Phenol Reduces Hypertonia and Enhances Strength: A Longitudinal Case Study

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Abstract

Phenyl alcohol blocks are used to relieve spasticity. Such nerve conduction blocks result from phenol-induced axonotmesis and could potentially affect muscle properties related to the ability to generate, maximize, and reduce force. This study assessed the 12-week longitudinal effect of phenol on position (stiffness) and velocity (damping) components of hypertonia, in addition to strength (peak torque and times to generate and reduce torque) in an individual with chronic elbow flexor spasticity following stroke. Phenol motor point injections of flexor muscles paradoxically increased the magnitude of flexion torque and decreased the times required to generate and reduce flexion and extension joint torques, in addition to reducing elbow extension stiffness and damping. Large reductions in the velocity related component of hypertonia (damping changes > 90%) occurred immediately following injection which is a finding that supports the velocity-dependent definition of spasticity. While the changes in damping were large and transient, changes in stiffness and strength variables were small, slower to occur, and maintained. This suggests secondary changes following nerve block, possibly facilitated by regular elbow use subsequent to spasticity reduction.

Keywords

Motor control; stroke; spasticity; torque; reaching; weakness

INTRODUCTION

Spasticity is a velocity dependent hyperexcitability of the stretch reflex¹ and contributes to increased joint resistance². Elbow flexor spasticity affects 40% of persons with stroke³ and can lead to pain and contractures, in addition to difficulties with dressing and hygiene. One approach to reducing spasticity has been to stretch the muscle by passive movement exercises or by splinting and casting. Another approach has been to use neuromuscular

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blockers to reduce hyperactivity of elbow flexors and to encourage use of hypoactive elbow extensors.

Phenyl alcohol (phenol) has been used extensively as a neuromuscular blocker and has been shown to reduce hypertonia of both upper and lower extremities following stroke⁴. The dispensing cost of phenol (RCDP, Edmonton, Canada) is 1% of Botox (Allergan, Oakville, Canada). Its administration through the “intramuscular motor point block” technique is safe and without surgery⁵. Phenol produces a long-lasting block of spastic muscle tone for weeks or months before slowly resolving⁵. Phenol induces axonotmesis (i.e., axonal and myelin degradation) thereby interrupting motor and sensory nerve conduction⁶; blocks persist until nerves have regenerated. In 23 elbows with flexor spasticity, Keenan and colleagues⁷ found that phenol blocks of brachioradialis and biceps muscles increased elbow range of motion by a mean of 53°. Using ethyl alcohol (a neurolytic agent similar to phenol) across 20 persons with elbow spasticity following stroke, Kong & Chua⁸ found an average 2-point grade reduction in hypertonia using the Modified Ashworth Scale (MAS)⁹.

Recent biomechanical models that partition position and velocity dependent components of hypertonia¹⁰ may provide additional information from standard clinical measures such as the MAS to measure the efficacy of phenol. With phenol acting to reduce spasticity of elbow flexor muscles via denervation, one might expect that it would weaken these same muscles and impair their ability to maximally develop force but evidence for these changes is scarce. Stroke-induced weakness can also impair the ability to quickly generate and reduce joint torque¹¹. Therefore, the objective of this study was to assess the effects of phenol on variables of hypertonia and strength (peak torque and times to generate and reduce torque). To achieve this, we contrasted baseline measurements with longitudinal data in one subject (i.e., case series).

METHODS

Clinical Assessment

Our candidate for phenol injection was a 72-year-old male with elbow flexor spasticity of the left arm resulting from an ischemic stroke four years previous. Upon incident, a CT scan demonstrated blocks in the right internal carotid and middle cerebral arteries; a second CT scan (11 days later) revealed low density changes at the right basal ganglia. The candidate was right hand dominant (pre and post stroke), independent in most activities of living, and recreationally involved in gardening. He had a severe flexor synergy of his left arm during gait which disrupted balance and had resulted in a fall the previous year (without injury). With the assistance of a cane he was able to ambulate 4 to 5 blocks. The clinical objective of administering phenol was to relieve spastic elbow flexor activity. A 26/30 Mini-mental test score indicated acceptable cognitive function¹² to participate in the study.

