requires time. Patient preparation is required and the procedure may be painful. Nerve or motor point location with a stimulator is necessary to restrict the dose of phenol, in order to maximise the effect of the drug and to reduce the risk of complications. The main adverse events are injection site pain, tissue necrosis and sensory dysaesthesia. Phenol is toxic and can damage surrounding structures. In the context of an obturator nerve block in the groin, post injection infection and ulceration may be very troublesome and expensive, requiring the patient to be admitted. Sensory dysaesthesia is extremely distressing and occurs when the phenol interferes with sensory nerve fibres. Several weeks of gabapentin or carbamazepine are required, which usually settles things down until the effect of the phenol diminishes. It can therefore be seen, that, although phenol is cheap, the costs of care can rise considerably if all the effects are accounted for and can even end up as very expensive if a complication occurs. Botulinum toxin, on the other hand, is more expensive, but the method of administration and the low complication rate make the drug the main cost pressure.

Phenol has for a long time been given intrathecally to patients with severe spasticity. The fact that it renders the patient incontinent of urine and faeces makes it suitable only for those in terminal phases of multiple sclerosis, who are already disabled by these

impairments. Sensory dysaesthesia can also occur, if it denervates sensory nerve roots, but this is less likely by this route than when injected peri-neurally. It is reasonably effective and is thus a very useful alternative to intrathecal baclofen administration in patients with late stage multiple sclerosis. It is given after a test dose of intrathecal baclofen to ensure that there is sufficient spasticity to reduce, and the patient is turned after the phenol is administered to ensure an even distribution of the drug.

Phenol is effective and 28 patients recently followed-up eighteen months after the injection showed that 89% had achieved the treatment goal (12) and that the effect of 4.5% phenol in aqueous solution is equivalent to that of 50% alcohol (13).

Intrathecal baclofen

The indications for providing an intrathecal baclofen (ITB) system are now well-known and the GABA-analogue acting directly in the spinal canal allows patients intolerant of larger doses of the oral agent to have a highly effective means of anti-spastic treatment delivered. Because of the cost and the small number of eligible patients, it will only be available for a few patients, but its effect has been shown (14). It is primarily used in paraplegics, typically with spinal cord injury, or in connection with multiple sclerosis, but its effectiveness has been shown in patients with tetraplegics as well and in severely brain-injured patients, where the burden of care can be reduced significantly by reducing severe spasticity (15). Hemiplegics have also been helped by ITB and reducing muscle tone by two points on the Ashworth score on the affected side has not resulted in an excessive muscle-weakening effect on the good side (16). The mean dose of ITB is 205 μg/day and the real cost of this technology is the price of the pump and implantation surgery. However, ITB cost needs to be set against its value and the treatment package needs to be evaluated over the eight-year life of the programmable pump. Both Postma et al. (17) and Sampson et al. (18) showed this value in separate studies and, in the former, hospitalisation in the treated group in the first year was 31.5 days compared to 18.7 days in a matched group. This covered the implantation of the pump, but highlighted the considerable costs in these patients without pumps. In subsequent years, reduced hospitalisation in the second year of having a pump in situ was compared to patients without, but patient matching was not fully controlled. Therefore, in terms of overall costs and quality adjusted life years (QALYs), the ITB patients came out quite well.

As with other anti-spastic treatments, we know very little about the long-term effect of ITB. A study of 22 ITB patients versus placebo was carried out to assess the effects on physical and mental health. Half were crossed over at thirteen weeks and measurements were carried out (19) (Table III).

This supports the clinical experience that many patients do improve in many other ways once they have started ITB treatment. They eat better, feel and look better and are in less discomfort from painful spasticity and muscle spasms. More studies are required to develop an evidence-based clinical pathway for ITB therapy, and clinical guidelines will be required along the same lines as those for BTX (2). In addition, well-designed cost-effectiveness studies will determine the real place for this treatment.

