RESEARCH ARTICLE

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Effect of Neural Tissue Mobilization on Sensory-Motor Impairments in Breast Cancer Survivors with Lymphedema: An Experimental Study

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Abstract

Background: Breast surgery, Axillary Lymph Node Dissection (ALND), radiation and chemotherapy may develop several complications such as axillary web syndrome, frozen shoulder, numbness, shoulder pain and range of motion restriction, lymphostasis, and lymphedema. Up to 77% report sensory disturbance in the breast or arm after breast surgery. These short- and long-term consequences have dramatic impact on physical function and quality of life in this population. **Aims:** The aim of the study was to determine the effect of neural tissue mobilization on sensory-motor impairments in breast cancer survivors with lymphedema. **Subjects and Methods:** This study was carried out by analyzing total 100 breast cancer survivor women, with lymphedema aged between 30-65 years of age who had undergone breast surgery mostly lumpectomy along with chemotherapy or radiation therapy. Participants were divided into two groups by random allocation. One group underwent neurodynamic mobilization and the other group conventional physiotherapy.The treatment protocol was given for 6 weeks. Parameters such ROM, pain, lymphedema and sensory-motor impairments were assessed at the baseline before the treatment and 6 weeks after the treatment. **Result:** The result from this study shows that there is significant improvement ($p<0.0001$, t-value 4.69) in mTNS of patients undergoing neural tissue mobilization,whereas there was no significant improvement ($p=0.05$, t-value 1.951) seen in patients undergoing conventional physiotherapy. **Conclusion:** This study concludes that effect of neural tissue mobilization has significant impact on sensory motor impairments as compared to conventional treatment protocol in breast cancer survivors with lymphedema.Pain and ROM showed similar difference with both the treatment protocols. It was also observed that patients with mild and moderate lymphedema showed significant improvement as compared to patients with severe lymphedema.

Keywords: Lymphedema- neuropathic pain- range of motion- sensory-motor impairments

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Introduction

Cancer is a group of disease resulting from uncontrolled growth and spread of abnormal cells which if further not controlled may result in death. It can be Genetic as well as epigenetic (Liliana et al., 2021). Cancer causes more deaths than AIDS, tuberculosis and malaria combined (Blecher et al., 2011). The overall 0–74 years risk of developing cancer is 20.2% (22.4% in men and 18.2% in women, respectively). A total number of 18 million new cases have been diagnosed in 2018, the most frequent of which are lung (2.09 million cases), breast (2.09 million cases), and prostate (1.28 million cases) cancers (Mattiuzzi and Lippi, 2019).

Breast Cancer is the most frequent malignancy worldwide in women and is curable in ~70-80% patient with initial stage, non-metastatic disease. Breast cancer is highly heterogeneous disease encompassing multiple types and subtypes majority of them responds to endocrine and generally have good prognosis and survival rate but significant proportion of breast cancer are triple negative breast cancer. Triple negative breast cancer is a subtype characterized by lack of expression of most targeted biomarkers such as Estrogen receptors (ER) Progesterone receptor (PR) human epidermal growthy factor receptor (HER-2) known for its more aggressive clinical behaviour poor prognosis higher recurrence rates and less survival rates (Wu and Hicks, 2021). It is common in Asian population and an estimated 1 in 7 women will develop breast cancer at some time in her life (Loh and Quek, 2011). The incidence of breast cancer (BC) among women has continued to increase within

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the last decade in spite of screening mammography and the reduction of mortality. Various forms of surgeries are done for management of breast cancer patients such as radical mastectomy, modified radical mastectomy and breast conserving surgery (De GRoef et al., 2016). Axillary lymph node dissection (ALND), another method is commonly employed as a procedure for diagnosing and treating positive lymph nodes.