The upper extremity portion of the Fugl-Meyer scale¹³ was used to describe motor impairment of his affected arm (maximum score = 66 indicating no impairment) and the MAS⁹ was used to grade elbow flexor tone (0 = no increase in muscle tone and 4 = rigid). The Fugl-Meyer score was 18 and the MAS grade was 4. The subject had no prior neuromuscular blocker treatments, had not received any physical therapy for his arm

impairment over the past year, and was not using any type of orthoses for his upper extremity. Aside from the phenol injection, he did not receive any additional treatments over the course of this study (medications or therapy). Local university and hospital ethics committees approved the study protocol.

Injection Technique

Phenol was injected into the biceps and brachioradialis muscles. Motor point block is the preferred administration of phenol⁵ and is achieved by direct injection into muscles, with the injection aimed at regions which are most sensitive to electrical stimulation (i.e., motor points)¹⁴. A 6% phenol aqueous solution was injected into four motor points of the biceps and a single motor point of the brachioradialis (0.5–1 mL/site). Motor points were identified by maneuvering a 3 Hz intramuscular stimulating electrode into regions of the muscle belly that produced visible contractions with a 1 mA current (i.e., electrically guided technique). Spasticity was immediately decreased following injection (clinical observation). No adverse effects to the phenol were observed or subsequently reported by the participant.

Assessments of Hypertonia and Strength

We described hypertonia by stiffness and damping. These two mechanical variables were determined by fitting a linear spring-damper model to the set of torque responses obtained from passively extending the elbow at a series of speeds (30, 60, 90, 120, 150, 180 deg/s) with an isokinetic dynamometer (KinCom, Chattanooga, TN). In this model, stiffness is the proportional relationship between joint resistance and extension angle. Damping is the proportional relationship between joint resistance and extension velocity. Increases in stiffness and damping correspond to a more resistive joint (i.e., increasing hypertonia). We have previously described this protocol in detail¹⁰. Stiffness and damping are valid measures of hypertonia and, over days, demonstrate high reliability [stiffness and damping intra-class correlations, ICCs(1,1), of 0.98 and 0.86] and measurement agreement [standard errors of measurements (SEM)s of 9.9 and 28.5%]¹⁰.

Our analysis of strength quantified both magnitude (i.e., peak torque) and time-dependent properties of the torque profile for isometric elbow flexion and extension actions. Peak torque was defined as the maximum isometric torque that could be sustained for a period of 250 ms. Times to generate and reduce torque were calculated as the durations between 10 and 70% of this peak torque value on the ascending and descending portions of the torque profile. We have described this protocol in detail previously¹¹ and reported high reliability and agreement over days with all ICCs(1,1) = 0.90 and SEMs = 20%¹¹.

Timeline of Assessments and Analysis of Time Series

Two baseline assessments were performed to establish measurement stability; these were performed 2 and 3 weeks in advance of injection to avoid factors (e.g., muscle soreness, fatigue) that may interfere with the phenol injection protocol. Follow-up assessments were performed at 2, 4, 8, and 12 weeks post injection. This testing interval has been used previously to test the effect of phenol injections for treating the spastic foot⁴.

Visual analysis of longitudinal data was used to evaluate the effectiveness of the intervention. As there was no discernable learning effect over the baseline measures, a mean of the two pre-injection baseline values was plotted on the graphs to represent the '0th' week. Graphically, all measurements were represented as a percentage of baseline means to facilitate comparisons between variables. We evaluated visual components of level, trend, slope, and variability¹⁵. A change in level was defined as an abrupt rise or fall in parameter magnitude that was sustained for two or more phases. Changes in trends and slopes were deemed to occur when the direction of the data path changed (i.e., increasing versus decreasing) and when the steepness of the data path changed. Variability was assessed both by the absolute change within baseline measures and by the degree of fluctuation in the time series following injection.

RESULTS

Hypertonia

Baseline measurements of stiffness (1.3×10^{-3} N·m/deg·kg) and damping (3.1×10^{-4} N·m·sec/deg·kg) were comparatively larger than those of an unaffected arm (mean values from previous study: stiffness = 2.2×10^{-4} N·m/deg·kg, damping = 6.8×10^{-5} N·m·sec/deg·kg)¹⁰ and were stable over pre-injection testing sessions (Figure 1). Stiffness and damping variables both decreased in response to the phenol injection, representing a reduction in joint resistance. Two weeks following injection, stiffness had decreased approximately 35% from its baseline value; it remained near this value for the remainder of the testing sessions (there was a slight increase at week 8). The change in damping was immediate (70% reduction at week 2 compared to baseline) and was maintained over weeks 2, 4, and 8 before returning to baseline in the 12th week.

