Effect of Cold Application and Tizanidine on Clonus: Clinical and Electrophysiological Assessment

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Abstract

Background/Objectives: Clonus is an involuntary rhythmic muscle contraction after sudden muscle stretch that occurs as a result of a lesion in the upper motor neurons. The real mechanism behind clonus remains obscure. The objective of this study was to investigate the effects of central-acting tizanidine treatment and peripheral extremity cooling on clonus.

Participants: Thirty-eight patients with upper motor neuron involvement and sustained clonus.

Methods: The 38 patients were divided into 3 groups: cold group ($n = 19$), tizanidine group ($n = 13$), and patient control group ($n = 6$). A separate group of 21 able-bodied volunteers served as controls for the cold group. The physiologic effects of cold application were measured in the able-bodied group and compared with the effects in the patients in the cold group. All participants were evaluated by clinical and electrophysiologic measurements.

Results: Changes in clinical and electrophysiologic measurements in the cold group were statistically significant compared with those of the tizanidine and patient control groups.

Conclusions: Subsequent and long-term cold application induced prolonged inhibitory effects on clonus. Tizanidine had no significant effect on clonus. Suppression of clonus by cold highlights the importance of peripheral input in relation to central mechanisms.

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Key Words: Spinal cord injuries; Spasticity; Clonus; Tizanidine; Tetraplegia; Hemiplegia; Cryotherapy

INTRODUCTION

Clonus is an involuntary rhythmic muscle contraction after sudden muscle stretch that occurs as a result of a lesion in the efferent motor pathways. It may be accompanied by spasticity and increased deep tendon reflexes (DTRs) (1). Severe clonus can cause difficulties in mobility and fatigue that affects work performance. Some patients may even lose their ability to stand or walk. Any mechanism or pharmacologic agent that can suppress increased reflexes and muscle tone may also be effective against clonus. The underlying mechanism remains obscure. Two hypotheses regarding clonus have been put forward. First, it occurs as a result of self-reexcitation of hyperactive stretch reflexes (2–4). Another theory is based on the idea that a central generator induces

rhythmic α -motor neuron activity, which was affected by the observed peripheral events (5–8).

The central α_2 adrenoceptor agonist tizanidine is a myotonolytic agent used in the treatment of spasticity. Tizanidine reduces spasm frequency and clonus; it is a therapeutic alternative for patients with spasticity associated with cerebral or spinal damage (9). Peripheral cooling has also been noted to dampen spasticity. Cooling inhibits ankle clonus by suppressing receptor activity and slowing nerve conduction, especially in group II fibers, on both muscle receptors and peripheral axons.

This study examines the effects of central-acting tizanidine treatment and peripheral extremity cooling on ankle clonus. Although the effects of cold application and tizanidine on spasticity have been well established, case-control studies about their effects on clonus are lacking in the literature. Moreover, because the effects of a single session of cold application on clonus have been evaluated in the literature, we focused on the effects of repetitive and long-term cooling on clonus. All patients were evaluated by several clinical and electrophysiologic measurements.

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METHODS

Approval for the study was obtained from the ethics committee of our hospital, and all of the patients gave written consent to participate in the study. Thirty-eight patients (mean age, 38 ± 16 years; 30 men and 8 women) with upper motor neuron involvement and sustained ankle clonus according to The Reflex Scale of the Modified Ashworth Scale were included. Exclusion criteria were unsustained ankle clonus, lower motor neuron involvement, previously performed tibial nerve blockage, use of antispasmodic medications, unknown etiology of disease, inability to cooperate, and insufficient ankle range of motion. Of these patients, 20 had hemiplegia caused by either trauma or cerebrovascular accident, 13 had either traumatic or demyelinating paraparesis, and 5 had either traumatic or vascular tetraplegia. Certain criteria affected which patients were assigned to each study group. Patients with peripheral vascular disease and cold intolerance were not assigned to the cold group. Patients with known liver function abnormalities were excluded from the tizanidine group because tizanidine is metabolized in the liver.

