Analgesic Efficacy of Dexmedetomidine as Adjuvant to Levo-Bupivacine in Ultrasound Guided Erector Spinae Plan Block for Modified Radical Mastectomy

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Abstracts: Background& aim: There are several advantages to properly managing post-masctetomy pain. With single shot interfascial plane blocks, local anesthetic adjuvants enhance analgesia duration. They improve the analgesic impact of local anesthetics. Dexamethasone, magnesium sulphate and dexmedetomidine, are examples of adjuvants with diverse modes of action. This research examined the analgesic effects of dexmedetomidine in women who had undergone a modified radical mastectomy (MRM). Methods and Patients: The research included forty women with histopathologically confirmed breast cancer. They were all scheduled for MRM and were randomly assigned to one of two groups: those who got levobupivacaine alone (group C) or those who received dexmedetomidine plus levobupivacaine (group D) during ultrasound (US)-guided erector spinae plane block (ESPB). The two groups were compared in terms of their hemodynamics, demographics, time until the first request for analgesia, numeric rating scale (NRS) scores, Richmond Agitation & Sedation scale (RASS) scores and total opioid use. Results: There were no statistically significant differences observed between the two groups in terms of baseline data. The set of participants referred to as group D had a statistically significant reduction in heart rate on many instances. Furthermore, it was discovered that group D had a substantial reduction in postoperative NRS ratings and a heightened degree of recovery from sedation, as shown by the RASS. Furthermore, it was noted that group D had a significantly reduced overall analgesic dose (9.12±0.46 vs. 6.24±1.37 mg; p= 0.02) and a prolonged duration until first analgesia (6.21±1.28 vs. 7.13±1.79 hours; p< 0.001). Conclusion: The use of dexmedetomidine in combination with levobupivacaine ESPB has been shown to enhance postoperative analgesia compared to the use of levobupivacaine alone. This improvement in postoperative analgesia leads to enhanced comfort levels for patients. Further research is necessary to corroborate these results via future studies conducted in several places.

Keywords: MRM, Dexmedetomidine, Levobupivacaine, Regional Block, US -Guided ESPB.

1. INTRODUCTION

In Egypt, Cancer of breast breast accounts for almost thirty nine% of all Cases of female cancer, making it the most prevalent female malignancy [1]. The breast cancer majority treatments involve surgery. However, it is a mutilating procedure that frequently results in extremely painful acute post-operative pain [2].

Patients undergoing mastectomy are somewhat frequently experiencing severe pain, with a Sixty% rate of incidence. Opioids are regarded as the gold standard in analgesics, but they frequently have a variety of side effects. Therefore, effective pain management is necessary to prevent post-mastectomy chronic pain syndrome and lessen acute discomfort [3, 4].

The current inclination towards anesthesia without the use of opioids underscores the recognition of the potential hazards linked to opioid administration. The prevailing opioid problem may be primarily attributed to the substantial prescription of opioids to patients, particularly for the management of chronic pain. Individuals who have modified radical mastectomy face the potential of developing chronic discomfort if the initial pain is not well treated. [5].

Regional nerve blocks for postoperative analgesia in breast cancer are available in some regions. Interscalene brachial plexus, Thoracic epidural, pectoral and paravertebral nerve blocks have shown favorable outcomes in providing postoperative analgesia for patients after breast cancer surgery. [6]. The erector spinae plane block (ESPB) guided by ultrasound (US) is a novel anesthetic method suggested by Forero et al. [7]

According to reports, there is evidence suggesting that the use of ESPB may have the potential to lessen pain after a MRM. procedure for breast cancer. Nevertheless, however the use of extended-acting local anesthetic drugs, the duration of anesthesia is sustained for a period of between eight and twelve hours. [8] Dexmedetomidine is an alpha-2 adrenergic receptor agonist with good selectivity[9].

It is worth mentioning that many meta-analyses have shown that the use of dexmedetomidine-assisted local anesthetic drugs has been associated with a faster start and prolonged duration of block in the context of brachial plexus block [10-12]. Nevertheless, there is a lack of comprehensive research regarding the effectiveness of combining dexmedetomidine with local anesthetic drugs in ESPB. The objective of this research was to evaluate the impact of dexmedetomidine, when used as an adjuvant in combination with ESPB, on the first instance of analgesia request and the overall analgesic needs in patients undergoing MRM.

