

EFFECT OF SNAGS MULLIGAN TECHNIQUE VERSUS LOW LEVEL LASER THERAPY ON PATIENTS WITH UNILATERAL CERVICAL RADICULOPATHY

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ABSTRACT

Background: Cervical radiculopathy is a condition caused by the compression of the nerve root in cervical spine that commonly manifests as neck pain and it may also radiate from the neck into the distribution of the affected nerve root. There is a significant amount of evidence available to support the benefit of physical therapy and manual techniques in general for patients with neck pain with or without radicular symptoms.

Objective: This study was conducted to assess the efficacy of Mulligan mobilization and low level laser therapy (LLLT) on pain intensity level, EMG dermatomal somatosensory evoked potential and functional level in patients with unilateral cervical radiculopathy.

Materials and Methods: Fifty patients of both genders with diagnosis of unilateral cervical radiculopathy, their ages ranged from 40 to 55. They were randomly assigned into two groups; Group A: Patients received SNAGS Mulligan technique, in addition to conventional program. Group B: Patients received LLLT, in addition to conventional program. The treatment was conducted at a frequency of three sessions per week for four weeks.

Results: Patients in both groups showed significant improvement post treatment in all the measured variables ; there was non-significant difference between two groups post-study in pain level where P-value was (0.128). There were no significant differences between two groups in amplitude, distal latency post-study, where P-values were (0.132) and (0.328) respectively. There were no significant differences between two groups in functional ability, where P-value was (0.156).

Conclusion: Study concludes that both LLLT and SNAGS Mulligan techniques have shown positive results and are effective in improvements in pain intensity, EMG dermatomal somatosensory evoked potential and functional level among Patients with unilateral cervical radiculopathy.

KEY WORDS: SNAGS Mulligan Technique, Low level laser therapy, Dermatomal Somatosensory Evoked Potential, cervical radiculopathy.

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INTRODUCTION

Cervical radiculopathy is a condition caused by the compression of the nerve root in cervical spine that commonly manifests as neck pain and it may also radiate from the neck into the distribution of the affected nerve root. It is the result

of compressive or inflammatory pathology from a space occupying lesion such as a disc herniation, spondylitic spur or cervical osteophyte. It might be unilateral or bilateral. Cervical radiculopathy constitutes 5 to 36% of all radiculopathies. Cervical radiculopathy affects both the

genders equally; the affliction is common during the fourth and fifth decade of the life. Males show early changes in cervical spine and subsequently leading to cervical radiculopathy, where as in females, the problem arises after the menopause [1].

Dermatomal somatosensory evoked potentials were a technique introduced in the early eighties. DSEP is effective in the diagnosis of the consequences of inflammation to sensory spinal roots, tumors of the cauda equina and radiculopathy. It involves stimulation of the skin areas innervated by individual roots. As innervation of individual roots (dermatome) partially overlap each other, the areas on the skin have been determined in which the overlapping is minimized. Dermatomal fields are excited by electrical stimuli with appropriate parameters, and the responses are recorded from the dermal surface of the skull of cortical representation associated with the sensory innervation. Responses are averaged and represent the negative or positive waves with reference to the isoelectric line. Latency response, i.e. the time of onset of each wave after stimulus application and their amplitude are recorded and compared [2].

There are different Mobilization techniques for neck pain, and mulligan's technique is one of them. It has two techniques Sustain Natural Apophyseal Glides (SNAGS) and Natural Apophyseal Glides (NAGS) [3]. Mulligan concept is the mobilization of the spine whilst the spine is in a weight bearing position and directing the mobilization parallel to the spinal facet planes. Mulligan has described a mobilization technique, spinal mobilization with arm movement, for improvement in cervical lesion resulting in pain and other signs below elbow. There is paucity of research evidence supporting its efficacy and are dominated by case report publication [4].

Vincenzino et al. [5] proposed that Mulligan techniques help in improving patient's symptoms by correcting minor positional fault and by neurophysiologic mechanism. According to paungmali et al. [6] MWM produces a hypoalgesia and concurrent sympathoexcitation. It has been previously proposed that the combination sympathoexcitation, non-opioid hypoalgesia and

improvement in motor function are indirect signs of possible involvement of endogenous pain inhibitory systems in manual therapy treatment effects.

