

Stellate Ganglion Block: Comparison of Different Doses of Ketorolac After Breast Cancer Surgeries

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ABSTRACT

Background: Despite advances in breast conservation therapy, upper limb edema is still a typical concern for those who have undergone treatment for breast cancer.

Objective: The purpose of this research was to evaluate the effects of a fixed dose of lidocaine combined with two different doses of ketorolac for stellate ganglion block (SGB) for decreasing pain and size of post mastectomy upper limb lymphedema after breast cancer surgery

Patients and methods: Forty patients that underwent mastectomy were randomly assigned to one of two research groups in this prospective randomized study (20 patients in each group) received either ultrasound guided SGB with solution of 4 ml lidocaine 2% & 15 mg ketorolac in total volume 10 ml (group 1) or ultrasound guided SGB with solution of 4 ml lidocaine 2% & 30 mg ketorolac in total volume 10 ml (group 2). Assessment was done after SGB for 3 weeks by collecting data of total analgesic consumption as primary outcome, first analgesic request, VAS score and arm circumference.

Results: Total analgesic dose /tablet was significantly decreased 19 (4-30) in group 2 versus 34 (20-63) in group 1, first analgesic request /hours 8 (5-54) in group 2 versus 4 (2-8) in group 1. At 2 and 3 weeks post-block, there was a significant reduction in group members' arm circumference both 5 and 10 centimeters above and below the elbow crease.

Conclusion: Higher dose of ketorolac could be associated with better analgesia, lower VAS score and with more upper limb lymphedema size reduction post-mastectomy.

Keywords: Upper limb lymphedema, Stellate ganglion block, Ketorolac.

INTRODUCTION

Lymphedema is a chronic condition that can arise as a result of axillary lymph node dissection (ALND) and is associated with a plethora of issues, including discomfort, impaired function, an unattractive appearance, and even psychological distress. Furthermore, it can negatively impact the quality-of-life (QOL) of breast cancer patients⁽¹⁾. In addition to psychological morbidity, women who suffer from lymphedema have experience of anxiety, depression and social isolation⁽²⁾. In spite of the advent of breast conservation therapy, arm swelling is still a prevalent issue for those who have undergone treatment for breast cancer. Complex decongestive therapy (CDT), also known as lymphatic physiotherapeutic intervention, is the gold standard for the effective management of lymphedema involving physical exercise, skin care, manual lymph drainage (MLD), bandages of compression, lymphedema self-management training throughout the long term as well as stocking compression. However, CDT is not useful for treating persistent large lymphedema when there is also an obesity component as the newly produced adipose tissue that persists under the skin after microsurgery frequently prevents successful limb reduction⁽³⁾.

Lymphedema is a condition that, if left untreated, can worsen over time, making an early diagnosis crucial. If the right therapeutic measures are taken quickly enough, it may be possible to stop the progression and even bring the limb back to normal⁽⁴⁾.

The stellate ganglion block (SGB) is a common method for relieving chronic pain. Anatomically, the inferior cervical ganglion sits between the seventh

cervical and first thoracic vertebrae. When the inferior cervical ganglion fuses with the first thoracic ganglion, the resulting structure is called a stellate ganglion and located anterior to the C7 transverse process, it is lateral to the longus colli muscle and the trachea, medial to the scalene muscles, and medial to the recurrent laryngeal nerve⁽⁵⁾.

Lymphedema patients can benefit from a stellate ganglion block (SGB), which was first used to treat the condition in 1983 by **Swedborg et al.**⁽⁶⁾ taking into account the hypothesis that the overlap between the sympathetic nervous system and the blocked veins causes the veins to relax and the post-capillary resistance to decrease, thereby releasing the collected interstitial fluid into the venous system⁽⁷⁾. When opposed to steroids, NSAIDs like ketorolac have fewer and milder adverse effects, yet they nevertheless provide analgesic, anti-inflammatory, and antipyretic relief. Inhibition of prostaglandin production is the primary mechanism by which ketorolac and other NSAIDs produce their pharmacological effects. Evidence suggests that NSAIDs may potentially operate centrally, despite the fact that their effects are primarily seen at the periphery⁽⁸⁾.

This study was done to compare between adding 2 different doses of ketorolac to fixed dose of lidocaine local anesthetic for stellate ganglion block as a method for decreasing pain and size of post mastectomy upper limb lymphedema after breast cancer surgery with total analgesia requirements in 3 weeks after the injection as a primary outcome. While, the first requested analgesia, visual analogue (VAS) score, the arm circumference after the block, lymphedema and breast cancer

questionnaire (LBCQ) score were the secondary outcome.

PATIENTS AND METHODS

At the Oncology Center, Mansoura University (OCMU), we conducted this randomized comparative study with blinding for both participants and researchers. Forty female patients aged between 20 to 70 years old with post mastectomy upper limb lymphedema were interviewed and enrolled in this study after obtaining written informed consent.

Inclusion criteria: Adult female (twenty to seventy years) of grades I, II ASA physical status complaining of post mastectomy upper limb lymphedema and post mastectomy chronic pain.

Exclusion criteria: Patients with infection at the area of injection, coagulopathies, distant metastasis, cardiac, diabetic or hepatic patients, hypersensitivity to NSAIDs, deformity at the site of injection and patients who refused to participate in the study.