2. METHODS AND PATIENTS

2.1. Investigation Design and Setting

The present research was conducted as randomized controlled trial (RCT) at South Egypt Cancer Institute. It was performed in the period between 2021 and 2022.

2.2. Patient Selection

The research included female patients who had been diagnosed with breast cancer and had a physical status of American Society of Anesthesiologists (ASA) I and II. The age range of the patients was between twenty-five and seventy years old. Additionally, the patients were planned to undergo either left or right MRM.

Patients who met any of the following criteria were excluded from the research: presence of skin infection in the vicinity of the needle puncture site,central or peripheral neuropathy, coagulation disorders, substantial impairment of organ function, morbid obesity (defined as a body mass index (BMI)less than thirty five kg/m2), and recent use of analgesic medications.

2.3. Randomization and Participants

A cohort of Forty female patients were recruited for the research project. The investigation's participants were assigned to groups in a randomized manner, with an equal distribution of individuals in each group. This randomization process was conducted using a computer-generated list of random numbers. The outcomes of the distribution were securely enclosed inside an impermeable envelope and entrusted to the research administrator for safekeeping. During the day of the surgical procedure, the individual responsible for monitoring the research provided the envelope to the anesthesiologist, who then administered the anesthetic solution.

The investigation included the enrollment of patients into two groups: Group C, which consisted of twenty individuals receiving twenty milliliters of 0.25% levobupivacaine administered into the interfascial plane below the erector spinae muscle (ESM) at the T5 level, and Group D, which consisted of Twenty patients receiving the same dose of 0.25% levobupivacaine as in Group C, along with an additional 1μ/kg of dexmedetomidine.

3. METHODOLOGY

Following a period of full fasting, during which standard monitors such as pulse oximeter, noninvasive blood pressure,capnography and electroencephalogram were used an intravenous (IV)cannula was then inserted and appropriately secured. The administration of an US-guided ESP block was performed on the patient while they were in a seated posture, taking into consideration the surgical site location. The ESP block was administered via a high frequency linear US transducer. The probe was positioned longitudinally, laterally to the fifth spinous process of the thoracic region. Subsequently, the erector spinae muscle, Trapezious muscle, and Rhomboideus major muscle were identified from the surface.

The accuracy of the needle tip placement was confirmed by administering about one milliliter of 0.9% normal saline in a caudad to cephalad direction. Following the identification of the appropriate tip location, the anesthesiologist administered a gradual infusion of twenty milliliters of levobupivacaine solution with a concentration of 0.25%. Subsequently, longitudinal fluid diffusion was detected in the region between the transverse and erector spinae muscle process, specifically categorized as group C. In the second group, the same process was replicated, with the addition of 1μ/kg of dexmedetomidine. Following the completion of the nerve block, the patient was positioned in the supine posture.

The administration of general anesthesia included the use of fentanyl at a dose of lμ per kilogram, propofol at a dose of two milligrams per kilogram, a muscle relaxant known as atracurium at a dose of 0.5 milligrams per kilogram, and either isoflurane or sevoflurane for inhalational anesthesia. No more narcotic, analgesic, or sedative agents were administered throughout the operating time. The research collected measurements of mean arterial blood pressure (BP), heart rate (HR), oxygen saturation, and endotracheal carbon dioxide levels.

3.1. Follow Up

The patient was transferred to the post anesthesia care unit after the surgery and was subjected to monitoring. The vital signs that were monitored included oxygen saturation and HR. The level of sedation was assessed using the RASS sedation score [13]. Levels of Pain were evaluated immediately after the operation and at specific time intervals (two, four, six, twelve and twenty-four hours) using the Numerical Rating Score (NRS) pain score [14]. The dosage and time of analgesia requested by the patient (demand dose one-two mg) were recorded when the NRS score was equal to or greater than three. Additionally, any side effects of the block were monitored for a duration of twenty-four hours after the surgery.