In recent years, the beneficial effects of low level laser therapy (LLLT) on clinical and electrophysiological parameters have been shown in several studies without any side effects [7,8]. LLLT may have the potential to induce biophysical effects within the nerve tissue. Studies on the stimulation of nerve regeneration and on nerve conduction by LLLT support the concept that this treatment might facilitate recovery of nerve and stimulate the regeneration of peripheral nerves [9, 10]. LLLT has also shown to have a role in pain and inflammatory process [11, 12].

The exact therapeutic mechanisms of laser therapy are not completely understood. Different experimental studies suggested that low-power laser therapy has anti-inflammatory and analgesic effects [12,13]. It is suggested that a neuronal activity inhibition might be responsible for the therapeutic effect, and the laser irradiation selectively inhibited nociceptive signals at peripheral nerves [14].

However, no study has been conducted to compare the effectiveness of these two approaches in treatment of cervical radiculopathy. So, this study has been designed mainly to compare the effectiveness of Mulligan mobilization and low intensity level therapy in patients with cervical radiculopathy.

MATERIALS AND METHODS

Fifty patients of both genders (30 female and 20 male) with diagnosis of unilateral cervical radiculopathy, their ages ranged from 40 to 55 years old were recruited from the out clinic of faculty of physical therapy, Cairo University after signing consent form prior to data collection in the period between Jan 2016 and May 2016. They were assigned into two groups randomly; Group A: Patients received SNAGs Mulligan technique, in addition to conventional program. Group B: Patients received low level laser therapy, in addition to conventional program [15, 16]. The treatment was conducted at a frequency of three sessions per week for four weeks [17]. Individuals were included if their ages ranged between 40 to 55 years old. All patients were

diagnosed as unilateral cervical radiculopathy at C6/C7 in chronic stage (more than 3 months) as the seventh (C7; 60%) and sixth (C6; 25%) cervical nerve roots are the most commonly affected [18]. Patients complaint from pain in the cervical spine and pain or paresthesia traveling from the neck into a specific region of the arm, forearm or hand [19]. The exclusion criteria for participants were Patients with spinal canal stenosis, Patients with vestibular insufficiency, Patients underwent to any cervical spine operations and Patients who have diabetic or peripheral neuropathy.

Instrumentation

EMG device neuro-Emg-micro 2channel, russian, sn 1051qy: Electrophysiological tests were performed using Neuro-EMG-Micro 2channel, Russian equipment. EMG used to measure amplitude in micro volt and latency in milli seconds of dermatomal evoked potential. Dermatomal somatosensory evoked potentials involve recording cerebral evoked responses from cutaneous stimulation of areas of known dermatomal innervation providing a pure sensory input to any level of the spinal cord [20].

Neck disability index (NDI): The NDI is a commonly used method to determine functional disability level of subjects with neck pain. It has test-retest reliability. The NDI is formed of 10 items; pain intensity level, personal care, lifting, reading, headaches, concentration, work, driving, sleeping and recreation [21].

Hot packs: Commercially available hot packs are usually made of bentonite, a hydrophilic silicate gel, covered with canvas. Bentonite is used for this application because it can hold a large quantity of water for efficient delivery of heat. These types of hot packs are made in various sizes and shapes designed to fit different areas of the body. They are stored in hot water kept at about 70° C to 75° C inside a purpose-designed, thermostatically controlled water cabinet (hydrocollator) that stays on at all times. This type of hot pack initially takes 2 hours to heat and 30 minutes to reheat between uses [22].

Assessment Procedure

Visual Analog Scale: It was used to measure the intensity of pain pre and post treatment. It is a vertical or horizontal line graduated by

different levels of pain starting from (0 - no pain) till (10- worst pain). The VAS is a reliable and valid tool for the quantification of perceived pain [23].

