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Poststroke Spasticity: Pathophysiology and Management An Accurate Evaluation of Spasticity

Emanuel- Andrei Piseru [1,3], Teodora Piseru [3,*] , Bogdan-Emilian Ignat [2,3] , Cristina Grosu [2,3] , Daniel Alexa [2,3] and Raul Andrei Cretu [2]

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1 Faculty of Medical Bioengineering, University of Medicine and Pharmacy "Grigore T. Popa", 700115 Iasi, Romania;
2 Faculty of Medicine, University of Medicine and Pharmacy "Grigore T. Popa", 700115 Iasi, Romania;
3 Neurology Department, Clinical Rehabilitation Hospital, 700661 Iasi, Romania

* Correspondence: Piseru Teodora: teodora.bondar@yahoo.com

Abstract: Stroke is a major contributor to long-term impairment and disability, affecting up to one-third of survivors and almost half of patients showing neurological deficit at six months. Spasticity affects approximately 25% of individuals within two weeks of a stroke and increases to 44% in patients who have had a second stroke. Severe or incapacitating spasticity affects 15% of post-stroke individuals. Poststroke spasticity is also linked to additional signs and symptoms of the upper motor neuron syndrome, such as simultaneous contraction of agonist and antagonist muscles, weakness of the muscles, and a lack of coordination. Spasticity arises due to aberrant neuroplasticity that develops after a stroke and there is currently no specific intervention method designed to address and correct this abnormal plasticity that takes place during the acute phase. Just before implementing any measures to deal with spasticity, it is crucial to evaluate the influence on the quality of life and level of severity. Several grading scales are used to measure spasticity such as the MAS and modified Tardieu scale.There are various therapeutic approaches that may be categorized into three main classes: physical, pharmaceutical, and surgical. Each class has a distinct purpose and is used at the appropriate moment to reduce the level of spasticity and improve the patient's health. Physiotherapy serves as a base of improving the patient's condition and facilitating the development of brain networks. The objective of post stroke spasticity management must include not only the reduction of muscle hypertonia, but also the evaluation of how post stroke influences functionality and overall mental health. Improper treatment or non-compliance may result in increased pain, joint contraction, and further disability. The goal is to assist the patient in achieving the best possible quality of life.

Keywords: Pathophysiology of Post-Stroke Spasticity; Management of Post-Stroke Spasticity; Evaluation of Post-Stroke Spasticity

1. Introduction

In Europe and worldwide, stroke ranks second in terms of mortality and is a major contributor to long-term motor impairment [1]. Up to one-third of stroke survivors remain physically dependent, and almost half of all patients show neurological deficit at six months [2]. Stroke survivors also have a high prevalence of long-term disability and consequences arising from that [3].

Most studies agree that within two weeks following a stroke, spasticity affects 25% of individuals [4]. After a year, the overall prevalence of spasticity rises to 44% in patients who have been hospitalized for a second stroke and to 38% in individuals who have survived a first stroke. Almost 15% of post-stroke individuals have been observed to have severe or incapacitating spasticity [3,5]. Spasticity is a condition that largely impacts the quality of life, and the most frequent side effects of spasticity are weakness of the muscles, pain, tendon retraction, and ankylosis [6].

Spasticity is a common symptom associated with many neurological disorders (Table 1) and is considered an important cause of persistent and acquired disability and cognitive impairment that negatively impact functional recovery for these patients [7]. In this article, we review the pathophysiology of post-stroke spasticity and focus on its latest treatment.

Possible causes
• Cerebral damage due to lack of oxygen • Cerebral palsy • Traumatic brain injuries • Multiple sclerosis • Neurodegenerative diseases • Toxicity (Phenylketonuria) • Spinal cord injuries • Strokes

Table 1. Possible causes that leads to spasticity.

The primary reason for this particular subject is that worldwide, the incidence of strokes is increasing, especially in young patients [8]. Comprehending the pathophysiology is crucial as it aids in determining the appropriate therapeutic strategy. We will examine the available treatment plans and determine the best course of action to assist the patient. A comprehensive and well-coordinated set of treatments, including affordable surgical and pharmaceutical procedures as well as rehabilitation initiatives is necessary for the best care of post-stroke syndrome (PSS). PSS refers to a variety of symptoms and complications that occur after someone has experienced a stroke [9]. In 1980 Lance et al. defined spasticity as a common complication of stroke. According to him, the disability observed during passive movements is "a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neuron syndrome" [10]. Later in 1994, Young comes up with a new definition that doesn't take into consideration the type of movement. Young stated that spasticity is "a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes that results from abnormal intra-spinal processing of primary afferent input" [11]. Upper motor neuron lesions due to stroke is always accompanied by positive and negative signs (Tabel 2), spasticity is part of the positive signs [10].

Negative signs
• Muscle weakness • Loss of coordination • Hypotonia • Fatigability • Loss of selective motor control
Positive signs
• Agonist/antagonist spastic co-contraction (during movement) • Extensor/flexor spasms • Positive Babinski sign • Clonus • Spasticity • Spastic dystonia • Increased tendon reflexes • Increased tone • Released reflexes • Exaggerated tendon reflexes

Table 2. Positive and negative signs observed in upper motor neuron lesion due to stroke

The initial symptom that a patient experiences following a stroke is weakness, and within the first six weeks following a stroke, 25% of individuals experience spasticity, according to a research by Wissel et al. Additionally, they noted that the elbow (79%), wrist (66%), shoulder (58%) and ankle (66%) are the most common sites of spasticity [12,13]. The combination of spasticity and weakness results in contractures, deformities of the joints, and restricted mobility, which make it much harder to perform everyday tasks [14]. Muscle contractures and spasticity are two different conditions, the first one results from structural changes in the muscles, whereas spasticity is primarily a neurological phenomen, involving dysregulation of the signals that control muscle movement. [15].

In individuals with spasticity, we often observe the following appearances in the upper limbs: internal rotation and adduction of the shoulder and forearm pronation along with flexion at the wrist, fingers and elbow (Figure 1). The most common appearance in the lower limbs is adduction and extension of the knee and ankle plantar flexion with an equinovarus foot. Spasticity can be observed in the muscle groups responsible for upper limb flexion and lower limb extension [16,17].

If the treatment is not administered properly or if the patient refuses to comply the quality of life may be negatively impacted by a number of events, particularly increased pain and joint contraction. The limitations appear within two to six weeks after a stroke and disabilities could continue to get worse for three to six months [18].