Sample size calculation: The percentage of patients needing analgesics by the third week was used to determine the sample size. Comparing two proportions in G*power 3.0.10(0.486 & 0.056) for control and intervention groups ,2-tailed, with α error = 0.05 and power = 80.0% and effect size = 1.06, and the calculated sample size was 16 patients in each group , the total number will be increased to be 20 patients in each group after adding 20% to avoid drop out.

Randomization: Using a closed envelope procedure, patients were randomly assigned to one of two groups (a convenient sample size of 20 patients per group):

Group 1: Patients received solution of 4 ml lidocaine 2% mixed with 15 mg ketorolac in total volume 10 ml.

Group 2: Patients received solution of 4 ml lidocaine 2% mixed with 30 mg ketorolac in total volume 10 ml.

Patient's preparations:

Routine investigations included bleeding profiles (bleeding time, clotting time, INR, complete blood count (CBC), kidney function as well as liver function tests were carried out. Demographic information, time since mastectomy (month), type of surgery, from their health records, we identified if they had lymph node dissection, if they had lymph node metastasis, and if they had radiation or chemotherapy.

Technique:

It is ultrasound guided lateral approach for SGB⁽⁹⁾. The patient was positioned in the supine position, put on monitor (pulse oximetry and blood pressure) and started I.V line for fluid replacement according to body weight and fasting hours. The neck was extended to

stretch the esophagus and move it medially. A minor rotation toward the opposite side of the process was acceptable. In this case, the block was performed on the same side as the injured limb. The patient's neck was thoroughly cleansed and dressed with sterile materials. Thyroid, trachea, carotid artery, internal jugular vein, vertebral artery, and longus colli muscle covered with prevertebral fascia were identified in a preliminary ultrasound scan (TOSHIBA UICW-660A Ultrasonography). The transverse process at C6 can be distinguished from those at C5 and C7 by the size and prominence of their respective anterior tubercles. Two milliliters of lignocaine at a concentration of 2% were injected topically to numb the skin. The spinal needle used was either 22, 23, or 25 G gauge. Needle was inserted medially until it passed through the deep cervical fascia, just above the longus colli muscle, keeping the puncture in the plane necessary to see the needle's tip at all times. When injecting the medications, ten millimeters were used while keeping an eye on the incision made between the carotid artery and the longus colli muscle. The patient was promptly seated. Two to four hours were spent in the recovery room evaluating the patient for any unexpected changes.

Signs of a successful block

An increase in body temperature of at least 1-degree Celsius, conjunctival flushing and lacrimation, nasal congestion and Guttman's sign "stuffiness of the nostril," anhidrosis, vasodilatation, and Horner's syndrome.

Assessment

The total analgesia requirement in 3 weeks after block and the first request analgesia after block were recorded from patients. Visual analogue (VAS) score was displayed as a horizontal line of 100 millimeters on which the patient's pain intensity was represented by a point somewhere between the extremes of "no pain at all" and "worst pain," yielding a range of scores from 0 to 100⁽¹⁰⁾. It was used before the block and 1, 6, 12, 18, 24, and 48 hours after the block, then after 1-, 2- and 3-weeks post-injection.

Arm circumference was taken four times, five centimeters and ten centimeters above and below the elbow crease to get a baseline reading. The OCMU held it again 1, 2, and 3 weeks following the block. Breast cancer and lymphedema questionnaire (LBCQ)⁽¹¹⁾ was performed in the OCMU before injection, at 1, 2, and 3 weeks after injection (**Table 1**). The number of patient's answers with yes about above symptoms before and after thoracic sympathetic ganglion block is the score. Any recorded complications related to the block as transient voice hoarseness and sensation of throat foreign body, Horner's syndrome, bruising, swelling and pain were recorded.

Table (1): Lymphedema and breast cancer questionnaire (LBCQ)

(11)

Question	Score
Do you have limited movement of your :	1) Shoulder
	2) Elbow
	3) Wrist
	4) Fingers
Do your arm or hand feel weak +/- Have you had	5) Aching
	6) Blistering
	7) Breast swelling
	8) Chest wall swelling
	9) Firmness
	10) Heaviness
	11) Tightness
	12) Increased temperature in your arm
	13) Numbness
	14) Rashes
	15) Redness
	16) Stiffness
	17) Swelling
	18) Swelling with pitting
	19) Tenderness

Ethical considerations:

The Institutional Review Board of Mansoura University Hospital in Egypt gave their permission to the study (MS.19.11.928). Patients were interviewed, and their signed informed consents to participate in our study were obtained. All

procedures in this study involving human participants were performed in conformity with the principles outlined in the Declaration of Helsinki, developed by the World Medical Association.

Statistical analysis:

We used SPSS (Statistical Package for the Social Sciences) version 22 to examine the data. Quantitative data was described as means and standard deviations, medians, and ranges, and given as numbers and percentages. Qualitative data was provided as counts and percentages. Quantitative data was checked for normality using the Kolmogorov-Smirnov test. The following tests were used to determine which statistical method was most appropriate for each data set: Categorical Chi-Square Test, Student's t-test and Mann-Whitney U-test for parametric and nonparametric testing comparing two study groups using a continuous variable. P ≤ 0.05 is significant.

RESULTS

In this prospective, randomized, and comparative trial, 40 patients who had developed upper-limb lymphedema after a mastectomy participated (after exclusion of 10 patients who were not fulfilling the inclusion criteria) at OCMU (Figure 1).