Three treatment groups were designed for patients with sustained ankle clonus: 19 patients (17 men and 2 women) participated in the cold group; 13 patients (10 men and 3 women) participated in the tizanidine group; and 6 patients (3 men and 3 women) participated in the patient control group. All participants in the 3 treatment groups received routine rehabilitation. The cold group patients received cryotherapy in addition to rehabilitation training; the tizanidine group received tizanidine and rehabilitation training; and the patient control group received only rehabilitation. To determine the effect of cold application on the electrophysiologic parameters of individuals without neurologic dysfunction, comparative cryotherapy data were gathered in a fourth group of 21 able-bodied volunteers (mean age, 35 ± 12 years; 11 men and 10 women).

Baseline demographics and course of intervention of each group are summarized in Table 1. In the cold group, the participants' lower extremities were submerged into a whirlpool held at 15°C for 20 minutes once a day for a total of 10 sessions. Lower extremity temperatures were measured immediately before and after the cooling process by a dermal thermometer at the level of the anterior tibialis muscle. An average decrease of 11°C in

skin temperature was obtained in all subjects. Patients in the tizanidine group were given 4 weeks of the medication at the maximum tolerable dosages that provided clinical improvement in spasticity while not interfering with the individuals' ability to participate in the rehabilitation program. The average tizanidine dosage was 12 mg/d (range, 8–24 mg/d). The most common side effect of tizanidine was sedation. Clinical and electrophysiologic evaluations were performed 2 hours after administration of tizanidine. Tizanidine dosage was titrated slowly initially, as well as during discontinuation. The patient control group, which consisted of subjects who received approximately 3 weeks of rehabilitation training, but neither cold therapy nor antispasmodic treatment, was evaluated at the beginning and at the end of the rehabilitation program. For comparison, a group of able-bodied volunteers underwent a single application of cryotherapy, during which the skin temperature of the lower extremities was decreased approximately 10°C .

Patient evaluation parameters included self-report with the spasm frequency scale, spasm severity, painful spasm, and interference with function (10). Clinical evaluation performed by the physician included the Ashworth Scale for the knees and ankles, deep tendon reflexes, plantar stimulation response, functional ambulation scale, and The Reflex Scale of the Modified Ashworth Scale (10,27). These evaluations are reported in Appendix I. Each patient underwent electrophysiologic evaluation both before and after the intervention (cryotherapy or tizanidine). Electrophysiologic evaluation included interburst latency, duration and amplitude of clonic burst, M-response latency and amplitude, H-reflex latency and amplitude of the gastrocnemius muscle after tibialis posterior nerve stimulation. H/M threshold rate, the F-response latency from the abductor hallucis muscle, and Achilles T reflex latencies and amplitude. Clonus of the tibialis anterior and gastrocnemius-soleus muscles was recorded with 2-channel and rectified EMG simultaneously, using signal triggering mode with a sampling rate of 100 ms, sensitivity of $200 \mu\text{V}$ per division (div) for both the first and second channels, analysis period of 200 ms/div, and lower limit frequency of 100 Hz at a set highest frequency of 3 kHz (Figure 1a). The interburst latencies of 3 clonic bursts (after the first burst, which was used as a signal trigger) were measured from onset to

Table 1. Baseline Demographics and Course of Each Intervention

	Male	Female	Total	Hemiplegia	Paraparesis	Tetraplegia	Intervention	Period
Patients	30	8	38	20	13	5		
Cold group	17	2	19	10	4	2	Cold application	10 sections
Tizanidine group	10	3	13	6	5	1	Tizanidine	4 weeks
Patient control group	3	3	6	4	5	2	Rehabilitation	3 weeks
Able-bodied controls	11	10	21				Cold application	Once

Figure 1. (a) Rectified EMG records of clonic bursts before cryotherapy (200 ms/div; 200 µ/div). Sol, soleus; TA, tibialis anterior. EMG records of a sample patient. (b) Rectified EMG records at the completion of the 10th cold application. Clonic bursts are abolished (200 ms/div; 200 µ/div). Sol, soleus; TA, tibialis anterior. EMG records of the same sample patient.

onset for each burst and noted as latencies of the first, second, and third clonic burst latencies. The duration of each clonic burst was measured from the onset to the end of EMG activity.