3.2. Statistical Analysis

The data was gathered and then analyzed with SPSS, specifically version 20, developed by IBM in Armonk, New York. The quantitative data were presented as the mean ± standard deviation (SD) and were analyzed using the Student t test for comparison. Nominal data is often represented in numerical form, namely as counts (n) and proportions expressed as percentages (%). The chi-square test was conducted on the provided dataset. The level of confidence was maintained at 95%, therefore indicating that a P value less than 0.05 was deemed statistically significant.

4. RESULTS

Table (1): Data of baseline of the studied groups:

	Group C (n= 20)	Group D (n= 20)	P value
Age (years)	48.90±8.62	46.65±11.77	0.42
BMI “kg/m2”	29.35±2.32	29.45±1.23	0.27
ASA:			0.75
I	13(65.0%)	13(65.0%)	
II	7(35.0%)	7(35.0%)	
SBP (mmHg)	138.25±9.77	136.00±10.31	0.46
DBP (mmHg)	81.0±5.23	79.50±11.90	0.26
Heart rate (b/m)	84.90±10.15	82.85±6.31	0.37
Operative time (min)	86.25±19.59	79.50±16.77	0.56

Data expressed as frequency (percentage), mean (SD). P value was significant if < 0.05. BMI: body mass index; ASA: american society of anesthesiologists; SBP: systolic blood pressure; DBP: diastolic blood pressure

Table 2: Changes in mean blood pressure in study groups

Time of assessment	Group C (n= 20)	Group D (n= 20)	P value
Intraoperative			
At induction	83.35±10.09	78.50±11.44	0.18
15-minute	81.90±8.48	77.15±11.4	0.78
30-minute	82.20±5.51	76.80±8.79	0.03
45-minute	83.90±6.67	79.45±9.43	0.23
60-minute	84.35±7.08	80.40±8.83	0.18
End of surgery	84.00±6.33	83.25±13.23	0.17
Postoperative			
Immediate	88.85±4.12	85.85±11.07	0.49
2-hours	90.90±6.43	84.85±10.58	0.06
4-hours	92.00±5.54	86.00±10.31	0.15
6-hours	90.90±7.51	88.45±9.38	0.67
12-hours	91.40±8.26	90.10±8.37	0.80
24-hours	90.10±9.04	91.15±9.54	0.80

Data expressed as mean (SD). P value was significant if < 0.05.

Table 3: Changes in heart rate in study groups

Time of assessment	Group C (n= 20)	Group D (n= 20)	P value
Intraoperative			
At induction	78.30±10.48	73.10±9.07	0.47
15-minute	76.85±9.33	67.55±5.87	0.02
30-minute	74.50±7.34	67.25±5.32	0.02
45-minute	73.85±7.26	67.45±5.79	0.03
60-minute	74.50±8.78	69.60±4.36	0.03
End of surgery	73.90±9.04	73.50±4.33	0.40
Postoperative			
Immediate	80.10±8.56	77.45±4.11	0.12
2-hours	80.10±8.96	77.30±6.08	0.14
4-hours	82.50±10.90	78.00±6.13	0.02
6-hours	82.50±9.98	75.40±5.04	0.03
12-hours	83.20±7.89	75.95±5.76	0.02
24-hours	82.40±6.53	76.10±5.00	0.02

Data expressed as mean (SD). P value was significant if < 0.05.

Table 4: Changes in ETCO2 and SO2 in the study groups

Time of assessment	Group C (n= 20)	Group D (n= 20)	P value
Intraoperative ETCO2			
At induction	33.10±2.61	32.05±0.75	0.06
15-minute	32.25±2.22	31.50±0.82	0.24
30-minute	32.50±1.63	31.55±0.94	0.33
45-minute	32.45±2.39	32.35±0.58	0.78
60-minute	32.35±1.26	32.30±0.47	0.17
End of surgery	32.30±1.62	32.15±0.36	0.78
Intraoperative SO2			
At induction	99.20±0.83	99.30±0.73	0.32
15-minute	99.45±0.68	99.20±0.83	0.43
30-minute	99.30±0.73	99.05±0.88	0.25
45-minute	99.25±0.71	98.85±1.08	0.23
60-minute	99.20±0.76	98.80±0.41	0.34
End of surgery	99.35±0.67	99.15±0.36	0.46
Postoperative SO2			
Immediate	98.90±0.55	99.15±0.67	0.19
2-hours	98.40±0.94	99.20±0.61	0.26
4-hours	98.55±1.05	98.95±0.75	0.16
6-hours	98.10±0.85	99.20±0.76	0.34
12-hours	98.45±0.28	99.05±0.68	0.25
24-hours	98.10±1.16	99.40±0.50	0.16