However, several consequences may develop after breast surgery, ALND, radiation and chemotherapy, such as axillary web syndrome, frozen shoulder, numbness, shoulder pain and range of motion (ROM) restriction, lymphostasis, and lymphedema (Johansson and Branje, 2010). Up to 77% report sensory disturbance in the breast or arm (Smoot et al., 2014). These short-term and long-term consequences have dramatic impact on physical function and quality of life in this population (Le VH et al., 2016; Norman et al., 2009; Shinde and Pati, 2020).

The lymphatic comprises a one-way transport system for fluids and proteins by collecting them from the interstitial space and returning them to blood circulation. As blood travels from the branching arteries down to the smallest capillaries, plasma fluid and proteins are forced out into the interstitial space most of exudatesget reabsorbed into the post capillary venules, but because of osmotic forces resulting from protein extravasation, there is small net fluid flux out of vasculature. This excess fluid is converted through the interstitium and into the initial lymphatics, which are freely permeable to macromolecules and thus serve a primary role in maintaining osmotic and hydrostatic pressure within the tissue space (Swartz, 2001)

Edema is a condition of tissue fluid imbalance often resulting from infection, trauma, surgery, and tissue grafting and Lymphedema occurs when the draining of lymphatic fluid ceases to work and fluids accumulate in the tissue. This leads to the development of swelling (Johansson and Branje, 2010). The pathological basis of edema can be described by considering lymph formation as passive process that is intrinsically linked to interstitial fluid movement and governed by mechanical forces. The first step in development of edema is an offset in mechanical equilibrium which occurs by blockage of lymph nodes, build-up of osmotic pressure within the interstitium, damage to lymphatic connection or changes in mechanical properties or composition of extra cellular matrix. Such swelling and imbalance are becoming more and more common as secondary effect of radiation therapy and surgical procedure such as mastectomy (Brennan et al., 1996).This condition may be reversible and effective treatment includes compression bandaging, wearing a sleeve/glove, manual lymphatic drainage and pneumatic pumping (Johansson and Branje, 2010; Jaju and Shinde 2019). If the edema is allowed to progress without treatment the volume will increase, and the arm will get heavy and cause discomfort and pain (Johansson andBranje , 2010; Casley-Smith, 1995). Breast cancer-related lymphedema results from impaired lymph transport due to surgical removal of or radiation-induced damage to axillary lymph nodes and lymphatic channels, which leads to accumulation of lymph in the UE, chest, or trunk (Smoot et al., 2014).

Neural tissue mobilization also called as neuro dynamics which refers to the communication between the different parts of the nervous system and to the nervous system relationship to the musculoskeletal system. Neurodynamic in the sense implied here is the mobilisation of the nervous system as an approach to physical treatment of pain. This mobilisation activates a range of mechanical and physiological responses in nervous tissue such as neural sliding, pressurisation, elongation, tension and changes in intraneural microcirculation, axonal transport, and nervous impulse movements (Shacklock, 1995). Women with lymphedema more frequently reported upper extremity symptoms such as pain, ache, numbness, or heaviness in the arm (Sandeep Shinde et al 2022). Sensory disturbances in the affected upper extremity following breast cancer treatment may result from nerve damage during surgery or following radiation, neuropathy due to chemotherapy, or perhaps lymphedema. Adverse neural tension may arise due to inflammation, nerve compression or impaired blood supply. There are studies which focuses more on the effect of neural mobilization on shoulder range of motion as to which the findings of this preliminary study is to focus on the effect of neural mobilization on the sensory-motor impairments in patients with lymphedema.

Materials and Methods

This study was done in a breast cancer survivor support group of tertiary care hospital in Karad. An ethical approval was obtained by Institution. Patients who have completed their treatment i.e chemotherapy, radiotherapy and surgery and have symptoms of sensory-motor impairments along with lymphedema were included in the study. Age group was ranged from 30-65 years old women.

Before initiating the study, all the participants were informed about the study procedure. A written informed consent was obtained from each participant. The demographic data, past surgical history and assessment was obtained from all subjects prior to the treatment given.

Pre test assessment was taken with the use of Visual analogue scale for pain, modified total neuropathy scale for sensory-motor impairments and range of motion. Figure 1.

