Rehabilitation medicine: 3. Management of adult spasticity

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Abstract

SPASTICITY REFERS TO AN ABNORMAL, velocity-dependent (i.e., how fast the joint is moved through its range) increase in muscle tone resulting from interruption of the neural circuitry regulating the muscles and is a common complication of cerebral palsy, brain injuries, spinal cord injuries, multiple sclerosis and stroke. The muscle stretch reflex is thought to play an important role in spasticity generation. Spasticity can have a significant detrimental effect on daily functions, such as feeding, dressing, hygiene, bladder and bowel control, and mobility; patients' need for support can also influence the cost of care. Thus, managing these patients appropriately or referring them to those with expertise in this area is important. In this article, I review the pathophysiology of spasticity and the evaluation and management of adult patients with the condition. Two hypothetical cases are presented to illustrate the management of spasticity.

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Cases

Mr. A is a 35-year-old man who has a traumatic C7 incomplete spinal cord injury resulting from a motor vehicle crash 3 years ago. (The injury was "incomplete" in that there is some preservation of motor and sensory function below the level of the lesion.) He lives independently in a wheelchair-accessible dwelling. Since the injury he has been taking baclofen (15 mg 4 times daily) to control his spasticity. In the last couple of months he has noticed his spasticity worsening. The muscles of his trunk and lower extremities go into severe extension when he transfers to or from his wheelchair, which puts him at high risk of falling. Self-catheterization has become difficult, because heightened tone in the adductor muscles of his lower extremities causes close approximation of his thighs. Transfer to a commode is also hindered by spasticity.

Mrs. B is a 67-year-old woman who had a stroke 18 months ago that resulted in spastic left hemiplegia. She has no useful function in her left upper extremity but is able to walk with a cane and a brace on her left ankle (ankle-foot orthosis). She is otherwise in good health and lives with her husband in a single-storey home. She enjoys going for walks with her husband. Over the last 6 months she has noticed a gradually increasing tightness in her left leg, and on several occasions she has tripped over the toes of her left foot, which has resulted in minor falls. Her husband is concerned that she may have a serious fall, leading to bone injury.

Pathophysiology of spasticity

The pathophysiologic basis of spasticity is not completely understood. Spasticity has been defined as a motor disorder characterized by a velocity-dependent increase in the tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex as one component of the upper motor syndrome.[1,2]

The stretch reflex arc is the most basic neural circuit contributing to spasticity. It consists of contractile muscle fibres and sensory and motor neurons (Fig. 1). The cell body of the sensory neuron — the afferent limb of the arc — is located in the dorsal root ganglion of the spinal cord. The afferent limb of the sensory neuron originates from a specialized receptor organ (the muscle spindle) in the muscle. The muscle spindle is sensitive to physical deformation; stretching the muscle evokes an impulse in the muscle spindle, which is transmitted via the sensory neuron to the grey matter of the spinal cord. Here the sensory neuron synapses with the motor neuron — the efferent limb of the arc. The cell body of the motor neuron lies within the anterior horn of the spinal cord, and the efferent limb exits via the anterior spinal root to innervate the contractile muscle fibres. The transmitted impulse results in muscle contraction. While agonist muscles contract in response to stretching, antagonist muscles must relax. Their relaxation is brought about via an inhibitory neuron within the spinal cord.

The alpha motor neuron and the muscle comprise the final common pathway in the expression of motor functions, including spasticity. There are numerous excitatory and inhibitory modulatory synaptic influences on this pathway. An imbalance in these influences results in hyperexcitability of the stretch reflex arc, which is thought to be the basis for spasticity. Some of the factors that play a role in suppressing hyperactivity of the final common pathway (Fig. 2) include cerebral inhibitory pathways (from the brain) and spinal mechanisms such as nonreciprocal Ib inhibition (from golgi tendon organ receptors in tendons), presynaptic inhibition of the Ia terminal (at the axoaxonic synapse between 2 axons), reciprocal Ia inhibition (inhibition of antagonistic muscles) and recurrent Renshaw inhibition (inhibitory feedback of the alpha motor neuron cell body by the inhibitory interneuron).[3]

In the medical treatment of spasticity, we use oral medication to try to modify one or more of the centrally mediated inhibitory influences on the final common pathway, or we try to modify the pathway itself by blocking the nerve (phenol injections) or neuromuscular junction (botulinum toxin injections). Gamma aminobutyric acid (GABA) is an important centrally acting neurotransmitter. Replenishing this transmitter with GABA analogues is the basis of action of baclofen, one of the medications commonly used in the treatment of spasticity.