Measurement of latency and amplitude of dermatomal somatosensory evoked potential procedures:

Patient was seated comfortably on a stool as the Mulligan technique was conducted. Skin overlying the dermatome, was carefully washed using methylated alcohol, and then dried by rubbing the skin with dry clean cotton wool to reduce skin resistance. The site of stimulation for C6 was about 7cm above the styloid process of the radius and for C7 between the second and third metacarpal bones. A bipolar electrode was used for stimulation with inter electrode distance of 2.5 cm with the stimulation cathode placed proximally. The sensory threshold for electrical stimulation was determined by increasing the intensity of electrical current until the patient reported its sensation as tolerable and painless stimulus intensity was usually set at 2.5 times above this level. Recording was done with 9 mm diameter tin/lead electrodes affixed with cream to abraded skin. The recording electrodes were placed at C3 and C4, while the reference electrode was placed at Fz and the ground electrode at Fpz. The cortical responses were amplified, average and displayed using an analysis time of 150ms. Filter setting of 2Hz to 1 KHz was utilized. Surface electrodes secured to the patients by filling the cub aspect of the electrode by an electrolyte paste, and then it was firmly pressed against the prepared skin. A cotton ball was placed on top of the electrode to prevent the paste from drying out and to allow a larger contact surface. Changes in the latency and/or amplitude of the response can indicate dysfunction in the neural pathway being monitored [24,25].

Intervention

Conventional physiotherapy treatment: It was given for all patients. The program included the following exercises: Stretching for Upper trapezius muscles and for neck rotators. The patient was asked to hold for 30 seconds, rest for 30 seconds and repeated three times and isometric strengthening exercises for neck rotators, extensors, side bending muscles. The

exercise was repeated for ten repetitions per session. In addition to, Electric hot pack was placed over the neck and upper part of shoulders musculature. This was being applied for ten min [26].

Mulligan (SNAGS) technique application group:

A pilot study was conducted on five patients and revealed that rotation Mulligan technique (SNAGs) was more effective than extension, flexion and side bending Mulligan techniques (SNAGs) ,so in the current study rotation Mulligan technique for C6,C7 was conducted accordingly. The patient seated comfortably on a stool. The therapist stand behind the patient and the medial border of one thumb’s distal phalanx is placed on the articular pillar on the chosen side of the suspected site of lesion. The thumb nail slope at approximately 45degree (in the direction of the eyeball). The therapist’s other thumb reinforces this. This means if the patient has lesion at cervical C6/7 so the therapist’s thumb was on the cervical 6th articular pillar. However when “SNAGGING” on the right ,the right thumb placed on the right pillar and push up with the left .When “SNAGGING” on the left the left thumb would be on the left pillar. The therapist’s other fingers comfortably placed laterally on each side of the neck or upper anterolateral thorax to prevent the neck from flexing. While the facet is being maintained, the patient was asked to turn his head slowly in the restricted painful direction. As the head rotates, the therapist follow with his hands to ensure that the mobilization take place with the movement then get the patient to apply sustained overpressure for few seconds at approximately 45degree in the direction of the eyeball. Mobilizations were repeated six times and the movements were re-assessed [27].

LLLT Treatment group: The parameters of the laser beams were chosen on the basis of preliminary results and previous studies. The optical output was tested before and after the end of the trial. Parameters value used, Wavelength 905 nm (red), Laser frequency 5,000 Hz, Maximum power output 25 mW, Diode surface 1 cm², Power density 12 mW/cm², Energy 2 J/point. Energy density 2 J/cm² at each point, Treatment time 120 seconds at each point, Daily energy

delivered 12 J, Total energy delivered 180 J. Application mode Probe held stationary in contact with skin, Anatomical site Local transforaminal (2.5 cm and 3.5 cm laterally from spinous process of involved (C6, C7) and the two next distal segments) [28,29].

Data Analysis: The Statistical Package of Social Sciences (SPSS) for windows version 19.0 was used to analyze the data. Analysis was done for 50 patients who completed the study. Paired t-test was used for comparing the pretreatment and post-treatment scores of each variable for both the groups (within group analysis). Independent t-test was performed to check the homogeneity of subjects before intervention and also to compare the effect of both the intervention on the various outcome (between group analyses). Statistical significance was set at P < 0.05. P value > 0.05 was considered as non-significant difference while P value < 0.05 was considered to have represented a significant difference. Value of confidence interval was set at 95%.

RESULT

General Characteristics of the Subjects: Data were collected from 50 subjects from both sexes. Subjects were divided into two equal groups. As shown in table (1) mean age, weight and height were (47.08±5.87) years, (73.64±8.05) kg, and (167.7±6.1) cm respectively for group A. The mean age, weight and height were (48.72±4.64) years, (76.84±5.6) kg, and (170.7±5.55) cm respectively for group B. There were no significant differences between two groups in their age, weight and height.