Data Collection Tools

Pain Intensity: It is a10-point numerical rating scale (0 = no pain; 10 = maximum pain) to assess the intensity of spontaneous neck and shoulder/axillary pain. The patients did not take analgesics or muscle relaxants for 24 hours prior to the assessment.

Range of motion for shoulder was measured by using goniometer. Since there are studies focusing on the different interventional protocols including neural mobilization for shoulder range of motion and time constraint, flexion and abduction were the only two components included in this study.

Measurement of lymphedema was done on the affected upper extremity (usually the one which was operated) and also comparison was done with non-affected side. The lymphedema was measured using an inch tape for segregation of the subjects into mild, moderate, severe

lymphedema.

Sensory-Motor impairments were assessed using the Modified Total Neuropathy Score.

Participants were divided into two groups by random sampling. One group underwent neurodynamic mobilization and the other group conventional physiotherapy. Conventional physiotherapy includes IFT and free active range of motion exercises. The treatment protocol was given for 6 weeks. After 6 weeks post test assessment for pain, sensory-motor impairment, and range of motion was taken.

Statistical analysis

All statistical analyses, including calculation of the mean and standard deviation of pain, assessment, range of motion and manual muscle testing was done using SPSS statistical software (version 21.0 for windows; SPSS, Inc., Chicago, USA). The collected data was statistically analysed using descriptive statistics as percentage, mean standard deviation and unpaired t-test (used to compare results of pre and post intervention of VAS, ROM and mTNS of both the groups). The shoulder mobility of the affected side was analysed and calculated by range of motion. Pain distribution was analysed and calculated using the standard deviation. For lymphedema, girth was measured using an inch tape and analysed by calculating the percentage.mTNSwas analysed using the mean and standard deviation. The outcome measures were assessed at the baseline before the treatment and 6 weeks after the treatment.

Results

The data collected was statistically analysed using descriptive statistics as percentage, mean standard deviation and unpaired t-test (used to compare results of pre and post intervention of VAS, ROM and mTNS of both the groups).

Demographic variables

100 women aged between 30-65 years of age had undergone breast surgery mostly lumpectomy along with chemotherapy or radiation therapy. Out of 100, 48% of women had mild lymphedema, 38% suffered from moderate lymphedema and 18% with severe lymphedema. Women between 51-65 yrs were affected more.

Lymphedema measurement

Lymphoedema was measured using an inch tape. It was observed that 50% patients of group 1 and 46% of group 2 suffered from mild lymphoedema. 32% and 36% of group 1 and group 2 respectively suffered from moderate lymphoedema. Few patients did not seek any preventive measures which accounted for 18% of the patients from both the groups suffering from severe lymphoedema. Table 1 shows Lymphedema Measurement.

Pain

The pain in the upper limb was the consistent finding in all Patients. They were assessed pre intervention and post intervention for pain through Visual Analog Scale (VAS) on activity and VAS at rest for both the groups. Patients of both the groups showed decrease in pain irrespective of different treatment protocols. At activity mean score for group 1 shows decrease in pain from 3.2 to 0.8 and group 2 from 3.2 to 0.42. At rest mean score for group 1 shows decrease in pain from 0.8 to 0.06 and group 2 from 0.8 to 1.05. Statistically it shows that there was extremely significant difference ($p<0.0001$) between pre intervention and post intervention assessment. Table 2 and 3 shows Pain distribution of group 1 and group 2 respectively.

Shoulder range of motion

The shoulder abduction range of motion is seen significantly affected followed by shoulder external rotation and shoulder flexion respectively. Group 1 has significant difference for flexion ($p<0.0001$, t-value 5.728) while for abduction there is very significant difference ($p=0.0072$, t-value 2.746).Group 2 has significant difference for flexion ($p<0.0001$, t-value 5.132) andabduction ($p=0.0223$, t-value 2.323). Both group showed improvement in range of motion and there is not considerable differences between two groups. Table 4 and 5 shows ROM of group 1 and group 2 respectively.