As regards demographic characteristics measurements of the studied groups, statistical analysis revealed no significant differences between the groups as regard information on the mastectomy procedure, time since the mastectomy, presence of lymph node metastases, the need for lymph node dissection, and the use of chemotherapy and/or radiation therapy (Table 2).

Table (2): Demographic characteristics, breast conserving surgery, time since mastectomy, modified radical mastectomy, breast conserving surgery, skin sparing mastectomy + LDF, lymph node metastasis and dissection, chemotherapy and radiotherapy of the studied groups

	Group 1 N=20	Group 2 N=20	P value
Age(years)	52.0±9.96	47.60±8.46	0.141
Height(cm)	160.5±2.42	162.25±4.35	0.062
Weight(kg)	81.35±9.98	74.05±14.41	0.07
BMI(Kg/m2)	30.57±3.39	29.04±4.95	0.263
Time since mastectomy (month)	10.6 ± 2.21	15.6 ± 3.32	0.49
Modified radical mastectomy (N)	18 (90%)	12 (60%)	0.39
Breast conserving surgery (N)	1 (5%)	4 (20%)	0.28
Skin sparing mastectomy + LDF (N)	1 (5%)	2 (10%)	0.35
Lymph node metastasis (N)	14 (70%)	17 (85%)	0.45
Lymph node dissection (n)	20 (100%)	20 (100%)	0.5
Chemotherapy (N)	20 (100%)	20 (100%)	0.5
Radiotherapy (N)	17 (85%)	11 (55%)	0.39

Data expressed as mean ± SD, number and percentage. **Group 1:** 15 mg ketorolac + 4 ml lidocaine 2%; **Group 2:** 30 mg ketorolac + 4 ml lidocaine 2%; N= number; P- Value considered significant if ≤ 0.05

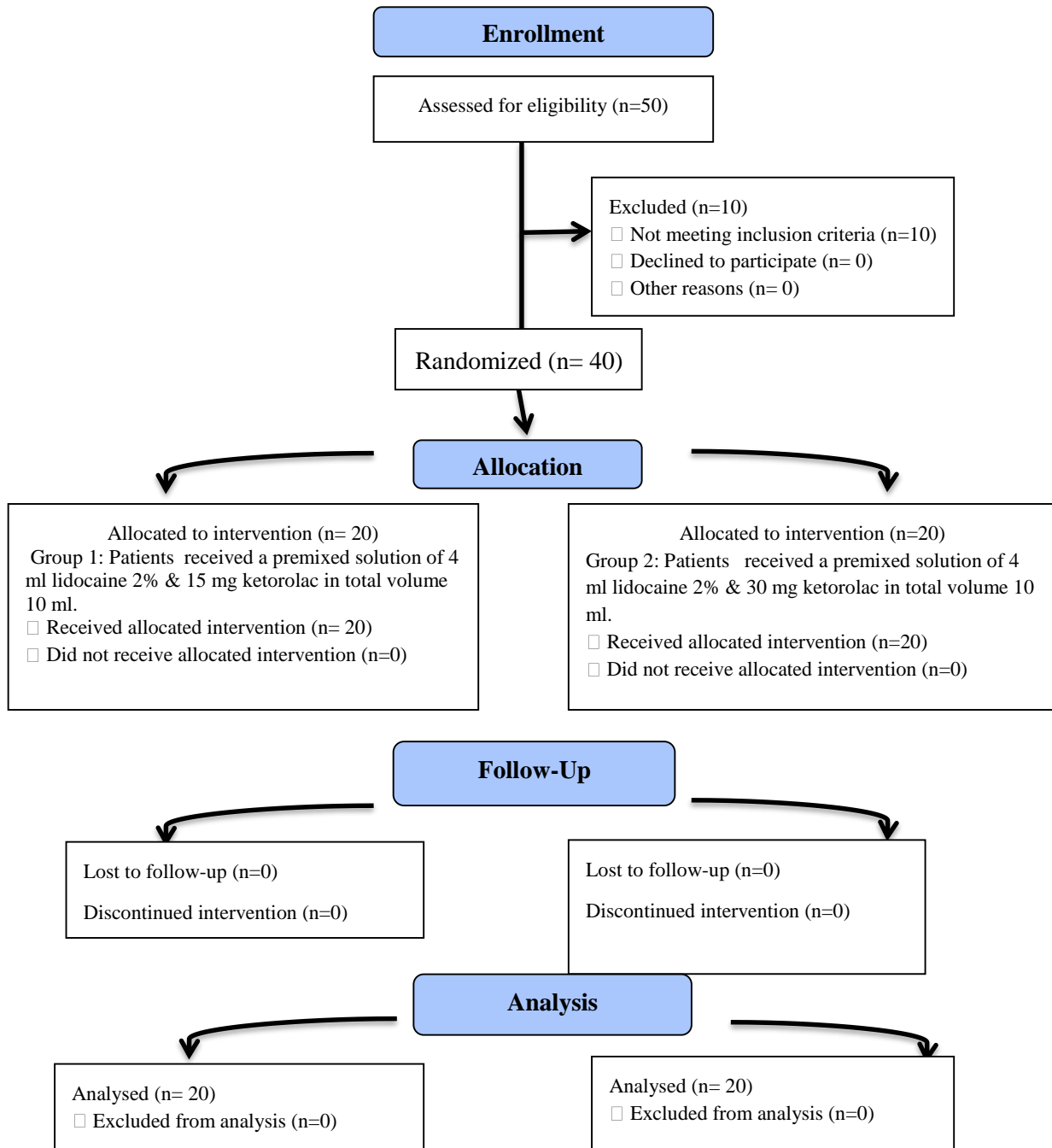


Figure (1): Consort flow chart of the studied groups.