Data expressed as mean (SD). P value was significant if < 0.05. ETCO2: endotracheal carbon dioxide; SO2: oxygen saturation

Table 5: Postoperative NRS and RASS score among the study groups

	Group C (n= 20)	Group D (n= 20)	P value
NRS			
Immediate	0.0	0.0	--
2-hours	0.900±0.78	0.30±0.17	< 0.001
4-hours	1.50±1.1	0.70±0.16	< 0.001
6-hours	2.55±1.31	2.20±0.76	< 0.001
12-hours	2.05±0.51	1.75±0.78	< 0.001
24-hours	1.95±0.68	1.45±0.51	0.03
RASS			
Immediate	0.0	-0.93±0.19	< 0.001
2-hours	0.0	-0.75±0.08	0.01
4-hours	0.0	0.0	--
6-hours	0.0	0.0	--
12-hours	0.0	0.0	--
24-hours	0.0	0.0	--

Data expressed as mean (SD). P value was significant if < 0.05. NRS: numeric rating scale; RASS: Richmond Agitation & Sedation scale

Table 6: Postoperative analgesic request in study groups

	Group C (n= 20)	Group D (n= 20)	P value
Number need to analgesia	6(30.0%)	2(10.0%)	< 0.001
Time to first request (hour)	6.21±1.28	7.13±1.79	< 0.001
Total dose (mg)	9.12±0.46	6.24±1.37	0.02

Data expressed as frequency (percentage), mean (SD). P value was significant if < 0.05.

Table 7: Post-operative side effect in study groups

Items	Group C (n= 20)	Group D (n= 20)	P value
Nausea	4(20.0%)	3(15.0%)	0.55
Vomiting	3(15.0%)	0.0	0.04
Sedation	0.0	5(25.0%)	0.01
Pruritus	3(15.0%)	1(5.0%)	0.36

Data expressed as frequency (percentage). P value was significant if < 0.05.

Majority of enrolled patients had ASA class-I. Two groups had insignificant variances as regard and operative time and baseline data (p> 0.05).

Changes in average BP in research groups (table two):

Two groups had insignificant variances as regard perioperative mean blood pressure (MBP) assessment with except of important lower MBP at 30-minute intraoperatively between group D (p= 0.03).

Changes in heart rate (HR) in research groups (table three):

Group D had significantly lower HR at assessment variant times with except at induction, immediate and two-hours postoperatively and surgery end and where both groups had comparable heart rate.

Changes in endotracheal carbon dioxide CO2and oxygen O2 saturation and in research groups (table four):

Two groups had insignificant variances as regard and intraoperative endotracheal CO2 and perioperative O2 saturation assessment (p> 0.05).

Postoperative RASS score and NRS and between the research groups (table five):

It was found that NRS was significantly lower in group D at assessment variant times with except of assessment of immediate post-operative where two groups had comparable NRS.

Also, RASS sedation score was significantly better in group D immediately and two hours after surgery but it was zero in two groups after the 2nd postoperative hour.

Postoperative analgesic request in research groups (table six):

Six (Thirty%) patients of group C required analgesia while only two patients in group D required analgesia with significant lower total analgesia dose in group D (9.12±0.46 VS. 6.24±1.37 (mg); p= 0.02). Also, duration to 1st analgesia was significantly longer in group D (6.21±1.28 vs. 7.13±1.79 (hour); p< 0.001).