Table III. Results of Middels' study (19)

One year effect size	Intrathecal baclofen	Placebo	p value
Sickness Impact Profile (Physical Health)	0.86	0	<0.05
Hopkin Symptom Checklist (Mental Health)	>0.80	0	<0.01
Ashworth score	1.40	0	<0.01
Pain score	0.94	0	<0.01
Health-related Quality of Life	0.20	0	NS

MANAGEMENT OF CHRONIC SPASTICITY

The management of spasticity is thus based on having clear goals. (The algorithm in Fig. 2 is applicable to patients in the long term.) The decision to stop treatment or to move from an active to a maintenance management programme is often difficult and there are no indications in the literature to guide the clinician. Another difficulty is that patients with progressive neurological diseases may have their spasticity governed by the disease rather than by their activities and while they may respond to spasticity treatment, the pattern of their symptoms and signs simply changes. It is therefore important to have both short-term and long-term goals and also that patients are assessed regularly to update those goals. When they do not achieve them, consideration can then be given to alternative means of management, such as surgery.

The most important feature in long-term care is good physical management. The use of oral agents should probably be maintained, where active signs of spasticity persist and focal spasticity treatment (BTX and phenol) should be given where the focal aims are clear. When a patient no longer responds, or does not maintain the benefits of previous treatment for a sufficiently long time to justify either expensive (BTX) or potentially harmful (phenol) treatments, then other means should be employed. For instance, a patient with a clenched fist following a stroke should probably not receive BTX treatment unless there are clear indications of the benefits of further injections as evidenced by progressive improvements beyond the three-month interval post-injection. Other treatments should thus be considered, such as splinting or even surgery to maintain the treatment goals.

OUTCOME MEASUREMENT

Identifying patients for long-term anti-spastic treatment is facilitated by accurate outcome measurement. The identification of clear treatment goals makes measurement of the treatment process necessary. Patients should not be given any treatment until

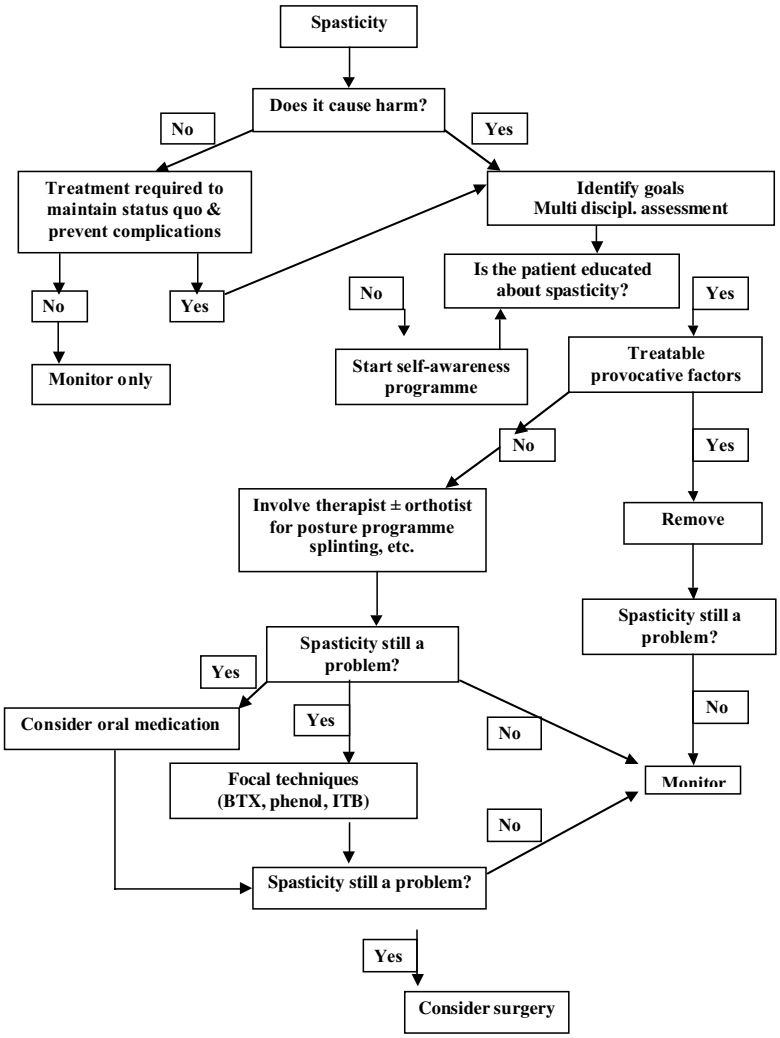

Fig. 2. Management of spasticity (24).