Table 1: General Characteristics of subjects in both groups.

General characteristics	Group A Mean ±SD	Group B Mean ±SD	t-value	P-value
Age (yrs)	47.08±5.87	48.72±4.64	-1.095	0.279
Weight (kg)	73.64±8.05	76.84±5.6	-2.13	0.081
Height (cm)	167.7±6.1	170.7±5.55	-1.78	0.11

Comparison of pre and post study for group A:

Neck disability index: As shown in table (2), the mean values and SD of NDI for group A pre and post-study was (31.55 ± 3.95) and (24.4 ± 4.31) degrees respectively. There was significant difference between pre and post-study in

NDI, where P-values were (0.000).

Pain level: The mean values and SD of pain pre and post-study were (8.24±1.09) and (5.52±1) respectively. There was significant difference between pre and post-study in pain level, where P-values were (0.000).

EMG tests

Amplitude: As shown in table (2), the mean values and SD of amplitude for group A pre and post-study was (1.54± 0.75) and (2.05± 0.9) degrees respectively. There was significant difference between pre and post-study in amplitude, where P-values were (0.000).

Latency: The mean values and SD of latency pre and post-study were (20.4±1.68) and (19.96±1.7) respectively. There was significant difference between pre and post-study in latency, where P-values were (0.002).

Table 2: Pre-study post-study mean values of measured variables for group A.

Group A	pre-study Mean ±SD	post-study Mean ±SD	t-value	P-value	
NDI	31.55 ± 3.95	24.4± 4.31	15.5	0	
Pain level	8.24±1.09	5.52±1	25.11	0	
EMG tests	Amplitude	1.54± 0.75	2.05± 0.9	-8.77	0
	Latency	20.4±1.68	19.96±1.7	3.48	0.002

Comparison of pre and post study for group B:

Neck disability index: As shown in table (3), the mean values and SD of NDI for group B pre and post-study was (31.13± 4.46) and (22.64± 4.13) degrees respectively. There was significant difference between pre and post-study in NDI, where P-values were (0.000).

Pain level: The mean values and SD of pain pre and post-study were (8.6±1.29) and (2.5±1.1) respectively. There was significant difference between pre and post-study in pain level, where P-values were (0.000).

EMG tests

Amplitude: As shown in table (3), the mean values and SD of amplitude for group pre and post-study was (1.48± 0.9) and (3.43± 1.6) respectively. There was significant difference between pre and post-study in amplitude, where P-values were (0.000).

Latency: The mean values and SD of latency pre and post-study were (21.74±1.62) and (19.5±1.49) respectively. There was significant

difference between pre and post-study in latency, where P-values were (0.002).

Table 3: Pre-study post-study mean values of measured variables for group B.

Group B	pre-study Mean ±SD	post-study Mean ±SD	t-value	P-value	
NDI	31.13 ± 4.46	22.64± 4.13	7.88	0	
Pain level	8.6±1.29	2.5±1.1	24.56	0	
EMG tests	Amplitude	1.48± 0.9	3.43± 1.6	-7.97	0
	Latency	21.74±1.62	19.5±1.49	6.66	0

Pre study means values between both groups:

Neck disability index: As shown in table (4), the mean values and SD of NDI for groups (A and B) before the study were (31.55 ± 3.95), (31.13 ± 4.46) degrees respectively. There was no significant difference between two groups pre-study in NDI, where P-values were (0.726).

Pain level: As shown in table (4), the mean values and SD of pain for groups (A and B) before the study were (8.24±1.09), (8.6±1.29) respectively. There was no significant difference between two groups pre-study in pain level, where P-values were (0.292).

EMG tests

Amplitude: As shown in table (4), the mean values and SD of amplitude for groups (A and B) before the study were (1.54± 0.75), (1.48± 0.9) respectively. There was no significant difference between two groups pre-study in amplitude, where P-values were (0.787).

Latency: As shown in table (4), the mean values and SD of latency for groups (A and B) before the study were (20.4±1.68), (21.74±1.62) respectively. There was no significant difference between two groups pre-study in latency, where P-values were (0.27).