Side effect of Post-operative in research groups (table Seven):

None of patients in group D suffered of vomiting while three (fifteen%) patients of group C suffered of vomiting with important variances (p= 0.04). Also, sedation was absent in group C, in contrast it was reported in five (twenty-five%) patients of group D (p= 0.01). Both groups had insignificant differences as regard pruritus and nausea frequency

DISCUSSION

Techniques for regional anesthesia offer better management of acute pain, which results in decrease chronic pain after MRM. Additionally, the use of efficient strategies for managing acute pain has been shown to have a positive impact on immune function. This is achieved by the reduction in the utilization of opioids, including morphine, which has been demonstrated to have detrimental effects on both cellular and humoral immune functions. Additionally, effective acute pain management also contributes to the mitigation of the stress response associated with surgical procedures. This effect could contribute to local recurrence higher rates following metastasis development and/or surgery [15].

long-acting amide local anesthetics. It is widely believed that ropivacaine has superior ability in possessing reduced potential for cardiac toxicity and differentiating sensory effects from motor ones, and. But, ropivacaine alone only has a limited effect on postoperative analgesia and is only used for a time brief period in nerve block. Ropivacaine and Dexmedetomidine were found to extend the duration of sensory block and improve peripheral nerve block [16].

The use of US instruments in contemporary anesthetic treatment has facilitated the development of novel regional procedures that rely on comprehensive understanding of the innervations of the breast. One such approach is the ESPB, first documented by Forero et al. [7].

In the present investigation we needed to assess the dexmedetomidine analgesic effect as an adjuvant combined with ESPB in MRM. Forty women were enrolled and were randomly subdivided into either received levobupivacaine with dexmedetomidine or levobupivacaine alone during ESPB. It was found that two groups had insignificant variances as regard data of baseline.

In line with the present research, Wang et al. studied a total of sixty women (thirty women in each group). They stated that the demographic data, site of surgery, operation time, duration of anesthesia intraoperative dosage of propofol and hospital stay among both groups were comparable in each group [6].

Nearly two groups in the present had comparable O2 saturation and hemodynamic but HR was significantly lower among group D. A previous research found similar findings and reported that HR of group D was lower after anesthesia induction, axillary dissection and pericarpectomy and at the surgery end [6].

Another research stated that as regarding heart rate and MAP, they were statistically significant lower in group D when compared with group C from 15 min after block up to 8 h postoperatively [17]. Mohamed et al. observed that addition of dexmedetomidine 1 μg/kg to bupivacaine in thoracic paravertebral block in patients undergoing MRM prolonged the duration of analgesia and reduced analgesic requirements with no serious hemodynamic adverse effects [18].

The hypotensive and bradycardic effects of dexmedetomidine, particularly at larger dosages, may be attributed to the activation of inhibitory 2 adrenoceptors in the medullary vasomotor center. This activation leads to a reduction in norepinephrine release and central sympathetic outflow. Bradycardia is brought on by both an elevate in vagal tone and a decline in sympathetic drive as a result of parasympathetic outflow central stimulation. None of those events occurred in our research [17].

Dexmedetomidine has anti-sympathetic properties via stimulating the vagus nerve, resulting in a decline in levels of plasma catecholamine. This mechanism contributes to the stable hemodynamics maintenance, demonstrated by reductions in both HR and BP. Several investigations have shown the potential of dexmedetomidine to reduce HR and BP [25], while conflicting findings have also been described in the literature. Hence, the precise correlation between dexmedetomidine and its impact on hemodynamics remains uncertain. [19, 20].

The main results in the present research is that group D had significantly lower total analgesia (9.12±0.46 VS. 6.24±1.37 (mg); p= 0.02). Also, duration to first analgesia was significantly longer in group D (6.21±1.28 vs. 7.13±1.79 (hour); p< 0.001). Also, NRS was significantly lower in group D at different times of assessment with except of immediate post-operative assessment where both groups had comparable NRS.

In line with the present research, a previous research stated that The combination of ropivacaine with dexmedetomidine at a dosage of 1 μg/kg−1 demonstrated superior analgesic efficacy compared to the administration of ropivacaine alone. The present research observed a statistically significant decrease in postoperative pain scores in group D compared to group C, in both resting and active phases. [6].

In a research conducted by Abdelaal et al., it was demonstrated that the inclusion of dexmedetomidine (100 μg) alongside levobupivacaine (20 ml of 0.375%) in transverse abdominis plane block following abdominoplasty resulted in a delay in the time at which the first analgesia request was made, in comparison to the administration of levobupivacaine alone (205±10.2 vs. 181±12.6 min; P<0.001). Additionally, the combined treatment was found to significantly reduce the total consumption of pethidine over a 24-hour period (136±13.4 vs. 172±15.8 mg; P<0.001). [21].