In the presence of a lesion in the upper motor neuron, in addition to the typical "upper motor neuron palsy" (i.e., spastic weakness), one sees a collection of symptoms — both positive (abnormal or exaggerated behaviours) and negative (performance deficits) — that constitute the upper motor syndrome (Table 1). Spasticity is a component of this syndrome (primarily representing the positive symptoms).[1]

Treating spasticity tends to unmask the negative symptoms and, thus, has a significant impact on a patient's level of functioning. Therefore, treatment of spasticity should be introduced gradually and aim at achieving an adequate balance between positive and negative symptoms to optimize function. For example, patients with spastic hemiplegia may be using the increased muscle tone in their weak lower extremities to bear their weight and possibly walk. Removing this increased tone by treating the spasticity might unmask the underlying weakness and prevent this function. Conversely, if spasticity is interfering with ambulation (e.g., by producing plantar flexed foot) then treatment is indicated.

Evaluation of the spastic patient

Spasticity develops gradually after the initial insult to the central nervous system. It usually becomes noticeable in the first few months, but the timing can vary depending on the underlying neurologic insult. Once recovery from the neurologic deficit stabilizes, the spasticity also tends to stabilize. Spasticity is not always detrimental. A weak flaccid limb can interfere with such daily activities as transferring, dressing, grooming and perineal care. Spasticity provides posture and tone to a limb that can assist with weight bearing even if the patient cannot walk. However, excessive tone may interfere with these activities. Thus, it is only when spasticity interferes with function or puts the individual at risk of hurting himself or herself that it needs to be treated.

- Spasticity is exacerbated by noxious stimuli, which increase the afferent input on the stretch reflex (Box 1).

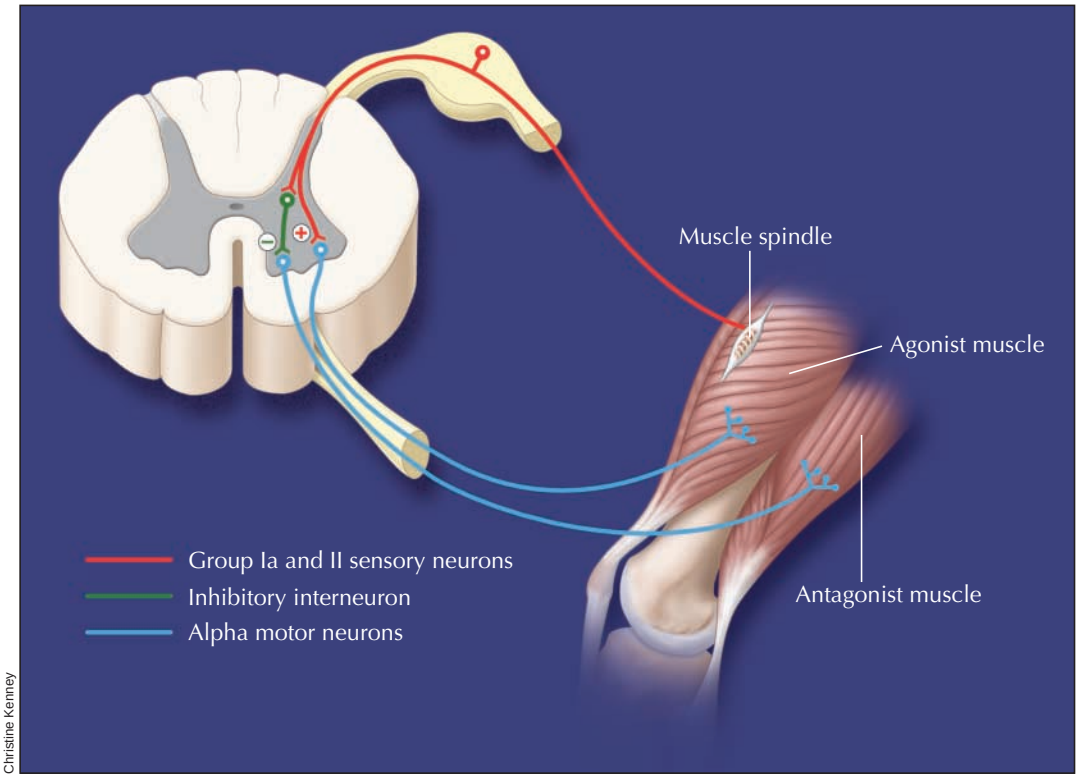


Fig. 1: The stretch reflex arc. When a muscle is stretched, an impulse is generated in the muscle spindle and is transmitted via the sensory neuron to the grey matter of the spinal cord. Here the sensory neuron synapses with the motor neuron, and the transmitted impulse results in muscle contraction. While agonist muscles contract in response to stretching, antagonist muscles must relax. Their relaxation is brought about via an inhibitory neuron within the spinal cord.