Comparing the first request of analgesia and total analgesia after SGB between studied groups, we found that group 2 showed significant decrease in total analgesia consumption after SGB compared to group 1 (19 versus 34) with (P<0.001) and also, there was an increase in first request of analgesia in hours in group 2 versus group 1 (8 h versus 4 h) after SGB (Table 3).

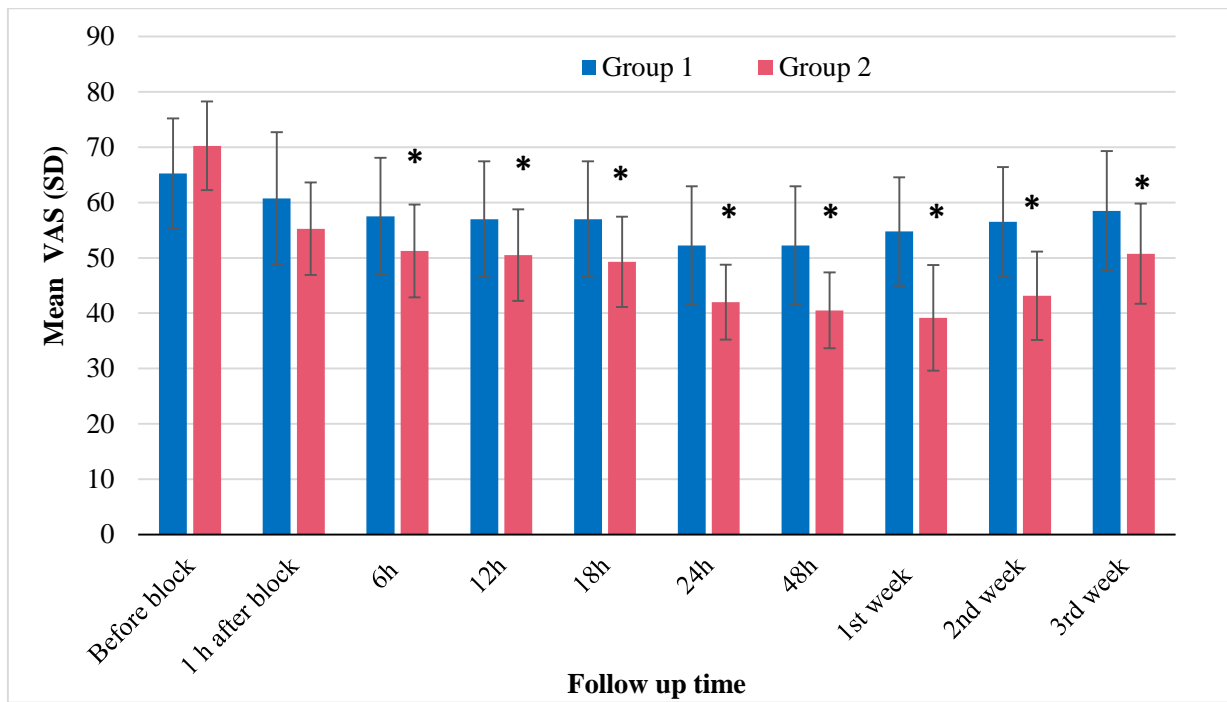
Table (3): Comparison of first request of analgesia and total analgesia after SGB between studied groups

	Group 1 (N=20)	Group 2 (N=20)	P value
First request of analgesia /h median (min-max)	4(2-8)	8(5-54)	0.001*
Total analgesic dose /tab median (min-max)	34(20-63)	19(4-30)	0.001*

N: number * Statistically significant differences when P-value ≤ 0.05.

Data expressed as median (min – max) range.

The visual analogue score (VAS) was used to evaluate pain intensity after SGB, and there were no statistically significant differences between the two groups before or 1 hour after block. While, there were statistically significant reductions in VAS score in group 2 compared to group 1 at 6 hours, 12 hours, 24 hours, 1 week, 2 weeks, and 3 weeks after block with SGB (P<0.05) (Figure 2).



* Statistically significant differences between studied groups

Figure (2): Comparison of mean visual analogue scale (VAS) pain score after SGB between studied groups.

In weeks 2 and 3 after SGB, there was a statistically significant decrease in arm circumference 5 cm above elbow in group 2 compared to groups 1. Among group1, no significant decrease of mean arm circumference regarding 5 cm above elbow from basal value (before block) compared to 1st, 2nd & 3rd week after block (from 34.52 ± 5.90 , 33.4 ± 5.7 , 32.65 ± 5.8 & 32.20 ± 5.98 respectively). While in group 2, there was statistically significant decrease of the mean arm circumference 5 cm from basal (before block) value compared to the 1st, 2nd & 3rd week post-operative (from 33.95 ± 2.5 , 32.4 ± 2.5 , 27.78 ± 2.44 & 28.38 ± 2.25 respectively)(Table 4).