Table 4: Pre-study mean values of subject's measured variables for both groups.

pre-study	Group A Mean ±SD	Group B Mean ±SD	t-value	P-value	
NDI	31.55 ± 3.95	31.13 ± 4.46	0.352	0.726	
Pain level	8.24±1.09	8.6±1.29	-1.06	0.292	
EMG tests	Amplitude	1.54± 0.75	1.48± 0.9	-2.84	0.787
	Latency	20.4±1.68	21.74±1.62	0.272	0.27

Post study mean values between both groups

Neck disability index: As shown in table (5), the mean values and SD of NDI for groups (A and B) after the study were (24.4± 4.31), (22.64± 4.13) degrees respectively. There was no significant difference between two groups post-

study in NDI, where P-values were (0.156).

Pain level: As shown in table (5), the mean values and SD of pain for groups (A and B) after the study were (5.52±1), (2.5±1.1) respectively. There was no significant difference between two groups post-study in pain level, where P-values were (0.128).

EMG tests

Amplitude: As shown in table (5), the mean values and SD of amplitude for groups (A and B) after the study were (2.05± 0.9), (3.43± 1.6) respectively. There was no significant difference between two groups post-study in amplitude, where P-values were (0.132).

Latency: As shown in table (5), the mean values and SD of latency for groups (A and B) after the study were (19.96±1.7), (19.5±1.49) respectively. There was no significant difference between two groups post-study in latency, where P-values were (0.328).

Table 5: Post-study mean values of subject's measured variables for both groups.

post-study	Group A Mean±SD	GroupB Mean±SD	t-value	P-value	
NDI	24.4± 4.31	22.64± 4.13	1.44	0.156	
Pain level	5.52±1	2.5±1.1	12.81	0.128	
EMG tests	Amplitude	2.05± 0.9	3.43± 1.6	-3.43	0.132
	Latency	19.96±1.7	19.5±1.49	0.988	0.328

DISCUSSION

There is a significant amount of evidence available to support the use of physical therapy interventions for patients with cervical radiculopathy, and the benefit of physical therapy and manual techniques in general for patients with neck pain with or without radicular symptoms [30]. This study to his study was conducted to assess the efficacy of Mulligan mobilization and LLLT on pain intensity level, EMG dermatomal somatosensory evoked potential and functional level in patients with cervical radiculopathy.

The findings in this research revealed a significant improvement post-treatment in both groups.

In Mulligan's group, the improvement in pain, shoulder mobility and functional disability could be because of Mulligan's mobilization with movement which is a combination of an active movement with simultaneous passive accessory

mobilization which helps in rapid restoration of movement. MWM technique found to be effective by neurophysiological mechanism of production of initial hypoalgesia based on stimulation of peripheral mechanoreceptors and the inhibition of nociceptors and altering sympathetic nervous system, and biomechanical concept of positional fault correction. This treatment technique produces a total and immediate pain relief during the treatment application. One explanatory mechanism underlying this manipulative therapy induced pain modulation is the activation of the descending pain inhibitory system within the central nervous system [31]. The active movement in this technique stimulates the proprioceptive tissues, such as the golgi tendon organ by tendon stretch.40 MWM repositions the joint, causing it to track normally [32]. MWM passively stretches the tightened soft tissues and shoulder capsule in adhesive capsulitis and thereby restores the normal extensibility of the shoulder capsule and tight soft tissues. This initial effect is sufficient to stimulate the long term changes in nociceptive and motor system dysfunction that are reflected in pain relief and improved function [33].

The Mobilizations with movement (MWM) for peripheral joints has been developed by Mulligan. MWM can be used in isolation or integrated with other manual approaches to improve the quality of joint intra articular gliding, neurodynamics and the facilitation of correct muscle recruitment. It is a combination of an active movement with simultaneous passive accessory mobilizations, to achieve painless movement by restoring the reduced accessory glide. In essence, the limited painful physiological movement is performed actively while the therapist applies a sustained accessory glide at right angles or parallel to the joint to restore a restricted, painful movement to a pain free and full range state. The combination of joint Mobilization with active movement may be responsible for the rapid return of pain free movement [34].

Neurophysiologic mechanism is another mechanism by which MWM has been believed to relieve pain. According to paungmali et al MWM produces a hypoalgesia and concurrent sympathetic excitation. This finding of initial sympatho

excitation was similar to that reported previously with oscillatory manual therapy of cervical spine. It has been previously proposed that the combination sympathoexcitation, non opioid hypoalgesia and improvement in motor function are indirect signs of possible involvement of endogenous pain inhibitory systems in manual therapy treatment effects [6].