Investigate such factors before initiating treatment.

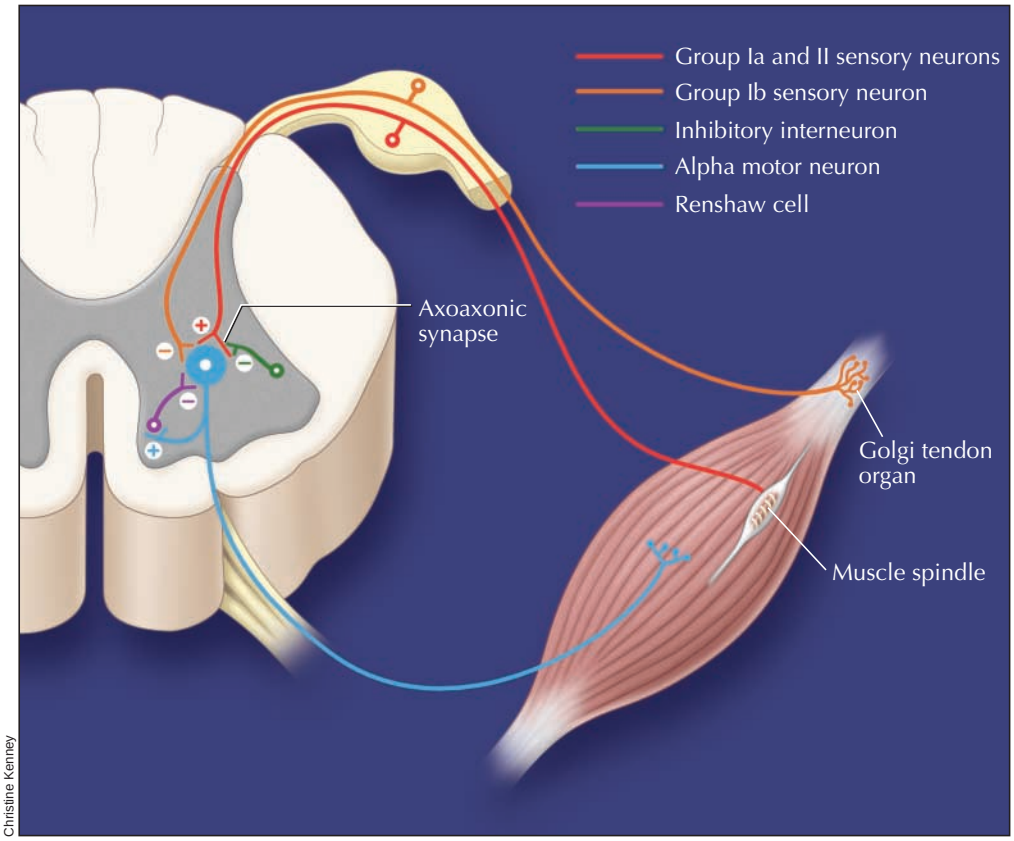
- Assess the severity of the spasticity. A mild increase in tone may not require any treatment and may, in fact, be beneficial to the patient. Severe, long-standing spasticity could result in fixed contractures, which often do not respond to treatment. The most widely accepted assessment tool is the modified Ashworth scale[4] (Table 2).
- Document the range of movement in the various joints involved in the pattern of spasticity. These base measurements will be useful later in monitoring the response to treatment.

Management of spasticity

Clearly identifying the goals of the patient and caregivers is crucial in treatment planning (Fig. 3). Before initiating treatment, consider the following questions proposed by Tizard[5] in cerebral palsy: Does the patient need treatment? What are the aims of treatment? Do the patient and caregivers have the time required for treatment? Will treatment disrupt the life of the patient and caregivers? Identify the functional objectives of treatment (e.g., improving gait, hygiene and other activities of daily living; pain relief; increasing ease of care; decreasing the frequency of spasms).