Table (4): Comparison of arm circumference 5 cm above elbow between studied groups and intragroup comparison in the studied groups

Arm circumference 5 cm above elbow	Group 1 N=20	Group 2 N=20	P value
Before block(basal)	34.52 ± 5.90	33.95 ± 2.5	0.69
1st week after SGB	33.4 ± 5.7	32.4 ± 2.5	0.48
2nd week after SGB	32.65 ± 5.8	27.78 ± 2.44	0.002*
3rd week after SGB	32.20 ± 5.98	28.38 ± 2.25	0.013*
Paired t test (comparison with basal value)	P1 < 0.001* P2 < 0.001* P3 < 0.001*	P1 < 0.001* P2 < 0.001* P3 < 0.001*	

N: number. SGB=stellate ganglion block. * Statistically significant differences when P- value ≤ 0.05 . P1=Significance between basal value and 1st week, P2= Significance between basal value and 2nd week, P3= Significance between basal value and 3rd week. Data expressed as mean \pm SD

With arm circumference 10 cm above elbow between studied groups, there was statistically significant decrease in arm circumference 10 cm above elbow in group 2 compared to group 1 before block, at 2nd week and at 3rd week after block. Among group 1, there was statistically significant decrease of mean arm circumference 10 cm above elbow from before block basal value compared to the 1st, 2nd & 3rd week after block (from 37.7 ± 5.9 , 35.6 ± 5.7 , 34.43 ± 5.63 & 33.75 ± 5.98 respectively). Among group 2, there was statistically significant decrease in the mean arm circumference 10 cm from basal before block compared to the 1st, 2nd & 3rd week after block (from 36.18 ± 4.85 , 34.2 ± 3 , 30.98 ± 2.27 & 30.78 ± 2.34 respectively) Table (5).

Table (5): Comparison of arm circumference 10 cm above elbow between studied groups and intragroup comparison in the studied groups

Arm circumference 10 cm above elbow	Group 1 N=20	Group 2 N=20	P value
Before block(basal)	37.7 ± 5.9	36.18 ± 4.85	0.3
1st week after SGB	35.6 ± 5.7	34.2 ± 3	0.37
2nd week after SGB	34.43 ± 5.63	30.98 ± 2.27	0.018*
3rd week after SGB	33.75 ± 5.98	30.78 ± 2.34	0.049*
Paired t test (comparison with basal value)	P1 < 0.001* P2 < 0.001* P3 < 0.001*	P1 < 0.001* P2 < 0.001* P3 < 0.001*	

* Statistically significant differences when P- value ≤ 0.05. P1=Significance between basal value and 1st week, P2= Significance between basal value and 2nd week, P3= Significance between basal value and 3rd week, Data expressed as mean ± SD

Regarding arm circumference 5 cm below elbow between studied groups, there were statistically significant decreases in arm circumference 5 cm below elbow in group 2 compared to groups 1 at 2nd week and 3rd week after block (P<0.05). Among group1 there was statistically significant decrease of mean arm circumference 5 cm below elbow from basal before block compared to 1st, 2nd & 3rd week after block (from 31.48 ± 5.9, 30 ± 6, 29.5 ± 6 & 29 ± 6.12 respectively). Among group 2 no significant decrease was found of mean arm circumference 5 cm below elbow from before block to 1st, 2nd & 3rd week after block (from 31.05 ± 2.76, 28.9 ± 2.76, 26.43 ± 2.9 & 25.78 ± 2.98 respectively) (Table 6).

Table (6): Comparison of arm circumference 5 cm below elbow between studied groups and intragroup comparison in the studied groups

Arm circumference 5 cm below elbow	Group 1 N=20	Group 2 N=20	P value
Before block(basal)	31.48 ± 5.9	31.05 ± 2.76	0.8
1st week after SGB	30 ± 6	28.9 ± 2.76	0.47
2nd week after SGB	29.5 ± 6	26.43 ± 2.9	0.049*
3rd week after SGB	29 ± 6.12	25.78 ± 2.98	0.041*
Paired t test (comparison with basal value)	1 < 0.001* 2 < 0.001* 3 < 0.001*	P1 < 0.001* P2 < 0.001* P3 < 0.001*	

* Statistically significant differences when P- value ≤ 0.05. Data expressed as mean ± SD.

As regards arm circumference 10 cm below elbow between studied groups, there was statistically significant decrease in group 2 compared to group 1 at 2nd and 3rd week after block (P<0.05). Among group 1, a statistically significant decrease was found of mean arm circumference 10 cm below elbow basal before block value compared to 1st, 2nd & 3rd week after block (from 29.2 ± 5.8, 28.25 ± 5.6, 28.23 ± 5.66 and 28.18 ± 5.68 respectively). Among group 2, there was statistically significant decrease of mean arm circumference 10 cm below elbow before block compared to the 1st, 2nd & 3rd week after block (from 28.6 ± 2.65, 27.3 ± 2.9, 25.35 ± 2.69 & 24.9 ± 2.7 respectively) (Table (7)).