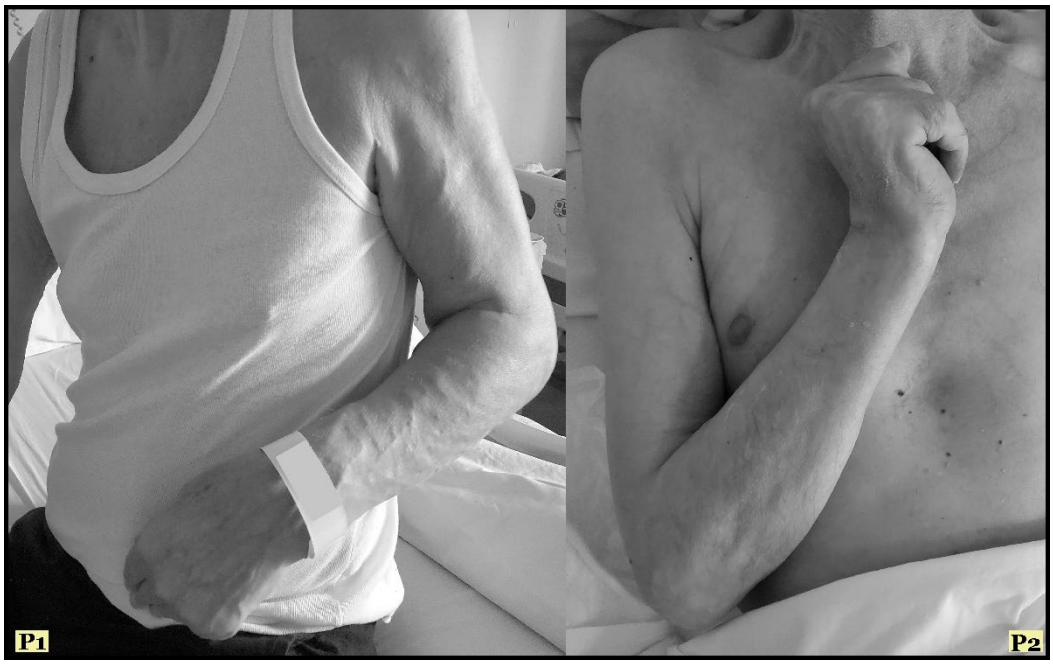

Figure 1. Spasticity observed in the upper limb in the moderate (P1) and severe stages (P2).

1. PHYSIOPATHOLOGY

The modulation of the stretch reflex is influenced by the supraspinal and spinal pathways, as well as factors such as activity, posture, and sensations. The initial increase in tone is primarily attributed to the elevated activity of spinal motor neurons, while subsequent changes are partially influenced by alterations in viscosity and elasticity within the immobilized muscles and joints [19]. Spasticity is a common disorder that arises following a stroke, primarily originating from neural factors. Its manifestation typically occurs within a period of six weeks following the onset of injury [20]. The presence of spasticity following a stroke is suggestive of significant connections to neural plasticity changes that occur following the initial cerebral injury [21,22].

Spasticity may arise as a result of two significant factors. The initial phenomenon is characterized by the presence of neuromuscular spindles exhibiting increased excitability. In the case of a patient with spasticity, engaging in active stretching of the muscles would result in a more severe stimulation of the afferent fibers associated with the spindles.The second case involves the stimulation of α motoneurons through an oligosynaptic pathway, which is caused by abnormal sensory inputs originating from the neuromuscular spindles at the spinal cord level [23]. The muscle contraction observed under isometric conditions following the dynamic phase of the stretch reflex in patients with spasticity is attributed to the activation of II afferent fibers [24,25]. These events exhibit a strong correlation with sensory input and are subject to change based on their origin within the central nervous system (CNS) [26].

Spasticity arises from an imbalance between excitatory and inhibitory fibers. Three primary regions have been suggested to be implicated in the manifestation of spasticity. In relation to active movements, changes in voluntary motor control may occur at the level of brainstem, the cerebral cortex and the spinal cord (Table 3) [27]. The upper cortical level is comprised of two distinct components: motor representation and the impulse to execute the movement [28].

SUPRASPINAL PATHWAYS
➢ The event of brain stem reflexes being released from cortical inhibition ➢ Excessive activation of non-adrenergic pathways arising from the locus coeruleus ➢ The excessive activation of serotoninergic pathways emerging from the raphe nucleus
SPINAL CORD
➢ The loss of recurrent inhibition, which is facilitated by the motor axon collaterals and Renshaw cell ➢ The process of reciprocal inhibition loss, which is facilitated by the afferent signals from antagonistic muscle spindles. ➢ Minimized reverse stretch reflex, stimulated by Golgi tendon organs ➢ The presynaptic inhibition of muscle spindle afferents is decreased
SPINAL MOTOR NEURONE
➢ The condition of denervation supersensitivity ➢ The occurrence of collateral sprouting
MUSCLES AND JOINTS
➢ The process of reducing the length of sarcomeres ➢ The degeneration of elastic tissue ➢ The formation of fibro-fatty deposits within the muscle tissue and tendons

Table 1. Pathophysiology of spasticity [29]

Strokes predominantly manifest at the cortical level, the brain stem being the second most affected region. Injuries at these levels are associated with the development of spasticity, clonus, hyperflexion, spasms, spastic dystonia, and spastic co-contractions [30]. The occurrence of a lesion is accompanied by subsequent impairment of the descending pathways and motor cortex, leading to a cascade of structural and functional reorganization processes in the perilesional, ipsilesional, and contralesional regions [31]. Patients with poor motor function exhibit a higher level of activation in the contralateral hemisphere to the affected site. The discovered alterations in neuronal plasticity are suggestive of the capacity of the central nervous system to reorganize the structure and functionality of neurons, including their synaptic connections, in response to stroke injury, as a compensatory mechanism [32]. The atypical suppression of communication between the two brain regions is associated with a decline in motor abilities among individuals who have experienced a stroke. This phenomenon is considered a form of maladaptive plasticity [33].

Neuroplasticity plays a crucial role in the restoration of motor function following cerebrovascular disease [34]. The consequence of this pathological neuronal reorganization may manifest as increased muscular activity and exaggerated reflex actions to peripheral stimulation [26]. The stretch reflexes are facilitated through the presence of excitatory connections between Ia afferent fibers originating from muscle spindles and α-motoneurons that innervate the associated muscles. Muscle spindles are stimulated by passive stretching, resulting in the discharge of Ia fibers. These fibers transmit inputs to the α-motoneurons through mostly monosynaptic, but also oligosynaptic pathways and subsequently these transmit an efferent impulse to the muscle, leading to its contraction [35].

In patients experiencing spasticity, three factors contribute to increased muscle tone: alterations in sensory input received by spinal motoneurons, alterations in reflex circuits that affect motoneuron excitability and modifications to intrinsic properties of motoneurons. In cases of patient immobilization, sarcomeres undergo substitution by connective tissue and adipose tissue. The pathological process ultimately results in the development of severe contractures and permanent impairment of joint mobility [36]. The excitability of the stretch reflex circuit is mainly controlled by both excitatory and inhibitory descending signals that originate from supraspinal sources [22]. In an individual with normal neurological function, the descending reticulospinal tract and vestibulospinal tract work together to maintain balanced regulation of excitatory and inhibitory signals [37]. Nerve impulse integration conducted by the motor units of the reduced muscle is affected at the spinal cord level. The efficiency of muscle contraction is primarily influenced by the motor unit dysfunction and impaired nerve impulse [10].