Physical and occupational therapy

Physical and occupational therapists play an important role in the evaluation, goal setting and management of patients with spasticity. Patients and caregivers are taught to avoid certain postures that promote spasticity. Bohannon[6] showed that standing in a tilt table reduces spasticity after spinal cord injury. (Note: A tilt table is one to which the patient is strapped; it is then tilted upright to allow the patient to stand.) Regular stretching is important to prevent contractures and to maintain the range of movement.



Christine Kenney

Fig. 2: Potential spinal mechanisms of suppression of hyperactivity in the final common pathway (alpha motor neuron and muscle). There are numerous excitatory and inhibitory modulatory synaptic influences on this pathway. An imbalance in these influences results in hyperexcitability of the stretch reflex arc, which is thought to be the basis for spasticity. Factors that play a role in suppressing hyperactivity of the final common pathway at the spinal cord level include nonreciprocal Ib inhibition (from golgi tendon organ receptors in tendons), presynaptic inhibition of the Ia terminal (at the axoaxonic synapse between 2 axons), reciprocal Ia inhibition by the inhibitory interneuron (inhibition of antagonistic muscles [see Fig. 1]) and recurrent Renshaw inhibition (inhibitory feedback of the alpha motor neuron cell body by the inhibitory interneuron).

Therapists should provide spastic patients with a regular, individualized stretching program. Braces may be used to maintain a spastic limb in a reflex-inhibiting posture and prevent contractures; serial casting may also be used for this purpose. Electrical stimulation (cutaneous, nerve, muscle and spine stimulation) and functional electrical stimulation[7] may have a role, although they are less commonly advocated.

Oral medications

Oral medications are important in the treatment of spasticity.[8–13] A number of randomized clinical trials have shown antispasticity medications to be efficacious in the management of spasticity, especially in spinal disorders (e.g., spinal cord injury or lesions and multiple sclerosis). Their efficacy in cerebral disorders (e.g., acquired brain injury and stroke) remains limited. The medications commonly used are baclofen (Lioresal), dantrolene (Dantrium), tizanidine (Zanaflex) and gabapentin (Neurontin). These drugs work centrally except for dantrolene, which acts peripherally at the level of the muscle. The dosing regimens, mechanisms of action and side effects of these medications are shown in Table 3.

Box 1: Factors that can increase spasticity

- Urinary tract infections
- Constipation
- Ingrown toe nails
- Pressure ulcers
- Poor fit in a brace or wheelchair

Baclofen is the medication most frequently prescribed for spasticity in cases of spinal cord injury and multiple sclerosis. Patients taking high doses of baclofen should be warned not to discontinue the medication abruptly because of the risk of withdrawal seizures and hallucinations.

Tizanidine is also a good first-line treatment. However, side effects at the onset of treatment tend to limit its use. It is best to start with a low dose of 2 mg at night and gradually add a 2-mg dose every second day until the patient is receiving 3 doses daily. The dose may then be increased gradually (to a maximum of 36 mg/d) to achieve the desired control of spasticity. This regimen may help avert dizziness, dryness of mouth and sedation.

Dantrium is effective in the management of spasticity, although it is used less frequently because of its rare association with liver toxicity. Liver function tests should be carried out before the start of treatment and every 3–6 months thereafter. If the spasticity fails to respond at the recommended maximum daily dose, if a second agent needs to be added or if side effects are troublesome, referral of the patient to a physiatrist should be considered.

Gabapentin is emerging as a useful alternative in spasticity management. Patients may require higher doses of this drug (2700–3200 mg/d), and its safety at this level over long periods in spasticity is unknown; thus, caution is advised.

Clonidine is used only as an alternative when other medications are ineffective; its use should be limited to very resistant cases. There are no double-blind, placebo-controlled studies to show its efficacy in spasticity.

Fampridine-SR (sustained-release 4-aminopyridine) is a potassium-channel blocker and has recently been shown to be helpful in managing spasticity in patients with spinal cord injuries.[14] Delta-9-tetrahydrocannabinol, the active ingredient in cannabis, has also been shown to be useful in spasticity; however, evidence of its efficacy compared with other medications requires evaluation.[15]

Injections of phenol or botulinum toxin

Focal treatment of spastic muscles has assumed an important role in the treatment of spasticity, especially in people with cerebral spasticity. The goal here is to block the final common pathway. Phenol injections have been used to block large nerves going to specific regions of the body that are spastic. Unfortunately, chronic dysesthesia and pain limit the use of this treatment. Other complications, such