H-reflex recordings were elicited with a sensitivity of 5 mV/div, analysis period of 5 ms/div, and a sampling rate of 100 µs. Stimulus amplitude was gradually increased in a stepwise manner in increments of 5 mA, starting at 0 mA. At each step, 10 recordings were obtained. T-reflex recordings were obtained with irregular hits on the Achilles tendon of low frequency using a triggered reflex hammer as the stimulus. Record settings

had a sensitivity of 2 mV/div, lowest frequency limit of 20 Hz, and highest frequency limit of 3 kHz. Sampling rate was set to 5 µs/div with an analysis period of 100 µs. At least 10 consecutive T-reflex responses were recorded, and the latency and peak-to-peak amplitude of the one with the highest amplitude was used. Sensitivity for the F-response recordings was 2 mV/div, with a lowest frequency limit of 50 Hz and a highest frequency limit of 3 kHz. Sampling rate was 5 µs/div, with an analysis period of 100 µs; 16 tracings were recorded. Latency of the F response with the shortest latency and amplitude of the F response with the highest amplitude were used.

The paired-sample *t* test was used to compare 2 means for each dependent group before and after intervention; if necessary, the Wilcoxon test was used. Within the context of the normality hypothesis, the *t* test was performed to study any statistically significant differences between the cold group and the able-bodied control groups regarding the measurements obtained. When comparing all groups, analysis of variance (ANOVA) was used for the variables compatible with the normality hypothesis, whereas for the incompatible variables, the Kruskal-Wallis test was used. For the variables found to be significantly different between the groups, the Scheffe multiple comparisons test was performed to determine which groups differed from the others.

RESULTS

In the cold group, statistically significant improvements were observed after cold application in the patient self-evaluation parameters and clinical measurements such as knee and ankle Ashworth Scores, spasm frequency scale, spasm severity and painful spasm, Reflex Scale ($P < 0.05$; Table 2).

The mean period for reemergence of ankle clonus after cold application was 50 hours (range, 1–7 days). The inhibitory effect of cold on ankle clonus persisted despite return of extremity temperature to normal. After cold application, clinically apparent ankle clonus was abolished in 16 of 19 patients, whereas electrophysiologic absence of ankle clonus was observed in 14 patients (Figure 1b). Of the 5 patients in whom ankle clonus persisted electrophysiologically, ankle clonus frequency was recorded at 6 Hz in 1, 5 Hz in 1, 1 Hz in 1, and 3 Hz in 2 patients. In those in whom ankle clonus persisted, a significant prolongation of latencies of the first and second beats was observed (Table 3).

Sural and tibial conduction velocities were slower after cold application. However, a significant delay of the latencies of the M response, H reflex, T reflex, and F response was observed; this was clearly recorded in all patients (Table 4). Comparison of patient feedback before and after tizanidine administration showed statistically significant improvements in spasm severity and knee and ankle Ashworth Scores. Significant decreases in spasticity values were also observed (Table 5). Overall, tizanidine did not have a significant effect on

Table 2. Patient Self-Evaluation Parameters and Clinical Measurements Before and After Cold Application

Measurements	Before Cold (Mean $\pm$ SD)	After Cold (Mean $\pm$ SD)	Significance (<i>P</i>)
Spasm frequency scale	2.27 $\pm$ 1.01	1.55 $\pm$ 1.09	0.006
Spasm severity	1.83 $\pm$ 0.85	1.50 $\pm$ 1.15	0.034
Interference with function	1.11 $\pm$ 0.83	0.83 $\pm$ 0.85	0.102
Painful spasm	1.00 $\pm$ 0.84	0.61 $\pm$ 0.77	0.020
Ashworth score (knee)	2.00 $\pm$ 0.84	1.60 $\pm$ 0.98	0.014
Ashworth score (ankle)	2.33 $\pm$ 0.61	2.00 $\pm$ 0.84	0.025
Functional ambulation scale	1.82 $\pm$ 1.84	1.88 $\pm$ 1.79	0.317
Plantar stimulation response	1.88 $\pm$ 0.47	1.88 $\pm$ 0.47	1.000
Reflex scale	6.00 $\pm$ 0.00	3.36 $\pm$ 0.95	0.000

Table 3. Clonus-Related Electrophysiologic Measurements Before and After Cold Application