Injury to the corticobulbar pathways, which integrate the brainstem and medullary reticular inhibitory centers, is often associated with dysfunction in the motor cortex and/or descending cortical spinal tract due to their relative proximity in the body. The bulbospinal pathways, especially the medial reticulospinal pathways, undergo a gradual increase in excitability due to the absence of inhibitory signals from the upper cerebral areas [38].

Reticulo-spinal hyperexcitability leads to unopposed stimulation of spinal stretch reflex circuits through excitatory descending inputs, leading to greater activity of spinal motor neurons and stretch reflex pathways [39]. Weakness is an immediate consequence of stroke due to injury of the motor cortex and descending cortical spinal tract. On the other hand, spasticity and related motor disorders develop and progress when the ipsilateral cortico-reticulo-spinal pathways in the opposite cortex become excessively excitable as a result of abnormal neuroplasticity [40]. The dorsal reticulospinal tract inhibits the spinal stretch reflex and runs alongside the cortical spinal tract in the dorsolateral funiculus. The medial reticulospinal tract and vestibular spinal tract descend into the ventromedial cord and mainly provide excitatory inputs. It is crucial to acknowledge that the dorsal reticulospinal tract is influenced by the motor cortex through corticoreticular fibers, which are located near the corticospinal tract [41].

In cases of stroke involving cortical and internal capsular lesions, impairment frequently occurs in both the cortical spinal tract and corticoreticular tract due to their very close anatomical proximity. This leads to a loss of cortical facilitatory input to the medullary inhibitory center, resulting in decreased inhibition from the dorsal reticulospinal tract. As a result, the facilitatory medial reticulospinal tract and vestibular spinal tract are not inhibited by the cortex, leading to increased excitability of the stretch reflex. Spasticity can be observed to some extent, regardless of the affected region [38]. Through the investigation of the fundamental processes causing spasticity, healthcare providers can create rehabilitation strategies that address the underlying causes of the condition, improving patient outcomes and performance.

2. CLINICAL EVALUATION

Recognition of spasticity relies on the observation of clinical characteristics within the context of a central nervous system disorder (Figure 2). Differentiating spasticity from other factors that result in elevated muscle tone, such as rigidity, catatonia, contractures, and oppositional and facilitatory paratonia, is extremely important.

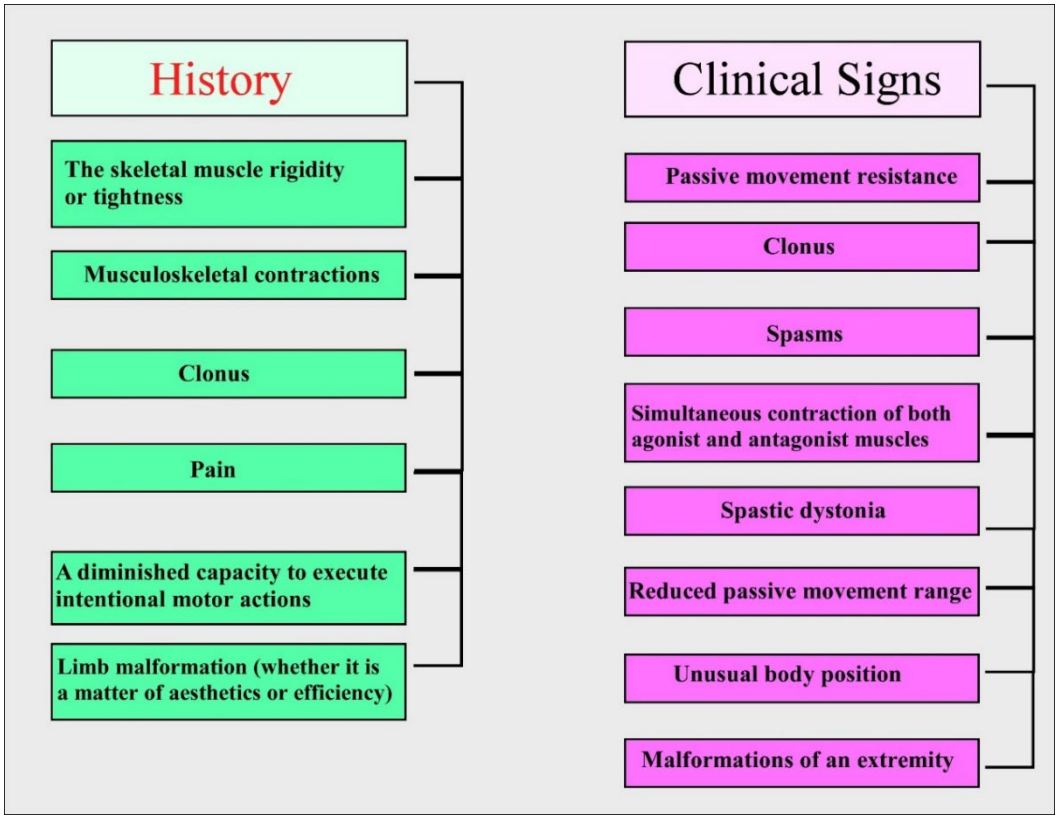

Figure 2. Clinical diagnosis in spasticity, what should we observe?

Spasticity can be evaluated visual, by clinical assesment and through electrofiziological methods as electromyography (EMG). An essential task for the clinician is to identify the trigger, quantify spasticity using appropriate scales, and observe the potential progression in the patient. Acute stroke specialists often do not prioritize the identification or treatment of spasticity. Therefore, physiotherapists frequently handle post-stroke patients who exhibit symptoms of spasticity such as muscle stiffness during the post-acute phase. To establish a definitive diagnosis, it is imperative to thoroughly investigate the patient's medical background and carefully observe their clinical manifestations. To diagnose spasticity, it is important to avoid relying solely on visual assessment. Instead, the patient should undergo a series of passive and active movements in various positions. Evaluating the intensity of spasticity is crucial after its identification (Figure 3), and we will provide a description for some methodes [42].