Modified Total Neuropathy Score (MTNS)

It includes six components which are sensory, motor,

Table 1. Lymphedema Measurement of the Affected Patients in Group 1 and Group 2

	Patients with lymphedema Group 1 (n=50) (%)	Patients with Lymphedema Group 2 (n=50) (%)
Mild	25 (50)	23 (46)
Moderate	16 (32)	18 (36)
Severe	9 (18)	9 (18)

Table 2. Pain Distribution of the Patients Affected Pre and Post Intervention at Activity and at Rest of Group 1

	Pre-intervention Mean±SD	Post-intervention Mean±SD	p-value	t-value
At activity	3.2±2.27	0.8±1.16	<0.0001	6.641
At rest	0.8±1.05	0.06±0.239	<0.0001	4.85

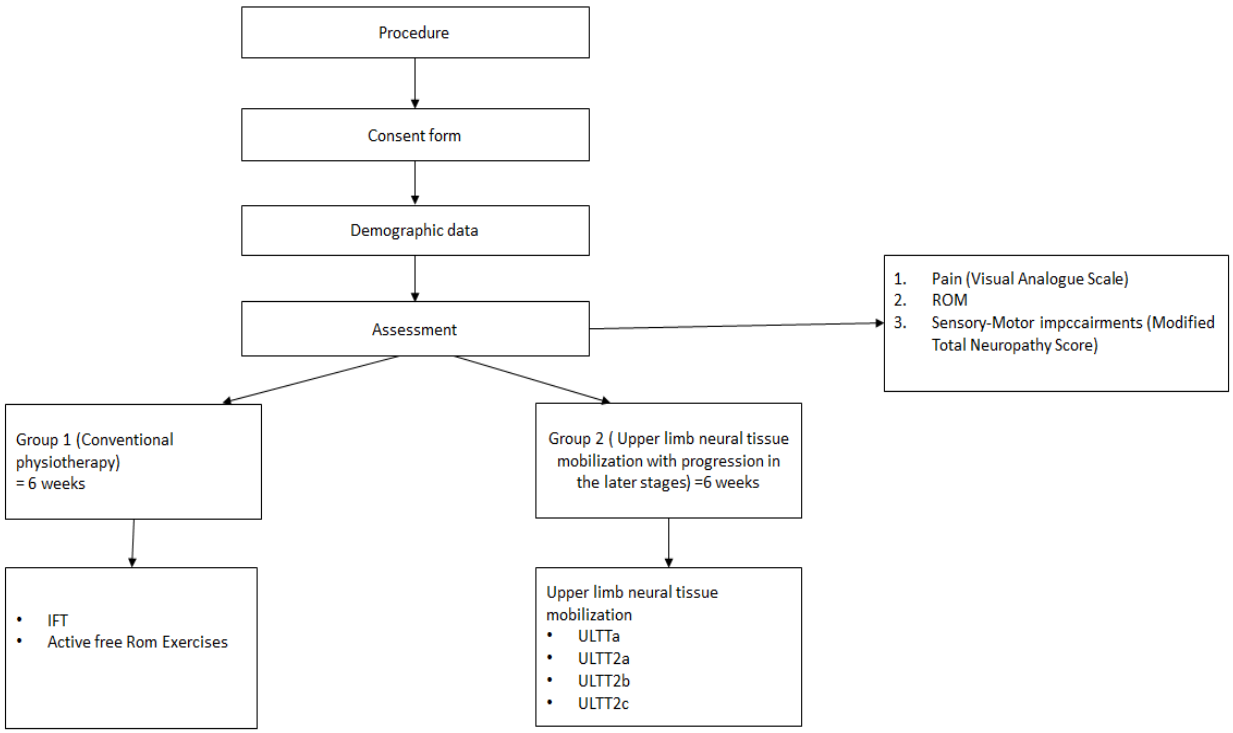

Figure 1. Procedure

Table 3. Pain Distribution of the Patients Affected at Pre and Post Intervention at Activity and at Rest of Group 2