Measurements	Before Cold (Mean $\pm$ SD)	After Cold (Mean $\pm$ SD)	Significance (<i>P</i>)
Clonus frequency (Hz)	5.84 $\pm$ 0.76	0.95 $\pm$ 1.8	0.000
Clonus first burst latency (ms)	202.00 $\pm$ 10.30	257.20 $\pm$ 30.15	0.043
Clonus second burst latency (ms)	170.40 $\pm$ 27.94	239.20 $\pm$ 96.70	0.043
Clonus third burst latency (ms)	150.00 $\pm$ 19.39	160.00 $\pm$ 47.52	0.710
Clonus duration (ms)	68.80 $\pm$ 9.44	71.20 $\pm$ 9.76	0.790
Clonus amplitude minimal (μ V)	299.40 $\pm$ 111.67	114.40 $\pm$ 39.02	0.029
Clonus amplitude maximal (μ V)	883.20 $\pm$ 119.27	551.60 $\pm$ 368.85	0.113

ankle clonus-related measurements (Table 6). Tizanidine administration did not have significant effects on the M response and H reflex, which were obtained in all patients after administration of the antispasmodic agent. When the clinical data before and after rehabilitation training were analyzed, no significant improvement was observed in any of the clinical measurements in the patient control group (rehabilitation only). The electrophysiologic measurements are summarized in Table 7.

Analyzing electrophysiologic evaluation in the group of able-bodied individuals after cold application, a significant delay was observed in the latencies of the H reflex, M response, and F response, as well as a significant decrease in sural and tibial nerve conduction velocities. The H reflex could be recorded in all subjects, both before and after cold application. The decreases in nerve conduction velocities were similar in both able-bodied controls and patients. However, with regard to reflexes, the only significant difference between the 2 groups was observed in the latency of the M response ($P = 0.049$). Changes in the Reflex Scale in the cold group were statistically significant compared with those of the tizanidine and patient control groups ($P = 0.000$). There was a statistically significant difference in ankle clonus frequencies among the 3 groups ($P = 0.002$). When the cold group was compared separately with the tizanidine and patient control groups, this difference was apparent ($P = 0.003$ and $P = 0.001$, respectively; Figure 2).

When the cold, tizanidine, and patient control groups were compared in terms of presence of ankle clonus, a statistically significant difference was obtained ($P = 0.000$;

Figure 3). According to the clinical evaluation, changes in the spasm frequency scale among the 3 groups were found to be statistically significant ($P = 0.037$). Decreases in interference with function and painful spasms were highest in the cold group; however, the tizanidine group had the most decrements regarding spasm severity. Both differences were statistically insignificant.

DISCUSSION

Because one of the aims of this study was to assess the effect of long-term cold application on ankle clonus, the clinical and electrophysiologic findings were performed at the beginning and at the end of 10 sessions. It was observed that, although ankle clonus was shortly suppressed after the first session, by the end of repetitive sessions, this effect lasted for an average of 2 days (range, 1–7 days). Therefore, cumulative suppressing effect on ankle clonus was achieved with long-term cryotherapy.

In a study by Bassett and Lake (11) on patients with upper motor neuron lesions, spasticity and clonus both decreased with the application of wet towels wrapped in crushed ice and with submergence in cold water. Measurable functional improvement has been reported in association with decreased spasticity after cold application. Knutsson (12), who studied the kinematics of spastic gait before and after cold application, reported that a decrease in spasticity of antagonistic spastic plantar flexors paralleled an increase in the late oscillation phase during dorsiflexion. Hedenberg (13), on the other hand, tested upper extremity functions of patients with hemiplegia before and after submergence in cold water

Table 4. Sensory and Motor Conduction and Reflex Response Measurements Before and After Cold Application