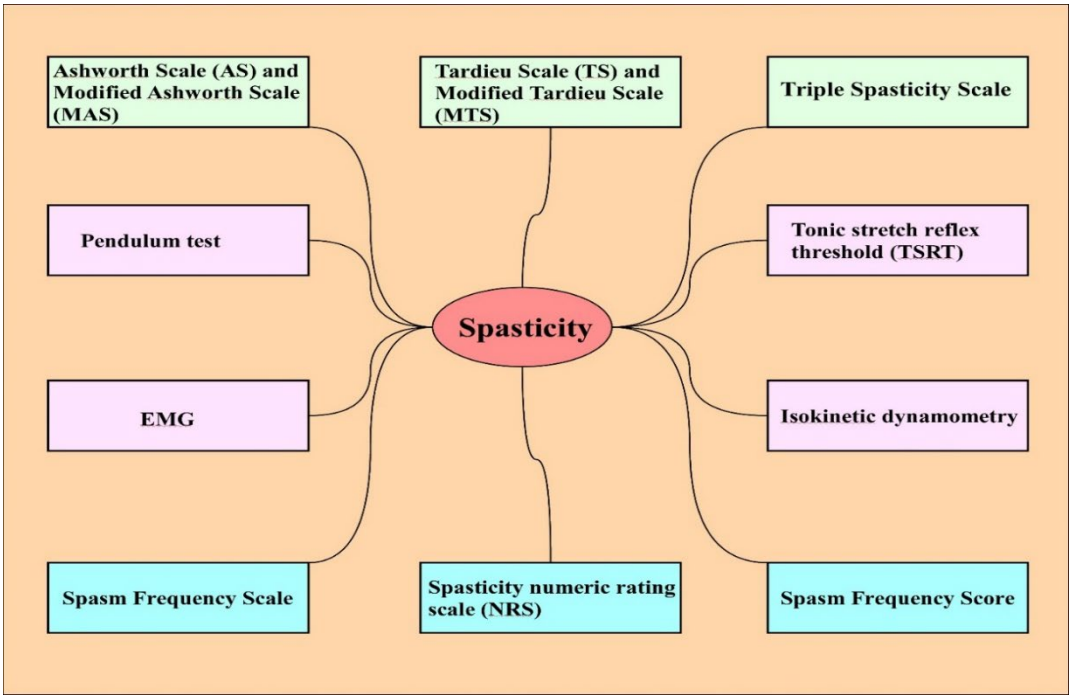

Figure 3. Instruments used for quantifying spasticity

3. SCALES AND SCORES

The Stroke Task force of the American Physical Therapy Association (StrokeEDGE) recommends the use of the Ashworth scale in post-stroke patients during the acute, sub-acute, and chronic phases. The Ashworth Scale (AS) includes five possibilities (Tabel 4), with a score ranging from 0 to 4, indicating the level of resistance experienced during the passive movement of the examined limbs. As the score increases, there is a corresponding increase in resistance [43].

	Ashworth Scale (AS)
0	There is no change in muscle tone.
1	There is a small rise in muscle tension when the limb is moved passively into flexion or extension.
2	There is a noticeable increase in muscle tension, but it doesn't interfere with the ability to move the limb by bending and straightening it.
3	There is a significant increase in muscle tension, making it challenging to move the muscles passively.
4	The limb is rigid and cannot be moved passively in either flexion or extension.

Tabel 2. Ashworth Scale (AS) [43].

Bohannon and Smith extended the Ashworth scale by incorporating an additional 1+ level to improve sensitivity. The modified Ashworth scale (MAS)(Tabel 5) has been widely used in clinical practice and research as a quantitative assessment tool for spasticity since its modification [44].

Resistance to passive movement is a complex measure that can be affected by various factors, spasticity being one of them. The Ashworth Scale (AS) is suitable for evaluating resistance to passive movement at an ordinal level. The modified Ashworth Scale (MAS) should be regarded as a nominal level measurement of resistance to passive movement until the uncertainty regarding the difference between the '1' and '1+' grades is resolved. These scales exhibit greater reliability in the upper limb [45]. Both scales are simple to accomplish, yet it lacks responsiveness to changes.

	Modified Ashworth Scale (MAS)
0	There is no change in muscle tone.
1	There is a small rise in muscle tension, with resistance at the upper limit of movement in flexion and extension.
1+	There is a small increase in muscle tension with a decline of less than 50% in the range of motion.
2	Slight increase in muscle tension observed with an immobility exceeding 50%, while maintaining full range of motion.
3	There is a notable rise in muscle tension, although range of motion remains intact, it can only be achieved with great difficulty and a substantial amount of time.
4	The limb is rigid and cannot be moved passively in either flexion or extension.

Tabel 3. Modified Ashworth Scale (MAS) [46]

Resistance to passive movement should not be confused with spasticity. The modified Ashworth scale was used to evaluate muscle tone by measuring the resistance encountered during the passive range of motion. This assessment does not involve specialized equipment and can be completed rapidly. The Modified Ashworth Scale (MAS) is currently considered the gold standard for clinical assessment of extremity spasticity. It is also most frequently used tool for evaluating the effectiveness of pharmacological and rehabilitation interventions in treating and managing spasticity in patients [46].

The Tardieu Scale and Modified Tardieu Scale (MTS)(Tabel 6) are used to evaluate muscle spasticity in patients with neurological disorders. The Tardieu Scale or MTS is used to measure spasticity by evaluating how a muscle responds to stretching at specific speeds. The examiner analyzed the response of the muscle group to stretching at a specific speed using two parameters: X (indicating the quality of the muscle reaction) and Y (indicating the angle of the muscle reaction).

	Modified Tardieu Scale (MTS)
0	There was no opposition encountered during the entirety of the passive movement.
1	Minor opposition during the passive motion phase; absence of a distinct "catch" at an exact angle.
2	Execute an intentional interception of the object at an exact angle, thereby stopping its passive motion, and subsequently let go of it.
3	There is a fatiguable clonus that occurs when pressure is maintained for maximum 10 seconds at a specific angle.
4	The individual exhibits unfatiguable clonus, which occurs at a specific angle and lasts over 10 seconds when maintaining pressure.
5	Joint fixed
	JOINTS ANGLES (The muscle undergoes minimal elongation (at an angle of zero) for all joints except the hip.)
R1	Angle of muscle reaction (the angle at which the catch occurs after a rapid increase in velocity, either during V2 or V3).
R2	Angle extent of complete range of movement (passive range of motion that occurs after a slow velocity stretch).
	VELOCITIES
V1	Performing the action at the slowest speed possible in order to minimize the activation of the stretch reflex.
V2	Velocity of the limb segment falling freely due to gravity
V3	As quickly as possible (exceeding the rate of the natural fall of the limb segment due to gravitational force)

Tabel 6. Modified Tardieu Scale (MTS) [47]

On the velocity scale, V1 assesses passive range of motion (PROM), only V2 and V3 are utilized for evaluating spasticity. Grading should consistently occur at a fixed time of the day, and the limb being tested should be consistently positioned in the same manner for repeated testing. The upper limb will be evaluated while the individual is seated. The lower limb will be assessed while the individual is lying on their back. Regarding the joints angles, a major difference between R1 and R2 indicates a substantial dynamic component with a higher potential for improvement. A small difference between R1 and R2 indicates a primarily immovable contraction in the muscle with a reduced capacity to adapt. The dynamic tone is indicated by the R1-R2, while MTS exclusively tests V1 and V3 [47].