Table 1: Symptoms of upper motor syndrome

Positive symptoms (abnormal or exaggerated behaviours)
Enhanced stretch reflexes
Increased muscle tone
Exaggerated tendon reflexes
Clonus
Released flexor reflexes
Babinski response
Mass synergy patterns (i.e., posturing of limbs and trunk in certain patterns, such as flexion of the upper limb and extension of the lower limb in a stroke patient)
Negative symptoms (performance deficits)
Loss of finger dexterity
Weakness
Loss of selective control of muscles and limb segments

Table 2: Modified Ashworth scale[4]

0	No increase in muscle tone
1	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of range of motion
1+	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the range of motion
2	More marked increase in muscle tone through most of the range of motion, but the affected part is easily moved
3	Considerable increase in muscle tone, passive movement is difficult
4	Affected part is rigid in flexion or extension (abduction or adduction, etc.)

as peripheral edema, skin sloughing and wound infection, have been reported.

More recently, botulinum toxin type A (Botox) injections have been used to block the final common pathway at the neuromuscular junction.[16,17] Botulinum toxin type A is better tolerated than phenol. Highly selective blockade of spastic muscles may be achieved by using electromyography to inject individual muscles. Once injected into a muscle, botulinum toxin is taken up by the presynaptic terminal at the neuromuscular junction and cleaved to form an active compound (in a few days) that interrupts the release of acetylcholine from the presynaptic terminal. This brings about blockade of the neuromuscular junction with resultant weakness (reducing muscle tone). After about 3 months the presynaptic terminal sprouts and re-establishes its communication with the muscle fibre (muscle tone returns). Thus, botulinum toxin type A takes effect about 1 week after injection and lasts about 3 months, after which muscle tone returns to baseline levels. It is a relatively safe medication and has few serious side effects. Muscle pain, bruising and transient fever may occur on the day of the injection but are self-limiting. Drug reactions are extremely rare, especially with the less antigenic newer products. Although botulinum toxin type A has recently been approved for use in focal spasticity in Canada, its high cost limits this use.

Referral to a physiatrist is warranted for phenol blocks and botulinum toxin injections.

Intrathecal baclofen

Side effects of oral medications may prevent their use at the optimum dose. In addition, some oral medications do not easily cross the blood–brain barrier. Intrathecal delivery of such drugs as baclofen[18,19] has successfully controlled spasticity in cases in which oral medications have failed to bring about the expected results. The medication is delivered via a programmable intrathecal pump that is usually implanted in the anterior abdominal wall. All other treatment options should be explored before consideration of an intrathecal pump; therefore, referral to a physiatrist is advised.

Surgical intervention

Surgical treatment[20] of spasticity tends to be reserved for the most refractory cases. Many destructive procedures such as myelotomy and cordotomy or cordectomy have been attempted, with variable results. Many orthopedic procedures, such as lengthening, releasing or transferring a tendon, are helpful in optimizing function and preventing contractures. Osteotomies may be undertaken to correct deformity. Selective dorsal rhizotomy in children with cerebral spasticity has produced encouraging results, although this procedure is not commonly advocated in adults.

The cases revisited

Case 1

Mr. A's spasticity has been relatively well controlled with baclofen for the past 3 years. The dose appears to be adequate (most people with spasticity require 40–80 mg/d, and in some cases a much higher dose). Clearly his history suggests a decline in function that must be addressed. Careful assessment reveals a urinary tract infection: urine culture produced significant growth of *Escherichia coli*. Mr. A is prescribed antibiotics, and eventually his spasticity decreases, which results in a return of his previous function.

If no noxious stimuli had been identified after adequate investigation, then the dose of the baclofen could have