Pain declined significantly in MWM group. A Paungmali (2004) showed that MWM produces sensory input sufficient to recruit and activate descending pain inhibitory systems that result in some or all of the pain relieving effects. It produces hypoalgesic effects during and following its application, as well as sympathoexcitatory effect [35]. Bill Vicenzino (2006) hypothesized that malpositioning of the ulna and radius occurs in relation to humerus in tennis elbow, the reduction of pain could be due to repositioning of the ulna and radius with respect to humerus achieved by lateral glide to elbow joint [36]. Both groups received conventional exercises. These exercises also might have shown the added effect in the both groups. In a recent study by Anap DB et al [37], 40 subjects were randomly assigned into 2 groups. One group was given MWM along with conventional physiotherapy and the other received conventional physiotherapy alone. They concluded that MWM treatment technique produced significant improvement in Pain free grip strength combined with the conventional physiotherapy ($t=5.45, p<0.01$).

The mechanism by which manipulation works is poorly understood. Manual therapy is used quite often for the spine and peripheral joints, despite of the inability of clinicians to accurately diagnose the pathway at which a manipulation is targeted. In people with low back pain and neck pain, spinal manipulation is thought to free motion segments that have undergone disproportionate displacements and to relax muscles by sudden stretching [38].

In low-level laser therapy's group, the improvement in pain, shoulder mobility and functional disability could be explained by many experimental and clinical studies that have shown analgesic and anti-inflammatory potential of low-level laser therapy (LLLT) in a dose-dependent manner [39,40]. It has been shown to be a low risk and safe treatment, but its true

efficacy is controversial. LLLT was demonstrated to modulate the inflammatory, proliferative, and remodeling phases of the healing process [41,42]. Important additional effects appear to include a direct influence on neural structures that are damaged by compression or inflammation, and this significantly improves nerve recovery [43].

Additionally, the peripheral nerve endings of nociceptors, consisting of the thinly myelinated A" and unmyelinated, slow-conducting C fibers, lie within the epidermis. This complex network transduces noxious stimuli into action potentials. Moreover these nerve endings are very superficial in nature and thus are easily within the penetration depths of the wavelengths used in LLLT. The cell bodies of neurons lie within the dorsal nerve root ganglion, but the elongated cytoplasm (axons) of the neurons extends from the cell body to the bare nerve endings in the surface of the skin. The direct effect of LLLT are initially at the level of the epidermal neural network, but the effects move to nerves in subcutaneous tissues, sympathetic ganglia, and the neuromuscular junctions within muscles and nerve trunks. LLLT applied with a sufficient level of intensity causes an inhibition of action potentials where there is an approximately 30% neural blockade within 10 to 20 minutes of application, and which is reversed within about 24 hours. The laser application to a peripheral nerve does have a cascade effect whereby there is suppressed synaptic activity in second order neurons so that cortical areas of the pain matrix would not be activated [44].

It has been shown that LLLT at the correct dose decreases mitochondrial membrane potential (MMP) in DRG neurons and that ATP production is then reduced [45] so perhaps the lack of ATP could be cause of this neural blockade. The most immediate effect of nociceptor blockade is pain relief which occurs in a few minutes and has been shown by the timed onset of a conduction blockade in somatosensory-evoked potentials (SSEPs). This inhibition of peripheral sensitization not only lowers the activation threshold of nerves, but also decreases the release of pro inflammatory neuropeptides [44].

Moreover, LLLT may have a direct effect on nerve structures, which could increase the speed of

recovery of the conductive block or inhibit A-d and C fiber transmission [45,46]. It is possible that laser-induced neural blockade may then lead to a long-term alteration in nociception [47], analogous to the prolonged analgesia seen in some patients after the administration of local anesthetics [48] and changes at the endorphin level [49]. However, the neuromodulation effects of LLLT are dependent on many conditions in relation to timing and mode of irradiation and rarely have been observed for 904 nm laser sources.

CONCLUSION

Study concludes that comparison between the groups where intervention given in form of LLLT and SNAGs Mulligan technique in patients with unilateral cervical radiculopathy did not show statistically significance differences between them, but both techniques have shown positive results and improvements in pain intensity, EMG dermatomal somatosensory evoked potential and functional level.

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Conflicts of interest: None

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