In a separate investigation, the utilization of dexmedetomidine in conjunction with paravertebral block was shown to result in a reduced need for opioids in the context of video-assisted thoracoscopic surgery. The present research observed a decrease in opioid intake, namely remifentanil and sufentanil, within group D as compared to group C. [22].

Consistent with these findings, Manzoor et al. conducted a research that showed the inclusion of dexmedetomidine in bupivacaine (thirty ml of 0.25%) in Pecs II resulted in a substantial increase in the duration of postoperative analgesia by almost 40% as compared to the use of bupivacaine alone (1024.0±124.9 vs. 726.4±155.3 min; P<0.001). The extended duration observed in this research may be ascribed to the use of dexmedetomidine at a dosage of 1 μg/kg, which is higher than the dosage of 0.5 μg/kg employed in this particular investigation. [23].

One of the objectives of the present improved rehabilitation program is to decrease the need for opioids during the perioperative period. The objective is to reduce the possible adverse effects linked to opioids. The use of regional nerve block is of significant importance in the reduction of opioid consumption. [22].

Dexmedetomidine's analgesic effects are influenced by a number of different mechanisms. Multiple mechanisms are thought to be at play in the lower postoperative pain score and decreased perioperative opioid use.

Dexmedetomidine's primary mechanism of action is to increase membrane hyperpolarization by activating sodium and potassium pumps [24].

The analgesic effects of perineuronal dexmedetomidine arise from its ability to strengthen cation channels that are triggered by hyperpolarization. This augmentation prevents the nerve membrane potential from reverting to the resting state, hence inhibiting future discharge. [25].

The administration of perineural dexmedetomidine resulted in a sixty% increase in the duration of ulnar nerve sensory block, whereas systemic dexmedetomidine led to a ten% extension of sensory block when compared to the administration of a placebo. Hence, the synergistic combination of local anesthetic drugs with dexmedetomidine results in heightened suppression of nerve transmission, leading to improved analgesic efficacy compared to the use of local anesthetic agents in isolation. [19].

As regard side effects in the present research, none of patients in group D suffered of vomiting while three (fifteen%) patients of group C suffered of vomiting with significant difference (p= 0.04). Also, sedation was absent in group C, in contrast it was reported in five (twenty-five%) patients of group D (p= 0.01). Two groups had insignificant differences as regard frequency of pruritus and nausea

A previous reported postoperative nausea and vomiting higher in group C. This may be owing to the use of more postoperative opioids in group C. Owing to performance of the block under US visualization, block-related complications such as pneumothorax and vascular injection did not occur [17].

To our knowledge, this is the first reported research that discussed effect of ESPB with the usage of dexmedetomidine on the RASS sedation scale. Here, we found that in the first postoperative two hours, group D had better RASS scale.

In a previous research assessed adding either ketamine or dexmedetomidine to bupivacaine 0.25% for Pecs-II block in patients underwent mastectomy. The authors reported that different studied groups had comparable RASS [26].

The present research acknowledges certain limitations. Relatively sample size and being conducted in single center, we didn’t assess effect of this procedure on frequency of chronic pain and we didn’t compare dexmedetomidine with other adjuvants as dexamethasone, ketamine and magnesium sulphate.

Another issue was the inability to test dexmedetomidine plasma concentrations in research subjects to establish if its impact was due to systemic absorption or was purely local. Furthermore, alternative dexmedetomidine dosages were not employed; a lower dose of dexmedetomidine might give the same analgesic benefit with fewer side effects.

Any yet, the main strength points of the current research are randomization and first research in our locality that assessed analgesic effect of dexmedetomidine as an adjuvant combined with ESPB in MRM

IN CONCLUSION

The use of dexmedetomidine in combination with levobupivacaine ESPB has been shown to enhance postoperative analgesia compared to the use of levobupivacaine alone. This improvement in postoperative analgesia leads to enhanced comfort levels for patients. Further research is necessary to corroborate these results via future studies conducted in several places.

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