Measurements	Before Cold (Mean $\pm$ SD)	After Cold (Mean $\pm$ SD)	Significance (<i>P</i>)
Sural sensory velocity (m/s)	51.45 $\pm$ 10.00	32.80 $\pm$ 8.75	0.068
Sural sensory amplitude (μ V)	12.19 $\pm$ 8.75	11.61 $\pm$ 6.70	1.000
Tibial motor velocity (m/s)	43.45 $\pm$ 3.03	30.85 $\pm$ 5.93	0.068
Tibial motor amplitude (mV)	9.10 $\pm$ 4.45	11.21 $\pm$ 5.66	0.068
M latency (ms)	4.59 $\pm$ 0.84	6.25 $\pm$ 2.11	0.003
M amplitude (mV)	16.02 $\pm$ 7.69	14.16 $\pm$ 10.90	0.447
H latency (ms)	31.31 $\pm$ 2.58	33.34 $\pm$ 3.41	0.002
H amplitude (mV)	5.96 $\pm$ 3.95	5.87 $\pm$ 6.01	0.949
H/M amplitude	37.07 $\pm$ 20.27	38.62 $\pm$ 23.15	0.717
H/M threshold	71.79 $\pm$ 19.83	87.14 $\pm$ 37.61	0.076
T latency (ms)	32.88 $\pm$ 2.70	36.42 $\pm$ 4.00	0.004
T amplitude (mV)	5.76 $\pm$ 2.25	3.88 $\pm$ 2.73	0.010
F latency (ms)	50.75 $\pm$ 8.23	58.38 $\pm$ 9.87	0.000
H reflex present (%)	100.00 $\pm$ 0.00	100.00 $\pm$ 0.00	1.000
T reflex present (%)	100.00 $\pm$ 0.00	100.00 $\pm$ 0.00	1.000

Table 5. Patient Self-Evaluation Parameters and Clinical Measurements Before and After Tizanidine Administration

Measurements	Before Tizanidine (Mean $\pm$ SD)	After Tizanidine (Mean $\pm$ SD)	Significance (<i>P</i>)
Spasm frequency scale	1.85 $\pm$ 1.28	1.38 $\pm$ 1.26	0.053
Spasm severity	1.69 $\pm$ 1.03	1.15 $\pm$ 0.80	0.028
Interference with function	0.85 $\pm$ 0.69	0.69 $\pm$ 0.75	0.165
Painful spasm	0.15 $\pm$ 0.37	0.07 $\pm$ 0.02	0.337
Ashworth score (knee)	1.92 $\pm$ 0.76	1.15 $\pm$ 1.07	0.020
Ashworth score (ankle)	2.15 $\pm$ 0.69	1.31 $\pm$ 1.18	0.020
Functional ambulation scale	1.77 $\pm$ 1.69	1.77 $\pm$ 1.69	1.000
Plantar stimulation response	1.77 $\pm$ 0.60	1.77 $\pm$ 0.60	1.000
Reflex scale	6.00 $\pm$ 0.00	6.00 $\pm$ 0.00	1.000

Table 6. Electrophysiologic Measurements Before and After Tizanidine Administration

Measurements	Before Tizanidine (Mean $\pm$ SD)	After Tizanidine (Mean $\pm$ SD)	Significance (<i>P</i>)
Clonus frequency (Hz)	5.77 $\pm$ 0.60	5.69 $\pm$ 0.48	0.337
Clonus first burst latency (ms)	208.92 $\pm$ 62.04	223.38 $\pm$ 20.62	0.441
Clonus second burst latency (ms)	186.15 $\pm$ 28.69	183.38 $\pm$ 17.35	0.721
Clonus third burst latency (ms)	174.92 $\pm$ 25.93	178.46 $\pm$ 20.51	0.584
Clonus duration (ms)	64.31 $\pm$ 5.93	61.23 $\pm$ 8.73	0.209
Clonus amplitude minimal (μ V)	271.69 $\pm$ 191.01	197.46 $\pm$ 90.58	0.188
Clonus amplitude maximal (μ V)	77.54 $\pm$ 263.41	599.08 $\pm$ 287.57	0.255

Table 7. Clonus-Related Electrophysiologic Measurements at the Beginning and End of 3-Week Rehabilitation Training in the Control Group