The triple spasticity scale (Tabel 7) is a composite of various methods used to measure muscle response, specifically focusing on the phenomenon that is dependent on velocity. The measurement assesses spasticity by analyzing tonic and phasic stretch reflexes, as well as evaluating passive resistance and dynamic muscle length. While the Triple Spasticity Assessment covers important aspects of spasticity, it may not capture the full spectrum of symptoms and functional limitations experienced by individuals with spasticity. Other factors such as pain, spasm frequency, and impact on activities of daily living may not be adequately assessed. The assessment primarily relies on qualitative observations rather than quantitative measurements, making it challenging to objectively quantify spasticity severity and track changes over time [48,49].

Triple Spasticity Scale		
	Grade	Summary
The resistance between a slow stretch and a fast stretch is higher (r1–r2).	0	There is no increased level of resistance.
	1	Slight change in resistance
	2	Moderate change in resistance
	3	Strong increased resistance
	4	Excessive and significant rise in resistance
Clonus	0	No clonus
	1	The duration of clonus is less than 10 seconds.
	2	Clonus duration exceeds 10 seconds.
Dynamic muscle length (R1–R2)	0	The angle variation between R1 and R2 is zero.
	1	The angle difference between R1 and R2 is less than one-fourth of the full range of motion.
	2	The angle difference between R1 and R2 is greater or equal to one-fourth and less than one-half of the total range of motion.
	3	The angle difference between R1 and R2 is greater or equal to one-half and less than three-fourths of the full range of motion.
	4	The angle difference between R1 and R2 is equal to or greater than three-fourths of the full range of motion.

Tabel 7. Triple Spasticity Scale: Slow stretch (less than 5°/s), fast stretch (as fast as possible). r1(r2)=0, no resistance; r1(r2)=1, mild resistance; r1(r2)=2, moderate resistance; r1(r2)=3, severe resistance; r1(r2)=4, extremely severe resistance [48]

The Penn Spasm Frequency Scale (PSFS) (Tabel 8) is a self-report assessment tool consisting of two components. It is often used to quantify the frequency of reported muscle spasms, serving as a measure of spasticity. The purpose of developing the PSFS was to improve the evaluation of spasticity by incorporating additional factors and gaining a more thorough understanding of an individual's spasticity status. This is because self-report measures of spasticity, in general, only show a moderate correlation with clinical examination [50]. The Spasm Frequency Scale utilizes the patient ability to quantify the frequency of their spasms within an established interval, usually lasting for 1 hour. The scoring system ranges from 0 to 4, with 0 indicating the absence of spasms within an hour, 1 indicating mild spasms caused by stimulation, 2 indicating complete spasms occurring less than once per hour, 3 indicating spasms occurring more than once per hour, and 4 indicating more than 10 spontaneous spasms per hour [49].

	Penn Spasm Frequency Scale (PSFS)	Spasm Frequency Score
0	No spasms.	No spasms.
1	There are no spontaneous spasms, but when there is intense sensory and motor stimulation, spasms occur.	Occurrence of one or a few spasms every day.
2	Intermittent involuntary muscle contractions and easily triggered spasms.	An average of 1 to 5 spasms occur daily.
3	Less than 10 occurrences of spontaneous spasms per hour.	5 to 10 episodes of muscular contractions per day.
4	There are more than10 occurrences of spontaneous spasms per hour.	Experiencing ten or more spasms per day or enduring continuous muscle contractions.

Tab. 8 Penn Spasm Frequency Scale (PSFS):Spasms are measured by the number of spontaneous flexor and exten-sor muscle spasms over a 1-hour period [50] [51].

Other scales that quantify spasticity are:

- The Spasm Frequency Score is a numerical scale ranging from 1 to 4 that measures the frequency of self-reported spasms experienced per day.The SFS is a modified version of Penn SFS (PSFS) that evaluates the self-reported frequency of spasms within the past hour [51].
- The Numeric Rating Scale for Spasticity (NRS-S) is a modified version of the Visual Analog Scale and the Numeric Rating Scale for Pain. The NRS was designed to gather data from the patient's viewpoint and encourages the patient to assess the intensity of their symptom on a scale ranging from 0 to 10. On a pain scale, 0 represents the absence of pain while 10 represents the most severe pain imaginable. On a scale of 0 to 10, 0 indicates the absence of spasticity, while 10 indicates the most severe level of spasticity. The NRS-S demonstrates significantly higher reliability across tests compared to the Ashworth Scale [49].

The Ashworth Scale is one of the most widely used clinical assessment tools for measuring spasticity, particularly in poststroke patients, due to several key reasons. First and foremost, its simplicity and ease of use make it highly practical for busy clinical settings. The Ashworth Scale provides a quick and straightforward method for healthcare professionals to evaluate muscle tone by assessing resistance to passive movement. This simplicity facilitates regular monitoring of spasticity levels during the course of treatment and allows for easy communication among healthcare team members. Additionally, the Ashworth Scale has demonstrated good reliability and validity in clinical research and practice, lending credibility to its widespread adoption. The Ashworth Scale's combination of simplicity, reliability, validity, and clinical relevance contributes to its prominence as the preferred scale for assessing spasticity in poststroke patients.

4. INSTRUMENTAL ASSESMENT

Several instrumental measurements are being used for classifying spasticity. One example of those is isokinetic dynamometry. Isokinetic contraction refers to the tension of muscles that occurs when there is a constant motion of limb movements around a joint. A specialized dynamometer is used to maintain a constant velocity of movements. The dynamometer's resistance is equivalent to the muscular forces exerted during the entire range of motion. This technique enables the calculation of muscular forces during dynamic situations and ensures the muscles are subjected to an ideal level of stress. However, when moving in the vertical plane, the dynamometer measures the torque that is the combined effect of the muscular and gravitational forces. The major problem relies upon the angular position and the torque potential of the muscle group being tested [52].

The instrumented pendulum test is a biomechanical assessment method for spasticity that is both objective and repeatable. The pendulum test was developed to provide an objective evaluation of knee spasticity by observing the leg's free oscillation after it is initially raised to a horizontal position and then released [53].