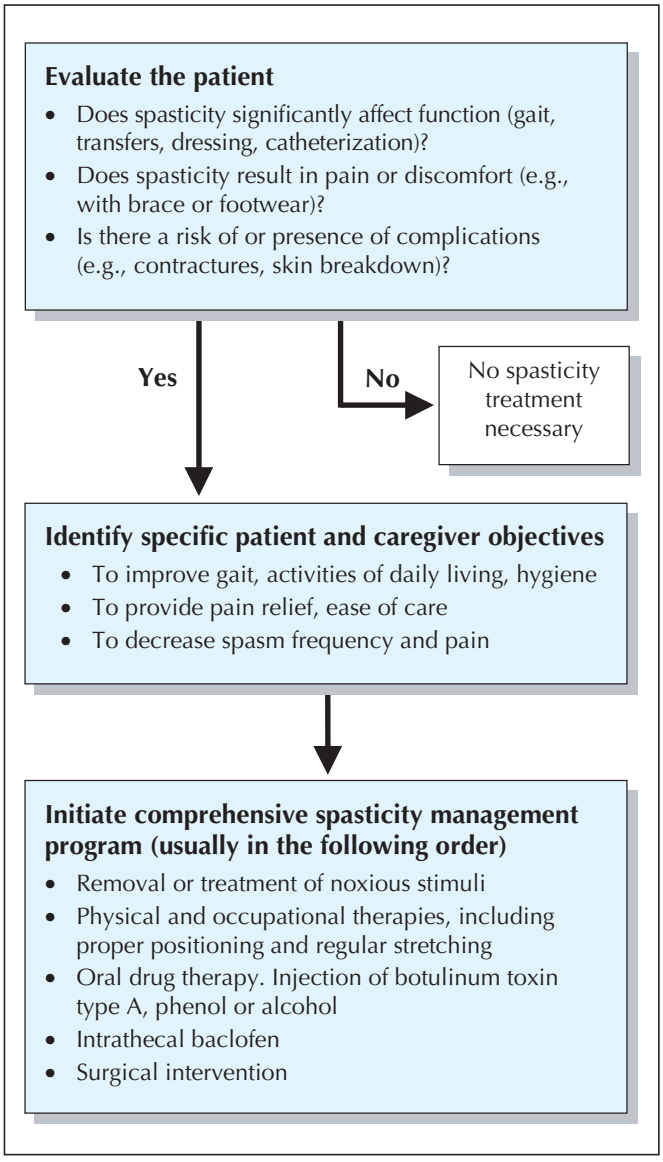


Fig. 3: Treatment planning for patients with spasticity.

Table 3: Dosing regimen, mechanism of action and side effects of drugs commonly used to treat spasticity

Drug	Initial dose	Daily maximum	Mechanism of action	Common side effects
Baclofen	5 mg 3 times daily	80 mg (can be higher if side effects are not a problem). Best divided into 4 doses	Centrally acting GABA analogue. Binds to $GABA_B$ receptor at the presynaptic terminal and thus inhibits the muscle stretch reflex	Daytime sedation, dizziness, weakness, fatigue, nausea; lowers seizure threshold *Withdrawal seizures and hallucinations with abrupt discontinuation*
Dantrolene	25 mg	100 mg 4 times daily	Interferes with the release of calcium from the sarcoplasmic reticulum of the muscle	Generalized muscle weakness, mild sedation, dizziness, nausea, diarrhea *Hepatotoxicity (liver enzymes should be monitored)*
Tizanidine	2–4 mg	36 mg	Imidazole derivative, with agonist action on alpha-2 adrenergic receptors in central nervous system	Dry mouth, sedation, dizziness, mild hypotension, weakness (less common than with baclofen) *Liver enzymes should be monitored*
Clonidine	0.05 mg twice daily	0.1 mg 4 times daily	Acts at multiple levels as an alpha-2 agonist in the central nervous system	Bradycardia, hypotension, depression, dry mouth, sedation, dizziness, constipation *Monitor pulse and blood pressure during treatment*
Gabapentin	100 mg 3 times daily	600–800 mg 4 times daily	GABA analogue. May have an indirect effect on GABA-ergic neurotransmission	Somnolence, dizziness, ataxia and fatigue

Note: GABA = gamma aminobutyric acid.

been increased to 20–30 mg 4 times daily, or a second agent such as dantrium could have been added. When oral medications fail or are limited by side effects, the patient should be referred to a physiatrist for consideration of alternatives, including an intrathecal baclofen pump. Because stretching plays a very important role in spasticity, any change in a patient's stretching routine may account for a decline. Referral to a physical or occupational therapist would be appropriate.

Case 2

Mrs. B is experiencing a gradual increase in spasticity, confined to her left lower extremity. As always, the physician should look diligently for noxious stimuli; however, spasticity could worsen for no obvious reason in the absence of noxious stimuli. The patient's main functional problem is increased plantar flexion, which is causing her toes to drag and resulting in falls. Oral medication therapy is not the first choice, as it tends to be less effective in treating cerebral causes of spasticity. Mrs. B is a good candidate for focal treatment of spasticity with botulinum toxin type A injections into her plantar flexors. If she responds well to the first set of injections, she will require repeat injections every 3–4 months to maintain safe ambulation. Referral to a physiatrist for the injections would be most appropriate. Her nonfunctional upper extremity does not require any specific treatment. Should she have difficulty cleaning her hand or experience pain because of marked spasticity, she may be a candidate for botulinum toxin type A injections in her upper extremity.

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