Measurements	Before Rehabilitation (Mean $\pm$ SD)	After Rehabilitation (Mean $\pm$ SD)	Significance (<i>P</i>)
Clonus frequency (Hz)	5.60 $\pm$ 0.55	5.80 $\pm$ 0.84	0.317
Clonus first burst latency (ms)	210.80 $\pm$ 40.56	193.20 $\pm$ 32.70	0.080
Clonus second burst latency (ms)	181.20 $\pm$ 27.48	162.40 $\pm$ 49.99	0.225
Clonus third burst latency (ms)	176.80 $\pm$ 22.16	165.60 $\pm$ 26.96	0.042
Clonus duration (ms)	63.60 $\pm$ 18.30	65.80 $\pm$ 13.50	0.786
Clonus amplitude minimal (μ V)	144.17 $\pm$ 80.37	164.20 $\pm$ 109.01	0.108
Clonus amplitude maximal (μ V)	417.20 $\pm$ 153.38	454.80 $\pm$ 289.92	0.456

Figure 2. Frequency changes for clonus in the cold, tizanidine, and control groups before and after intervention.

and after cold application and noted significant improvements in functional capacities. Dimitrijevic et al (8), however, reported no changes in clonus frequencies with cold application. Miglietta (14) showed that the longer the period of cold application, the longer it took for clonus to recur. The average periods of recurrence of clonus observed after 10, 20, and 30 minutes of cold application were 28 (range, 15 to 45 minutes), 48 (range, 10 minutes to 2 hours), and 85 minutes (20 minutes to 6 hours), respectively.

Our results are similar to the above-mentioned studies regarding the inhibitory effects of cold application. According to our study, cold application has an important inhibitory effect on ankle clonus, as well as decreasing its frequency. Cold application induced prolonged inhibitory effects on clonus. This can be termed as the “prolonged effect,” a first in the literature. The following mechanisms may help to explain this phenomenon. (a) There is a persistence of ankle clonus inhibition even after a cooled muscle has returned to body temperature; in other words, failure of clonus to return despite the absence of peripheral input suggests presence of a central effect. It also supports the idea that intermittent blockage of peripheral input may result in modifications of central organization. Moreover, the decrease in Ashworth Scores for ankle movements also supports the idea that the prolonged effect of cold application may occur at the level of the spine. (b) Receptor adaptation may be another factor. However, there is no evidence supporting the long-term effects of cold on receptors. Similarly, there is no proof that adaptation to cold is not prolonged.

In a study by Ottoson (15), it was observed that spontaneous discharge in the spindles abolished after rapid cooling. Spindular response to stretch was reported to increase in a linear fashion as the temperature was increased from 3°C to 32°C. The highest frequency of discharges was observed at 30°C. It was also observed that the responsiveness of the cooled spindles after stretch was not parallel to the changes in the amplitudes of the static and dynamic components of the receptor potential. Despite the diminished spindular response, there was no change in the amplitudes of the static and dynamic

Figure 3. Presence of clonus before and after intervention in the cold, tizanidine, and patient control groups.

components. It was professed that this phenomenon could be explained by an increase in the threshold of the nerve fiber and/or a relatively prolonged refractory period. Beres-Jones (4) suggested that EMG activation patterns and burst characteristics across muscles were similar during stretch-induced ankle clonus, non-weight-bearing standing, and stepping. They recorded synchronous EMG co-activation patterns for the soleus, medial gastrocnemius, and tibialis anterior muscles during stretch-induced ankle clonus. They did not find a positive correlation between clonic EMG frequency and amount of loading. They proposed that clonus can occur at stable frequency independent of changes in peripheral events that modulate muscle lengthening and loading.

Some authors professed that clonus is unaffected by peripheral events and that it only occurs through a central “generator,” which probably lies somewhere in the spinal region, with a high possibility of there being more than 1 in the patients with complete spinal cord injuries (16). Hagbarth et al (17) failed to show a difference in dynamic spindle sensitivities of patients with spasticity compared with normal individuals. Clonus is sustained by stretch reflexes occurring as a result of discharges during muscle relaxation. Whether dynamic fusimotor activity plays a role in the development of clonus remains controversial (18). Rack et al (19) showed that clonus frequencies changed from 2.7 to 5.7 Hz with different mechanic loading. When the load was changed even further, the amplitude of the movement decreased abruptly, and the movement that remained was no longer a regular and forceful clonus. When stretch reflexes operate with high gain, limbs may break into spontaneous clonus. Clonus may develop in normal individuals as a result of exerting massive effort against an inappropriate challenge, thus preventing voluntary control. In everyday life, clonus of this type occasionally does occur when a large force is exerted against an awkward load, and it may seriously interfere with voluntary control.