Additional details can be obtained by integrating measurements of muscle torque or stiffness with an analysis of neuromuscular (EMG) responses. The electromyographic (EMG) is used as a response to stretch, tendon reflex (T reflex), and electrical stimulation of the peripheral nerve (Hoffmann reflex or H reflex) and F-wave. The T-reflex measures the stretch reflex by observing muscle reactions to tendon percussion. The magnitude of the response is contingent upon the amplification of the primary neuromuscular spindle nerve endings [54]. The H-reflex is a method of assessing the excitability of alpha motor neurons by measuring the threshold spinal reflex response in muscles following electrical stimulation of the peripheral nerve [49]. Individuals experiencing spasticity exhibit heightened excitability of alpha motor neurons, resulting in amplified amplitude of both the H-reflex and the M-response. Consequently, these individuals can have their H-reflex, M-response, and H/M ratio measured. Quantitative information regarding spasticity can be obtained by recording the H-reflex, F response, and H/M or F/M ratios. The neurophysiological characterization of the increased activity of the stretch reflex in patients with spasticity is marked by an elevation in the 'H max/M max' ratio. This may be caused by an excessive enhancement of the H-reflex during voluntary muscle contraction and/or the absence of inhibition during muscle relaxation [55].

The surface electromyography (sEMG) technique is valuable for evaluating spasticity in the upper extremities of individuals who suffered a stroke. Surface electromyography (EMG) can be utilized to estimate stretch reflex responses as well as to identify the amplitude as well as duration of stretch-induced reflex activity. The presence of certain factors such as subcutaneous fat distribution, orientation of muscle fibers, electrode placement, and skin resistance can create noticeable limits among individuals [56]. The undamaged nervous system controls locomotion by determining the specific point within the biomechanical range of a joint (muscle length/joint angle) at which muscle contractions, the stretch reflex, and other proprioceptive reflexes initiate.

The Tonic Stretch Reflex Threshold (TSRT) is the position that represents the "spatial threshold". Following a stroke, the capacity to control task-specific TSRTs is compromised. A manifestation of this dysfunction in individuals with spastic hemiparesis is the incapacity to extend the upper angular limit of the TSRT beyond the biomechanical range in order to induce muscle relaxation [57]. As a result, the abnormal activation of motor neurons starts after the TSRT point. Patients with spasticity experience greater resistance, or spasticity, when attempting to move the limb beyond the TSRT angle, whether through passive or active methods. In the medical field, the measurement of Tonic Stretch Reflex Threshold (TSRT) has been incorporated into a portable device known as the Montreal Spasticity Measure (MSM) [56].

5. NONPHARMACOLOGICAL TREATMENT APPROACH

Currently, the choices for managing spasticity include physical therapies like prolonged stretching, proper positioning, exercises, and pharmaceutical interventions involving oral spasticity drugs, targeted treatments and in some cases, surgical interventions.

Neuromotor rehabilitation begins in the early stages following a stroke to facilitate the formation of new connections towards normal functioning. Furthermore, alongside the neural remodeling intervention, there is a focus on improving muscle strength and preventing spasticity.The optimal approach for addressing spasticity is typically implemented during the chronic phases, with the primary objective being to enhance the individual's quality of life and achieve certain objectives (Tabel 9) [58].

Increase the degree of movement and active function
Prevent muscle stiffness/Reduction of muscle hypertonia
Decrease discomfort
Raise the level of hygiene
Improve awareness in patients with consciousness disorders
Improved walking pattern and speed
Improve posture
Reduce physical caregiver burden and nursing care
Prevention of medical complications
Increased independence in performance

Tabel 9. Treatment objectives [42]

The patient may gain advantages from shockwaves, thermotherapy, neuromuscular electrical stimulation, muscle strengthening, robotic orthoses, and specialized aerobic and fitness training (Tabel 10).

- Neuromuscular electrical stimulation
- Orthotics
- Stretching
- Body weight–supported treadmill training
- Robot-assisted
- Neurofacilitatory techniques
- Functional electrical stimulation
- Resistance training programs
- Constraint-induced movement therapy
- Neural prosthesis
- Aquatic therapy
- Electroacupuncture
- Physical modalities (vibration, thermotherapy, shockwave therapy, magnetic stimulation, heat and cold therapy)

Tabel 10. Rehabilitation Techniques

Prior to initiating spasticity prevention or correction, it is imperative to eliminate all stimuli that have the potential to induce spasticity (Tabel 11). The therapist's involvement is crucial in performing the stretching exercises to preserve muscle length and instruct the patient on a set of exercises to continue independently at home once they regain partial motor control.

Position and therapy
• Inadequate seating • Inappropriate orthotics
Traumatic
• Post-traumatic syringomyelia
Skin issues
• Pressure ulcers • Ingrown toenails • Skin infections • Injuries
Visceral issues
• Constipation • Urinary tract infection • Urinary tract calculi • Deep vein thrombosis

Tabel 11. Factors contributing to worsening spasticity

Physical therapy and physiotherapy are essential components in the management of patients suffering from post-stroke spasticity [59]. Orthoses are devices that can be incorporated into the patient's routine of activity to provide additional support in maintaining proper leg alignment. An orthosis offers a significant benefit in terms of its long-lasting efficacy, as it can be applied and maintained for extended periods of time without the need for a physiotherapist to be present [60]. Neuromuscular electrical stimulation provides immediate advantages by delivering electrical impulses that focus on agonist muscle groups, thereby decreasing spasticity in muscles with opposing actions. According to certain studies, neuromuscular stimulation following the administration of botulinum toxin may lead to the diffusion of the substances, resulting in better results [61]. The purpose of the passive movements carried out by therapists is to reduce motor excitability while improving the viscoelastic properties of the muscles and tendons, improve muscle length, increase joint range of motion and to reduce contracture, pain and spasticity [62]. This allows for a comprehensive mobilization which additionally trains the surrounding tissues. The observed outcomes are reliant upon the active participation of both the therapist and the patient. The exercises do not worsen the patient's condition, specifically in relation to spasticity [63]. An basic exercise involves maintaining a standing position for thirty minutes. This exercise not only reduces spasticity but also provides additional benefits such as enhancing bone mineral density and improving pulmonary, intestinal and urinary tract function. It is crucial to maintain the standing position under favorable conditions, failing to do so can exacerbate spasticity, despite the numerous advantages associated with maintaining this position [64].

Transcutaneous Electrical Nerve Stimulation is a physical therapy technique that involves the application of electrical stimulation to the affected area [65]. Has been demonstrated to decrease spasticity in antagonist muscles. The effect appears to be associated with the synthesis of β-endorphins, which could potentially reduce the excitability of motor neurons. Transcutaneous Electrical Nerve Stimulation may enhance cortical synaptic reorganization and motor output by augmenting sensory input through the activation of Aβ-fibers with larger diameters [66].

Supplementary interventions such as hydrotherapy, cryotherapy, thermotherapy, vibratory stimuli, neurodevelopmental inhibitory techniques, and robotics can be used to induce muscle relaxation and decrease the severity of spasticity [67]. Shockwave and transcranial direct current stimulation, have demonstrated encouraging efficacy in decreasing spasticity [68,69].