	Pre-intervention Mean±SD	Post-intervention Mean±SD	p-value	t-value
At activity	3.2±2.27	0.42±0.90	<0.0001	8.023
At rest	0.8±0.04	1.05±0.19	<0.0001	5.031

and pin, vibration, motor function and deep tendon reflex. Group 1 shows a significant difference ($p<0.0001$) between pre intervention and post intervention assessment by using neural tissue mobilization for treating sensory motor impairments in breast cancer survivors with lymphedema. Group 2 shows insignificant difference ($p=0.0540$) between pre intervention and post intervention using the conventional treatment protocol. Only the motor function component for both the groups showed significant difference despite of using different treatment protocols.Table 6 and 7 shows mTNS of group 1and group 2 respectively.

Discussion

The purpose of this study was to investigate the effect of neural tissue mobilization in comparison with other conservative techniques for the treatment of sensory motor impairments in breasts cancer survivors with lymphedema. Breast cancer survivors after breast surgery, ALND, radiation and chemotherapy may develop axillary web syndrome, frozen shoulder, numbness, shoulder pain and range of motion restriction, lymphostasis and lymphedema (Johansson and Branje, 2010).

Table 4. ROM Affected Pre and Post Intervention of Group 1

	Pre-intervention Mean±SD	Post-intervention Mean±SD	p-value	t-value
1. Flexion	166.6±9.185	175.3±5.471	<0.0001	5.728
2. Abduction	133.1±10.2	138±10.4	0.0072	2.746

Table 5. ROM Affected Pre and Post Intervention of Group 2

	Pre-intervention Mean±SD	Post-intervention Mean±SD	p-value	t-value
1. Flexion	166.6±9.18	174.5±5.79	<0.0001	5.132
2. Abduction	133±10.2	137±8.87	0.0223	2.323

Table 6. mTNS Affected Pre and Post Intervention of Group 1

	Pre-intervention Mean±SD	Post-intervention Mean±SD	p-value	t-value
Sensory	1.34±1.002	0.4±0.8081	<0.0001	5.163
Motor	1.04±0.9249	0.3±0.6776	<0.0001	4.564
Pin	1.2±1.385	0.4±0.7848	0.0008	3.465
Vibration	1.14±1.212	0.34±0.6884	<0.0001	4.058
Motor Function	1.26±0.694	0.44±0.644	<0.0001	6.123
DTR	0.84±0.9971	0.34±0.7982	0.0067	2.768
Total score	6.8±5.521	2.2±4.031	<0.0001	4.696

Table 7. mTNS Affected Pre and Post Intervention of Group 2

	Pre-intervention Mean±SD	Post-intervention Mean±SD	p-value	t-value
Sensory	1.34±1.002	1.34±1.002	>0.9999	0
Motor	1.04±0.9249	0.5±0.7890	0.0022	3.141
Pin	1.2±1.385	1.12±1.319	0.7681	0.2951
Vibration	1.14±1.212	1.12±1.189	0.9338	0.08328
Motor Function	1.26±0.6943	0.38±0.6667	<0.0001	6.465
DTR	0.84±0.9971	0.34±0.6884	0.0044	2.918
Total score	6.8±5.521	4.8±4.81	0.054	1.951

Many studies report that most cases of lymphedema develop during the first 1-2 years after primary treatment. Adverse neural tension may arise due to inflammation, nerve compression, or impaired blood supply to the area. Up to 77% report sensory disturbance in the breast or arm (Smoot et al., 2014). Lymphedema was measured of affected upper extremity, which was the side usually operated in breast cancer surgery and it was compared with the non-affected upper extremity. Our study found that an age groupbetween 51-65 yrs was affected more than the other age groups. Pain was experienced more on activity and was relieved at rest irrespective of the presence of lymphedema.