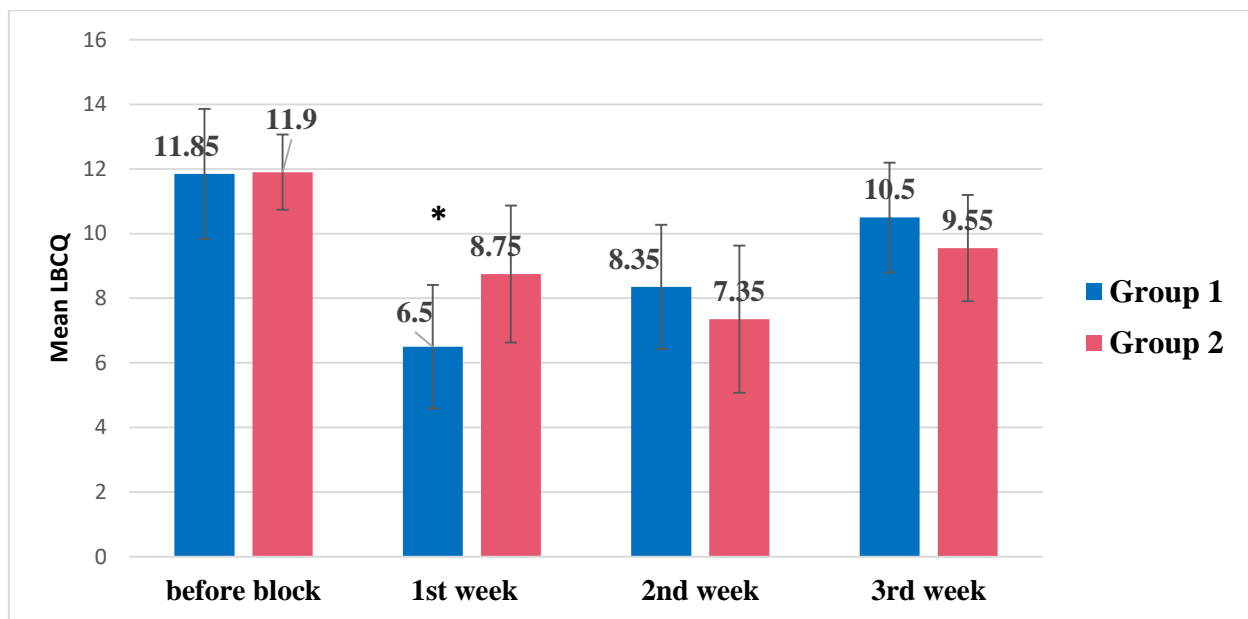
Table (7): Comparison of arm circumference 10 cm below elbow between studied groups and intragroup comparison in the studied groups

Arm circumference 10 cm below elbow	Group 1 N=20	Group 2 N=20	test of significance
Before block(basal)	29.2 ± 5.8	28.6 ± 2.65	0.68
1st week after SGB	28.25 ± 5.6	27.3 ± 2.9	0.5
2nd week after SGB	28.23 ± 5.66	25.35 ± 2.69	0.05*
3rd week after SGB	28.18 ± 5.68	24.9 ± 2.7	0.029*
Paired t test (comparison with basal value)	P1 < 0.001* P2 < 0.001* P3 < 0.001*	P1 < 0.001* P2 < 0.001* P3 < 0.001*	

* Statistically significant differences when P-value ≤ 0.05. Data expressed as mean ± SD. Data expressed as mean ± SD.

A comparison of LCBQ score between studied groups showed no statistically significant difference among both groups before block period while LCBQ score increased significantly in group 2 compared to group 1 in the 1st week after block (P<0.001). In addition, such increase gradually decreased to be non-significant in the 2nd and 3rd weeks after block (P>0.05) (Figure 3).

No patients in either group experienced any adverse effects from the stellate ganglion block procedure or the investigational medication used in this trial.



* Statistically significant differences between studied groups

Figure (3): Comparison of lymphedema breast cancer questioner.

DISCUSSION

This prospective, randomized, comparative study aimed to compare the effects of varying doses of ketorolac with a set dose of lidocaine in a stellate ganglion block on pain and the extent of lymphedema in the upper limbs following mastectomy.

Not much is understood about the mechanism of SGB in lymphedema caused by breast cancer. The autonomic control of lymphatic vessels due to SGB is one proposed mechanism. Various nerve fibers, both sympathetic and parasympathetic, innervate lymphatic vessels. Patients with breast cancer-linked lymphedema have reduced contractility of collecting lymphatic channels. Vascular constriction is triggered by neurotransmitters found in sympathetic nerve fibers of lymphatic vessels. The lymphatic system may be affected by SGB's modulation⁽¹²⁾. In animal studies, it was found that after SGB, both the brachial artery and vein blood flow were improved, suggesting that SGB can improve venous blood flow. As a result, that SGB may enhance venous flow, which in turn helps alleviate lymphedema caused by breast cancer⁽¹³⁾. As lymphedema is characterized by a persistent inflammatory response, it is possible that SGB has a role in modulating the immune system. Extreme inflammatory changes were seen in a lymphedema animal model. A boost in SGB's ability to modulate the immune system by the use of corticosteroids is possible⁽¹⁴⁾. No statistically significant differences were seen in the current study between groups with respect to age, sex, or any of the anthropometric measures used (height and weight). In a study by **Thapa et al.**⁽¹⁵⁾, those 54 patients were all set to undergo general anesthesia for orthopedic surgery on their upper limbs, all patients underwent ultrasound guided SGB before the block, and there were no statistically significant variations in terms

of age, gender, or other anthropometric variables between the groups (height, weight and BMI).