Since recent developments in robotics, there has been a growing interest in utilizing robotic orthoses for support. A study conducted by Okuno T. et all. demonstrates the additional benefits and advantages associated with their use. Approximately 85% of

stroke survivors experience immobility in their upper extremities, with 25% of them eventually losing any function in the arm within 5 years of the stroke's start. Okuno conducted an experiment involving the integration of the Robot Hybrid-Assisted Limb robot (HAL) and Botulinum Toxin Injections (BoNTs) in individuals who have had a stroke. The study demonstrated that the use of HAL had positive benefits on the active range of motion in individuals who had received previous BoNT injections. If the joint remained rigid due to severe spasticity, it would not have been feasible to utilize HAL due to its mechanical constraints on safety. The long-term effects were also observed at the end of the first year. However, it remains uncertain if the combination therapy was superior to BoNT injections combined with standard rehabilitation alone [70]. A fundamental limitation of the study is its small sample size of 15 subjects, which undermines the ability to provide statistically meaningful findings.

Xiang Qian Shi et al. launched a study to examine the effectiveness of a soft robotic hand that can effectively bend and straighten the fingers in individuals with chronic stroke and various levels of rigidity in their muscles. The study demonstrated the clinical impact of using a soft robotic hand to enhance the functional ability of the weakened upper limb in individuals who have experienced a long-term stroke. In his research, sixteen participants were enlisted for a 20-semester course of rehabilitation. The study showed substantial improvement in voluntary motor function and muscular coordination in the impaired upper limb. Also, they discovered a moderate improvement in voluntary motor control around the joints of individuals' weaker upper limbs, increase in muscle coordination for accurate manipulation of fingers in tasks such as grasping, gripping, and pinching items, as well as improved control and agility of the weaker upper limb [71].

Wei Rong conducted a study in which he associated an electromyography-driven robot system with neuromuscular electrical stimulation (NMES) to examine its efficacy in post-stroke rehabilitation. The results of the study demonstrated that the utilization of both NMES and a robot can enhance the accuracy of finger movements, promote the contraction of finger muscles, and reduce excessive muscular activity in the elbow joints. The level of muscle co-contraction in the finger and elbow joints, as indicated by the Modified Ashworth Scale decreased. The 20-session training resulted in improved upper limb function. The system evaluations revealed that the robot component mostly improved motion precision, while the NMES component primarily boosted voluntary effort for finger movement and reduced excessive muscular activity in the elbow joint [72].

While the data acquired on the usage of biomechanical orthoses was statistically significant, the limited sample size limits the precision of the results. Therefore, additional investigations are necessary to gain more conclusive findings.

6. PHARMACOLOGIC TREATMENT

Pharmacologically, there exists a limited selection of drugs that can aid in reducing spasticity. The healthcare provider must assess the patient's state and determine the goal of treatment based on the possible adverse effects before starting an appropriate therapeutic plan. Low patient compliance and unfavorable outcomes result from using the wrong dosages (Figure 4).

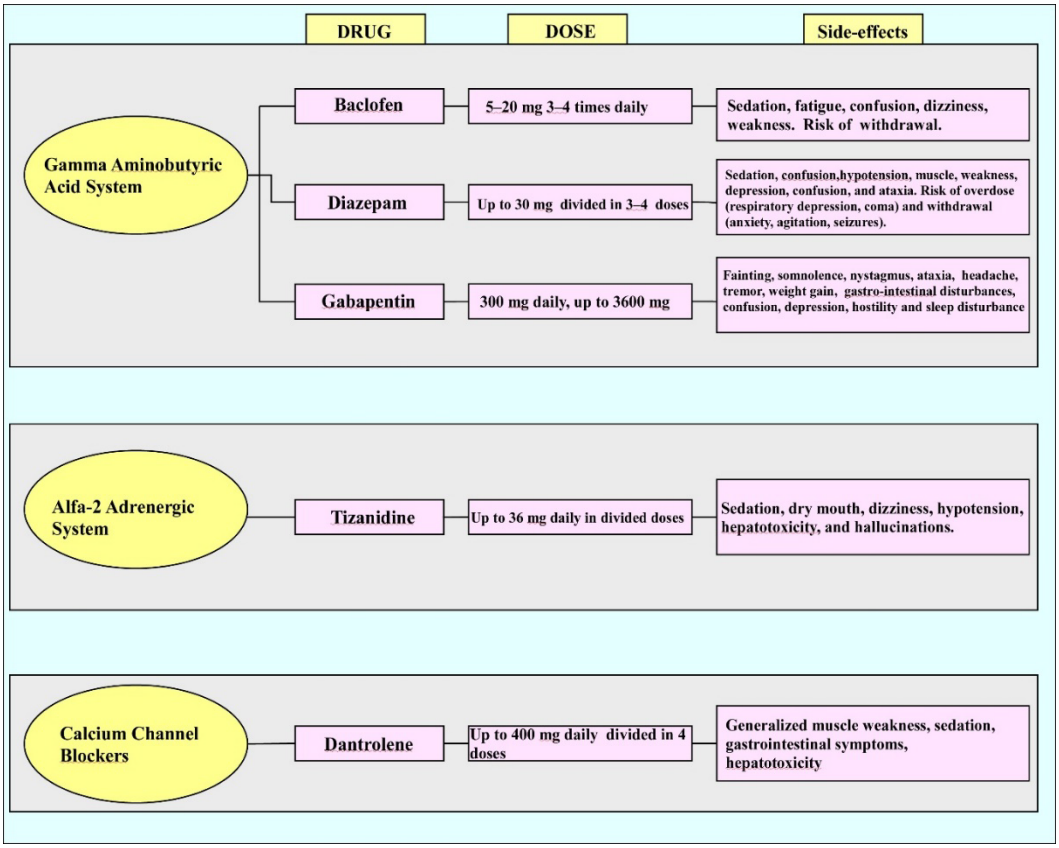

Figure 4. Pharmacologic treatments for spasticity.

When it comes to administering drugs, the best strategy is to start therapy with modest doses and gradually raise it until the desired outcome is achieved. When a drug is given, it is important to determine the kind of spasticity the patient has as well as any potential side effects. Ideally, the substances is given until the maximum acceptable dose is reached and for a sufficient amount of time to provide the intended result. A rapid cessation of substances may result in a rebound effect that exacerbates spasticity. One of the most widely used oral treatments for spasticity is the gamma-aminobutyric acid (GABA) agonist Baclofen [73]. Lowering calcium influx and inhibiting the release of excitatory neurotransmitters such as aspartate and glutamate are two effects of baclofen. After passing across the blood-brain barrier, baclofen binds to GABAb receptors both presynaptically and postsynaptically in the spinal cord. Stretch reflexes that are monosynaptic are more effectively suppressed than those that are polysynaptic [74]. When used by someone who has seizures, baclofen should be used cautiously as it lowers the threshold for seizures. Rebound spasticity may occur 48 hours after stopping baclofen [29].