All the participants showed decrease in range of motion of flexion and abduction before treatment.Since there are studies focusing on the different interventional protocols including neural mobilization for shoulder range of motion and time constraint, flexion and abduction were the only two components included in this study. Goniometer was used to assess the range of motion. Using the VAS, pain assessment was taken and it was observed that patients with pain also had restricted range of motion. One possible results is that the chemotherapy or radiation therapy can cause peripheral neuropathy due to sensory axonal damage, with reduced amplitude of sensory nerve action potentialsand changes in afferent activity, leading to widespread pain sensitivity (Argyriou et al., 2012; Partridge and Winter, 2004; Wampler, 2006; Wolf, 2008).

The women with lymphedema more frequently reported upper extremity symptoms such as pain, ache, numbness, or heaviness in the arm. Sensory disturbances in the affected upper extremity following breast cancer treatment may result from nerve damage during surgery or following radiation, neuropathy due to chemotherapy, or perhaps lymphedema. Sensory symotoms (tingling, numbness, neuropathic pain and myalgias), motor symptoms (hand dexterity, walking, climbing, combing hair etc.,), pin level sensibility, vibration sensibility, motor functions and reflexes were scored with the use of Modified Total Neuropathy Score.

Patients were randomly divided into two groups. One group was treated with neural tissue mobilization and other group with conventional physiotherapy for 6 weeks. Post intervention assessment shows that patients treated with neural tissue mobilization showed significant difference in decreased pain, improve range of motion and decrease in mTNS as compared to pre intervention assessment. Decrease in neural tension, increased blood supply and free gliding of the nerves lead to improvement in these symptoms Patients treated with conservative treatmentwhich more focuses on the relieving pain and increases ROM showed significant improvement in ROM, strength and decrease in pain as compared to improvement in sensations and other motor functions. For both the groups it was also observed that patients with mild and moderate lymphedema showed significant improvement as compared to patients with severe lymphedema which is a lifelong complication and difficult to treat. There are studies which show the effect of neural mobilization on shoulder range of motion. After assessing the patients it was noted that most of the patients suffering from lymphedema be it mild, moderate or severe had sensory-motor impairments. There are many studies which show the effects of neural tissue mobilization on pain, range of motion and other conditions and focus less on sensory-motor impairments. Our study focuses

on neural tissue mobilization as an intervention to treat sensory-motor impairments in breast cancer survivors with lymphedema and showed significant improvement.

Several limitations should be recognised in this study. Range of motion for elbow and wrist are not assessed which can be assessed and noted for future studies. The findings of the current study show the need for rehabilitation programs in combination with neural tissue mobilization for the treatment of sensory-motor impairments in breast cancer survivors. In view of our results, the health care providers should take in to account neural tissue mobilization as an intervention to treat sensory-motor impairments in breast cancer survivors with lymphedema.

In conclusion, on the basis of results neural tissue mobilization has showed significant improvement in patients with mild and moderate lymphedema as compared to patients with severe lymphedema.This study concludes that effect of neural tissue mobilization has significant impact on sensory motor impairments as compared to conventional treatment protocol in breast cancer survivors with lymphedema.Pain and ROM showed similar difference with both the treatment protocols. It was also observed that patients with mild and moderate lymphedema showed significant improvement as compared to patients with severe lymphedema.

Abbreviations

ALND, Axillary Lymph Node Dissection; IFT, Interferential Therapy; ROM, Range of Motion; VAS, Visual Analogue Scale; BC, Breast cancer; mTNS, Modified Total Neuropathy Score

Author Contribution Statement

Joshi Devanshi conducted literature review for this manuscript, developed an introduction section of manuscript, conducted the discussion of the study, findings, collected data and analysed the data. Dr. Shinde Sandeep provided a description of the background information, collected data and analysed the data and participated in prescription of the manuscript, all the authors read and approved the final manuscript.

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Ethical Committee

The study was approved by institutional ethical committee of Krishna Institute of Medical Sciences Deemed to Be University, Karad, Maharashtra.

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Statement conflict of Interest

The authors claimed that there are no conflicts of interest concerning the content of the present study.

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