Anti-inflammatory drugs like ketorolac work by blocking the production of prostaglandins. Anti-inflammatory drugs like ketorolac work by blocking the production of inflammatory molecules including prostaglandins and thromboxane A2. These molecules are produced by the cyclooxygenase enzymes (COX-1 and COX-2). For this reason, nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently recommended for pain and inflammation caused by diseases that are prostaglandin-mediated⁽¹⁶⁾. Additionally, nonsteroidal anti-inflammatory drugs (such as ketorolac) are administered perineurally in conjunction with local anesthetics to increase the duration of pain relief after the block wears off⁽⁸⁾. Parenteral ketorolac and an opiate are generally well tolerated, with few adverse effects beyond drowsiness, headache, dizziness, nausea, dyspepsia, and abdominal pain. There is also a low risk of gastrointestinal and operative site bleeding and acute renal insufficiency. Some people also experience itching, diarrhea, sweating, self-limiting wheezing, edema and hyperkalemia⁽¹⁷⁾. Interestingly, the current study compared the first request analgesia and total analgesia between studied groups. Group 2 was demonstrated to be associated with as a highly statistically significant increase in first request analgesia/h (8 h versus 4 h) and a highly statistically significant decrease in total analgesia compared to group 1 (19 versus 34). The current study found no statistically significant differences in VAS score between groups before or 1 hour after the block, but did find statistically significant decreases in VAS score in group 2 compared to group 1 at 6 hours, 12 hours, 24 hours, the first week, the second week, and the third week after the block. Denoting that

higher dose of ketorolac could be associated with lower VAS score and less pain post mastectomy.

Sayed and Mahmoud⁽¹⁸⁾ in their study on patients undergoing shoulder arthroscopy to see how the addition of dexamethasone or ketorolac to a bupivacaine and lidocaine mixture affected post-block analgesia and intraoperative hemodynamics. They found that VAS baseline showed insignificant difference among all groups. While VAS at 4, 8 and 12 hours were significantly lower in the dexamethasone group in comparison with other groups, but there was insignificant difference between ketorolac and control groups at the same after block hours while they noticed that the time to first analgesic was 10.95 ± 1.05 hours in the ketorolac group and 11.7 ± 3.53 hours in the control group it was insignificant difference between ketorolac and control group. In a study performed at Intermountain Health Care reported that, Ketorolac is chemically stable when added to local solutions of lidocaine or bupivacaine, which is important since it extends the duration and improves the quality of analgesia following foot surgery as compared to plain 1.73 percent lidocaine or 1.73 percent lidocaine with intravenous ketorolac⁽¹⁹⁾.

However, when **Reinhart et al.⁽²⁰⁾** compared plain lidocaine versus ketorolac plus plain lidocaine, they found that the ketorolac plus plain lidocaine provided longer-lasting and higher-quality analgesia following foot surgery, evidence that ketorolac were less likely to use opioids for pain and required less rescue medication. Consistent with the findings of **Basenko et al.⁽²¹⁾**, they found that administering 30 mg of ketorolac with 40 ml of bupivacaine 0.25% for brachial plexus block significantly increased the duration of analgesia following block.

The current studied groups were compared based on their arm circumference 5 cm above the elbow. At 2- and 3-weeks post-block, group 2 showed statistically significant reductions in arm circumference 5 cm above the elbow compared to group 1. At 2- and 3-weeks post-block, group 2 showed statistically significant reductions in arm circumference 10 cm above the elbow compared to group 1. In the second and third week after the block, group 2 showed statistically significant decreases in arm circumference 5 cm below the elbow compared to group 1. Group 2 also showed statistically significant reductions in arm circumference 10 cm below the elbow compared to group 1 at weeks 2 and 3. Patients' circumferences began to drop after the second injection in research by **Kim et al.⁽²²⁾** where a sequence of blocks was established to sustain a lasting effect and patients reported feeling less edema and pain. In a study by **Zhang et al.⁽²³⁾**, they discovered that three SGBs performed at 2-week intervals were successful for enhancing BCRL in the upper arm and forearm, and that the use of corticosteroids in SGB had good effects in reducing upper arm circumference faster and dramatically. Also, another study by **Seo et al.⁽²⁴⁾**, after three consecutive SGBs with 1% lidocaine 4 mL and 40

mg triamcinolone 1 mL, they found a significant reduction in the upper arm and forearm circumferences of patients with BCRL, additionally, upper and forearm circumference decreased noticeably following the initial SGB where three successive injections were administered every two weeks, and the circumference was assessed two weeks after SGB. After 3 consecutive SGBs, there was a decrease in circumference at 1 month, however it is unclear if the effects of SGB are long-lasting.

Results from the Lymphedema and Breast Cancer Questionnaire (LBCQ) were compared in the present study. Neither group differed from the other statistically during the pre-block period, but in the first week following the block, group 2 showed significantly higher LCBQ than group 1. Furthermore, such an increment steadily declined until it was no longer statistically significant in weeks 2 and 3 after the block.

CONCLUSION

From the results of the current study we concluded that higher dose of ketorolac when added to fixed dose of lidocaine local anesthetic for Stellate ganglion block as a method for decreasing pain and size of post mastectomy upper limb lymphedema after breast cancer surgery, it could be associated with better quality of pain relief as reduction of total analgesic consumption, prolonged time to first analgesic, lower VAS score and with more size reduction of the upper limb lymphedema without causing any adverse effects, also higher dose of ketorolac was associated with lower LCBQ score in 1st week after block.

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Conflict of interest: No conflicts of interest throughout the execution of this work.

Author contribution: Authors contributed equally in the study.