this has been documented. Unfortunately, measuring spasticity is difficult, as there are no direct measures. The inadequacy of the Ashworth score has already been described above (9) and the only really accurate measure, which follows the definition of spasticity, is the Wartenberg Pendulum test, but this is not applicable at the bedside (21). The Tardieu test has been around for many years and has advantages over the Ashworth (22). Having said that, the latter is reliable between observers and in test-retest situations, but this is of little value, if it does not measure what it sets out to measure. The Tardieu scale measures the angle at the point of resistance during a rapid velocity stretch. If there is an overactive stretch reflex, a 'catch' is felt and the assessor records the dynamic and static muscle length and the joint angle at the catch and full at range of movement. It was modified by Held & Pierrot-Deseilligny (23) and inter- and intra-rater reliability studies have been validated by Boyd & Graham and renewed clinicians' interest in the scale (24).

Other formal and goal-specific outcome measures can be employed, such as the FIM, Barthel and nine hole peg test, goal attainment and patient satisfaction scores, but Brashear's study (8) breathes new life into a search for relevant functional tools. Measuring what was expected is important, but how much improvement does it take to convince health payers that the extra cost justifies the treatment outcome? Many agents, such as BTX, are viewed erroneously as expensive, but their value is more important than the basic cost of the drug or intervention. Comparative costs and prevention of other unnecessary treatments need to be included in the equation, and treatments lasting many months or years need to be put in perspective. The impression is that BTX and ITB are very efficacious in this respect. Phenol is too, as long as it does not produce side effects, which can be costly to correct. The overall comparator is against the cost and impact of surgery, as this is invariably the final endpoint of the natural history of spasticity. The problem is that we neither know the long-term outcome of antispastic treatments nor the natural history of spasticity and, until there is a direct measure of spasticity, it will always be difficult to convince health service managers of the value of treatment. One way to look at patient outcomes is through the improvement not only of their lives, but of society as a whole, i.e. 'Great Britain Ltd' in the UK. Let us therefore show an example of some of the benefits and possible ways to measure them (see Case History on next page).

CONCLUSION

Modern anti-spastic treatment is highly effective and advances have been made to show its functional benefit and its cost-effectiveness. There is still insufficient knowledge about the natural history of the impairment, but functional benefits have now been seen with BTX and ITB. In addition there is little indication as to who will require anti-spastic medication and who can be managed physically. Keeping an eye on the future, it has become apparent that having clear goals and an appreciation of the long-term aims of treatment allows the clinician to develop more specific outcome measures. In the immediate future, having specific targets can help clinicians to communicate to the patient prior to any procedure. Both BTX and ITB have a huge role to play in the management of the spastic patient and it is up to the treatment provider to ensure good communication and to explain the treatment aims to avoid excessive expectations.

CASE HISTORY OF MARGARET G.

- 59 years old, multiple sclerosis for 20 years
- Bilateral adductor & hip flexor spasticity
- Cared for by husband as sole carer
- Problems
  - Painful spasms
  - Falls during transfers because of muscle spasms
  - Nocturnal spasms keeping Margaret and her husband awake
  - Urinary incontinence from adductor spasms induced traction on catheter tube
- Aim of treatment
  - Ease day and night care by reducing spasms
  - Make transfers safe and protect husband's back
  - Manage incontinence
  - Reduce pain

150 U Botox® botulinum toxin type A injected into each psoas major muscle and a bilateral obturator nerve block using 6% phenol in aqueous solution. Excellent result.

OUTCOMES FOR MARGARET G.

Patient	*Service*
• Less analgesia	Decreased catheter changes by nurses
• Better posture	
• Seating comfort	Cheaper & simpler wheelchair seating
• Now continent	Returned to day centre – now continent
• Better sleep & QoL for Margaret & husband	Night time carer not required. Husband sole
• Carer	No formal respite care required. No falls No hospital admissions for MG or husband

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