In another study undertaken by Rossi et al (20), afferent fibers from the gastrocnemius-soleus muscles

were blocked by compression. They observed that 10 minutes after the first application of compression, clonus was completely suppressed, without any change in the T reflex (without any sign of blockage of the afferent and efferent fibers of the monosynaptic arc). There is no doubt that the T reflex is produced by the discharge of the Ia afferent fibers and that these are the first to be blocked by compression. Their interpretation was that clonus is sustained by the discharge of a subpopulation of Ia afferent fibers, which are more susceptible to compression than those of the monosynaptic reflex.

In response to cryotherapy, we showed persistence of H and T reflexes with prolonged latencies, as well as decreases in the stimulation threshold and H/M ratio, but with a marked inhibitory effect on clonus. This suggests that clonus may be generated by mechanisms somewhat different from the peripheral and central components of the H and T reflexes.

The centrally active drug, tizanidine, when administered at maximally tolerated dosages to our patients, had

no significant effect on clonus. Pharmacologic and electrophysiologic studies have shown that tizanidine affects spinal polysynaptic reflexes. This action arises from agonistic activity of the compound at noradrenergic α_2 receptors, resulting in both direct impairment of excitatory amino acid release from spinal interneurons and a concomitant inhibition of facilitatory caerulospinal pathways. Also, tizanidine selectively blocks group II pathways, which have a role in spasticity (21,22). Several studies in the literature have reported that centrally active antispastic drugs do not have significant effects on clonus; however, some studies have shown that baclofen has more dramatic effects than other drugs (23–26). The suppression of clonus by cold highlights the importance of peripheral input with regard to central mechanisms. Better results may be obtained in the treatment of clonus and spasticity by using centrally and peripherally effective mechanisms simultaneously. Furthermore, “the prolonged effect of cold” supports the presence of spinal neuroplasticity and adaptation in individuals with neurologic impairments.

APPENDIX I: PATIENT SELF-REPORT AND CLINICAL EXAMINATION SCALE DEFINITIONS (10,27)

Spasm Frequency Scale (Modified from Penn)

- 0 No spasms
- 1 Spasms induced only by stimulation
- 2 Infrequent spontaneous spasms occurring less than 1 per hour
- 3 Spontaneous spasms occurring more than 1 per hour
- 4 Spontaneous spasms occurring more than 10 per hour

Spasm Severity

- 1 Mild
- 2 Moderate
- 3 Severe

Interference With Function

- 0 Does not interfere with function
- 1 Makes function difficult
- 2 Prevents function

Painful Spasm

- 0 Causes no discomfort or pain
- 1 Causes moderate discomfort or pain
- 2 Causes severe discomfort or severe pain

Ashworth Score

- 0 No increase in tone
- 1 Slight increase in tone giving catch when the limb is moved in flexion or extension
- 2 More marked increase in tone, but limb easily flexed
- 3 Considerable increase in tone, passive movement difficult
- 4 Limb rigid in flexion or extension

Plantar Stimulation Response

- 0 No visible activity/flexor response
- 1 Flicker of movement/extensor response
- 2 Slight knee or hip movement
- 3 Knee lifted from support
- 4 Movement elicited by light touch

Functional Ambulation Scale

- 0 Patient cannot walk, or requires help of 2 or more people
- 1 Patient requires firm continuous support from 1 person who helps carrying weight and with balance
- 2 Patient needs continuous or intermittent support of 1 person to help with balance or coordination
- 3 Patient requires verbal supervision or stand-by help from 1 person without physical contact
- 4 Patient can walk independently on level ground, but requires help on stairs, slopes, or uneven surfaces
- 5 Patient can walk independently anywhere; patient can walk on any surface without any support, regardless of inclination

The Reflex Scale

- 0 None
- 1 Hyporeflexia
- 2 Normal
- 3 Pathologically brisk but no clonus
- 4 Unsustained clonus, less than 4 beats
- 5 Unsustained clonus, more than 4 beats
- 6 Sustained clonus

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