Strength

For elbow flexion, baseline values of peak torque (0.10 N·m/kg) and times to generate (0.92 s) and reduce (1.32 s) torque were impaired relative to an unaffected arm (mean values: peak torque = 0.43 N·m/kg, generation time = 0.46 s, reduction time = 0.46 s)¹¹. Pre-injection baseline variation was low (Figure 2). Following injection, there were moderate and functionally positive changes to elbow flexion parameters that persisted over the testing period. Generation and reduction times decreased to between 50 and 80% of their baseline values (i.e., increased ability to modulate torque in a timely fashion) and peak torque increased by over 50%.

Baseline values of elbow extension variables (peak torque: 0.12 N·m/kg, generation time: 0.74 s, reduction time: 0.79 s) were also impaired (unaffected means: 0.40 N·m/kg, 0.43 s, 0.38 s)¹¹ but stable in baseline assessments (Figure 3). While there was a similar response following injection for time-dependent parameters of elbow extension (values remaining between 50 and 80% of baseline), the peak extension torque decreased slightly before returning to its baseline value. Slight increases in extension generation and reduction times occurred at week 8; coincidentally, this was the same period as the observed increase in stiffness.

DISCUSSION

This 12-week longitudinal case study investigated the effects of phenol injection on muscle-joint function (i.e., hypertonia and torque variables). We found that the elbow joint was less resistive to passive movement following injection but this change disappeared after 12 weeks. We also found improvements in both time-dependent and magnitude dimensions of elbow flexion, in addition to improvements in the generation and reduction times of elbow extension in response to the phenol injection.

Reductions in Hypertonia

The changes in hypertonia over time suggest that phenol had its most profound effects in this single subject immediately following the injection (i.e., damping and stiffness minima) and that its effects waned at 12 weeks. This duration of effectiveness is within the ranges found in prior studies⁵. Hypertonia is an increase in the passive resistance to movement and results from spasticity (i.e., hyperreflexia) and/or changes to the viscoelastic characteristics of muscular and connective tissues². Spasticity is believed to be velocity dependent¹ and is the target of neuromuscular blockers. Our findings of a dramatic (changes > 90%) reduction in damping, a velocity dependent parameter, support this definition of spasticity. The transient nature of this damping reduction may reflect the recovery of nerve conduction and the re-emergence of spasticity. The mild but persistent changes to stiffness (changes < 40%) could be due to secondary changes to muscle and connective tissues, facilitated by more regular use of the elbow once spasticity is reduced. Long-term spasticity has recently been associated with muscle fiber changes to sarcomere length and stiffness¹⁶ and such characteristics may be amendable to change with activity.

Positive Strength Changes

Changes in strength (i.e., torque) variables followed the hypertonia changes with increases in peak torque observed for elbow flexion, rather than the expected decrease in torque. These positive changes in both time-dependent and magnitude parameters of elbow flexion are likely secondary to reductions in hypertonia and the promotion of regular use of elbow flexors over an increased range of motion. Greater elbow use may increase the descending drive on motoneurons¹⁷ and may also have had a re-normalizing effect on the length-tension relationship of muscle, which is altered in persons with stroke¹⁸. Recent findings by Landau and Sahrmann¹⁹ indicate that central regulation of firing patterns (e.g., motor unit recruitment, rate modulation), not muscle wasting, is the primary cause of weakness following stroke. The early changes in strength are suggestive of central adaptations.

Clinical Implications and Conclusions

Phenol appears to paradoxically improve both temporal and magnitude dimensions of muscle strength, in addition to reducing hypertonia. Central adaptations may underlie improvements in strength. Our findings were for a single subject and should be explored further by a study of randomized control trial design. Future studies also need to measure the effects of phenol injection on other dimensions of muscle function (e.g., passive range of motion and active length-tension relationship) and on measures of activity and participation.

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Figure 1.

Timeline of hypertonia variables (stiffness and damping) during passive extension of the elbow. Data are normalized by baseline values (pre-injection mean values). Baseline variability is graphed on the left.

Figure 2.

Timeline of elbow flexion muscle strength variables (peak torque, generation time, and reduction time). Data are normalized by baseline values (pre-injection mean values). Baseline variability is graphed on the left.

Figure 3.

Timeline of elbow extension muscle strength variables (peak torque, generation time, and reduction time). Data are normalized by baseline values (pre-injection mean values).

Baseline variability is graphed on the left.