REFERENCES

1. **Abass M, Gismalla M, Alsheikh A et al. (2018):** Axillary lymph node dissection for breast cancer: efficacy and complication in developing countries. *Journal of Global Oncology*, 4: 1-8.
2. **Stocks M, Freeman M, Addiss D (2015):** The effect of hygiene-based lymphedema management in lymphatic filariasis-endemic areas: a systematic review and meta-analysis. *PLoS Neglected Tropical Diseases*, 9 (10). <https://doi.org/10.1371/journal.pntd.0004171>
3. **Lin H, Huili Q, Qian W et al. (2020):** Lymphedema in survivors of breast cancer. *Oncology Letters*, 19 (3): 2085-2096.
4. **Gosain R, Pollock Y, Jain D (2016):** Age-related disparity: Breast cancer in the elderly. *Current Oncology Reports*, 18(11): 69-73.
5. **Perrine D, Votta-Velis G, Borgeat A (2016):** Ultrasound indications for chronic pain management: an update on the most recent evidence. *Current Opinion in Anesthesiology*, 29 (5): 600-605.

6. **Swedborg I, Arnér S, Meyerson B (1983):** New approaches to sympathetic blocks as treatment of postmastectomy lymphedema (report of a successful case). *Lymphology*, 16 (3): 157-163.
7. **Borman P (2018):** Lymphedema diagnosis, treatment, and follow-up from the view point of physical medicine and rehabilitation specialists. *Turkish Journal of Physical Medicine and Rehabilitation*, 64 (3): 179-97.
8. **Gupta A, Bah M (2016):** NSAIDs in the treatment of after block pain. *Current Pain and Headache Reports*, 20 (11): 62. doi: 10.1007/s11916-016-0591-7
9. **Serna-Gutiérrez J (2015):** Ultrasound-guided stellate ganglion block. *Rev Colomb Anesthesiol.*, 43: 278–282.
10. **Hawker G, Mian S, Kendzerska T et al. (2011):** Measures of adult pain: Visual analog scale for pain (VAS pain): numeric rating scale for pain (nrs pain): McGill pain questionnaire (mpq): short-form McGill pain questionnaire (sf-mpq): chronic pain grade scale (cpgs): short form-36 bodily pain scale (sf-36 bps): and measure of intermittent and constant osteoarthritis pain (icoap). *Arthritis Care & Research*, 63 (11): 240-252.
11. **Choi E, Nahm F, Lee P (2015):** Sympathetic block as a new treatment for lymphedema. *Pain Physician*, 18 (4): 365-372.
12. **Lee Y, Park H, Lee Y et al. (2018):** The Effect of Stellate Ganglion Block on Breast Cancer-Related Infectious Lymphedema. *The Korean Journal of Hospice and Palliative Care*, 21 (4): 158-162.
13. **Han H, Yang E, Lee S (2019):** Sodium Selenite Alleviates Breast Cancer-Related Lymphedema Independent of Antioxidant Defense System. *Nutrients*, 11 (5): 1021. doi: 10.3390/nu11051021
14. **Seo K (2015):** Effects of stellate ganglion block on breast cancer-related lymphedema: comparison of various injectates. *Pain Physician*, 18: 93-99.
15. **Thapa D, Dhiman D, Ahuja V et al. (2018):** Tramadol sparing effect of dexmedetomidine as an adjuvant with lignocaine in before block stellate ganglion block for after block pain relief following upper limb surgeries. *British Journal of Pain*, 12 (1): 26-34.
16. **Maslin B, Lipana L, Roth B et al. (2017):** Safety considerations in the use of ketorolac for postoperative pain. *Current Drug Safety*, 12 (1): 67-73.
17. **Cloesmeijer M, van Esdonk M, Lynn A et al. (2020):** Impact of enantiomer-specific changes in pharmacokinetics between infants and adults on the target concentration of racemic ketorolac: A pooled analysis. *British Journal of Clinical Pharmacology*, 87 (3): 1443-1454.
18. **Sayed S, Mahmoud A (2018):** Dexamethasone versus Ketorolac as Adjuvants to Interscalene Brachial Plexus Block in Shoulder Arthroscopy Under General Anesthesia. *The Medical Journal of Cairo University*, 86: 1947-1953.
19. **Prasad G, Khanna S, Jaishree S (2020):** Review of adjuvants to local anesthetics in peripheral nerve blocks: Current and future trends. *Saudi Journal of Anaesthesia*, 14 (1): 77-84.
20. **Reinhart D, Stagg K, Walker K et al. (2000):** After block analgesia after peripheral nerve block for pediatric surgery: clinical efficacy and chemical stability of lidocaine alone versus lidocaine plus ketorolac. *Regional Anesthesia & Pain Medicine*, 25 (5): 506-513.
21. **Basenko I, Tchuev P, Budnyuk A et al. (2006):** Use of Ketorolac as adjuvant in brachial plexus block with bupivacaine: A-472. *European Journal of Anaesthesiology*, 23: 123. https://journals.lww.com/ejanaesthesiology/Citation/2006/06001/Use_of_Ketorolac_as_adjuvant_in_brachial_plexus.438.aspx
22. **Kim J, Park H, Cho S et al. (2015):** The effect of stellate ganglion block on intractable lymphedema after breast cancer surgery. *The Korean Journal of Pain*, 28 (1): 61-3.
23. **Zhang X, Oliveri J, Paskett E (2020):** Features, Predictors, and Treatment of Breast Cancer-Related Lymphedema. *Curr Breast Cancer Rep.*, 12 (4): 244–254.
24. **Seo K, Suh M, Hong S et al. (2019):** The new possibility of lymphoscintigraphy to guide a clinical treatment for lymphedema in patient with breast cancer. *Clinical Nuclear Medicine*, 44 (3): 179-185.