Benzodiazepines (Diazepam) increase the affinity of GABA-A receptors in order to exert their effects. Pre-synaptic inhibition rises as a result, and the spinal reflex route is subsequently reduced [74]. These drugs cause muscle weakening and sleepiness even when they decrease muscle hypercontraction. Its use is restricted throughout the day due to drowsiness and behavioral adverse effects [75].

Although they are not commonly thought of as first-line treatments for spasticity, antiepileptic drugs like pregabalin and gabapentin can be utilized as adjuvant therapies, especially in cases when central neuropathic pain is present [42]. The anti-convulsant gabapentin shares structural similarities with GABA. At large doses (2400–3600 mg per day), this substances has been demonstrated to be beneficial in reducing spasticity, despite the fact that it is often used to treat neuropathic pain [74].

Tizanidine is a drug that acts as an agonist for α-2 receptors. It works by increasing noradrenergic activity in the spinal cord and brain, as well as enhancing the pre-synaptic

inhibition of motor neurons [76]. It suppresses the activity of stimulating spinal interneurons and pathways originating from the locus coeruleus. Due to the potential for liver damage, it is crucial to regularly assess liver enzymes throughout the initial four months of treatment [77].

Dantrolene inhibits the release of calcium from the sarcoplasmic reticulum and disrupts the process of contraction-excitation coupling in muscle fibers [78]. Unlike other substances used to treat spasticity, this medicine has a direct effect on muscle tissue and is less likely to cause sedation when the daily dose does not exceed 300mg [29].

Additionally, there are a range of injectable medicines that can be used to successfully relieve spasticity. These treatments involve the administration of botulinum toxin, phenol/alcohol, and intrathecal baclofen. In 1977, Dr. Alan B. Scott administered botulinum toxin by injection to cure strabismus, but initial approval for the use of botulinum toxin in spasticity was granted in 1989 [79]. Subsequently, there has been a notable increase in scientific investigation about botulinum toxins, resulting in the development of newer formulations that have a wider range of uses [80,81]. Botulinum toxin inhibits the release of acetylcholine (ACh) from the motor terminals, resulting in the inability of skeletal muscles to contract, despite the continued arrival of action potentials at the motor end plate [82].

Presynaptic nerve terminals are the site where the heavy chain of botulinum toxin attaches and internalizes. Nerve branching and reinnervation, which occur over a span of several months, reverse the observed effect [29]. Botulinum toxin, when injected into skeletal muscle, induces specific muscular weakening in the targeted area [83]. It has the benefit of specifically reducing spasticity without causing the adverse effects of overall weakness or drowsiness. Prior to administering the injections, it is essential to engage in a comprehensive discussion with the patient and their caregiver regarding the treatment strategy and objectives [84]. The injection tehnique is done with ultrasound and/or EMG guidance by trained profesionals. Postinjection therapies, such as physiotherapy are utilized to optimize the advantages of botulinum toxin injections. The impact is not as instantaneous and the duration is not as prolonged compared to chemical neurolysis [85,74]. In addition, Simpson et al. shown that BoNTs is both safer and more effective than Tizanidine. They reported a greater reduction in muscle tone in the upper limbs and a lower occurrence of side-effects. In addition to affecting muscle tone and enhancing the effectiveness of physiotherapy methods, administering BoNT can also provide pain relief [86].

The spinal cord's GABAergic neurones are capable of absorbing a very little amount of baclofen that has been administrated oral. Intrathecal baclofen (ITB) therapy is a method that allows for the direct delivery of a GABA agonist to the spinal cord, with the purpose of suppressing spasticity while limiting any negative side effects via a programmable pump that is surgically implanted beneath the skin in the abdominal region [87]. It is commonly used to address persistent spasticity in the lower part of the body, after receiving proper therapy with at least two oral antispasticity drugs simultaneously [88]. This method shows inability in reducing muscular hyperactivity in patients with severe spasticity [89]. It should be considered for patients between 3 to 6 months after stroke [90].

Neurolysis is performed by injecting phenol into the peripheral nervous system, which causes the destruction of neural tissue by altering the structure of proteins in axons and membranes of both sensory and motor nerve fibers [91]. This process ultimately results in the loss of nerve supply and the degeneration of muscle spindles. These method is useful in managing spasticity that arises in important strong muscle groups proximal to the torso. It is imperative to do this procedure entirely under the supervision of an ultrasound scan or nerve stimulator. A solitary administration usually produces long-lasting effects extending many months and can be repeated if considered necessary in specially trained centers [92].

The primary reason for surgical intervention in spasticity is severe spasticity or functional impairments resulting from spasticity-related complications. These surgical procedures, including myelotomy, tenotomy and cordectomy, are performed to reduce

muscular contraction.The outcomes of surgery can vary and are reliant upon each patient. Osteotomies can also rectify articulation deformities. Orthopaedic surgery may successfully reduce the adverse effects of spasticity through targeted manipulation of tendons, such as extending, releasing, or transplanting a specific tendon [93]. Neurosurgical procedures encompass neurotomy and selective dorsal rhizotomy. The aberrant sensory nerve roots are recognized and separated, while the motor nerves remain undamaged. Neurotomy is mostly used to treat spasticity in the lower limbs, specifically in the distal region [94]. Selective dorsal rhizotomy involves cutting the aberrant nerve fibers in the lumbar region that show an inappropriate response to electrical stimulation. This procedure leads to a general improvement in spasticity throughout the lower body [95]. Phamacological and nonpharmacological treatment of poststroke spasticity plays a crucial role in the comprehensive rehabilitation of stroke survivors. The primary aim of these interventions is to mitigate the debilitating effects of muscle stiffnes, which can significantly impact mobility and quality of life.All physicaltherapy methods and medication shouls be used together, offering more tailored and sustained relief for patients, enhancing functional outcomes and facilitate greater independence.

7. CONCLUSIONS

The complex mechanisms and origin of spasticity makes the comprehension of its pathophysiology and therapeutic mechanism quite challenging. To ensure optimal treatment, the patient must undergo a comprehensive clinical evaluation to accurately classify the severity of spasticity. For effective treatment, it is crucial to utilize physical therapy and drugs to prevent potential immobilization of the patient, which can result in both physical and mental impairment. Every patient is distinct, and the treatment approach is determined by the clinician based on the specific pathology. While there are only a couple of treatments available for patients with spasticity, the precise mechanism of action remains incompletely understood. Therefore, it is imperative to further investigate and improve the research of spasticity in the future. This has the potential to offer new approaches that could improve the severe spasticity observed in patients. Mean while physical therapy combined with medication or different other techniques seem to be the solution for treating posttroke spasticity and therefor multidisciplinary therapeutical plans should provide a greater independence and better quality of life for this patients.

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