Original Article

Effectiveness of intravenous dexmedetomidine compared to intercostal nerve blocks in patients undergoing simple mastectomy with axillary dissection under general anaesthesia.

Dr. Dabasis Kumar¹, Dr Sabina Yeasmeen², Dr Md Miraj Hossain³,
Dr Montosh Kumar Mondal⁴, Dr AKM Faizul Hoque⁵, Dr. Muhammad Nazrul Islam⁶,
Dr.Ashfaqul Islam⁷, Dr. Mohammad Mahabubuzzaman⁸.

¹Assistant Registrar (Anesthesiology), National Institute of Traumatology and Orthopaedic Rehabilitation (NITOR), Sher-e-Bangla Nagar, Dhaka, Bangladesh. ²Associate Professor, Department of Anaesthesia, Analgesia and Intensive care medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. ³Assistant Professor, Department of Anaesthesiology, KhwajaYunus Ali Medical College and Hospital, Enayetpur, Sirajganj, Bangladesh. ^{4,5}Associate Professor, Department of Anaesthesia, Analgesia and Intensive care medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. ⁶Specialist, Dept. of Anaesthesiology, United Hospital limited, Dhaka. ⁷Resident, Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU, Shahbagh, Dhaka. ⁸Anesthesiologist, National Institute of Traumatology and Orthopaedic Rehabilitation (NITOR), Sher-e-Bangla Nagar, Dhaka, Bangladesh

Corresponding Author: Dr. Dabasis Kumar, E-mail: sabinay0970@gmail.com

Abstract:

Background: General anaesthesia is used for breast cancer surgery. The downside of general anaesthesia includes inadequate pain control and a high incidence of nausea and vomiting. General anaesthesia with intravenous dexmedetomidine or intercostal nerve block reduce the incidence of postoperative pain.

Objective: To evaluate the effectiveness of intravenous dexmedetomidine compared to intercostal nerve blocks in patients undergoing simple mastectomy with axillary dissection under general anaesthesia. Methods: It was a single-blinded prospective randomized comparative study. This study was conducted at the Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from March 2018 to March 2019. A total of 60 patients suffering from breast cancer admitted in the Department of General Surgery of BSMMU Dhaka and scheduled for simple mastectomy with axillary dissection, were enrolled in this study. Results: Age, height and weight were almost identical between two groups. Duration of anaesthesia and surgery were almost similar between two groups. The mean heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure did not significantly fluctuate in subsequent baseline follow up and 15 minute and at 160 minutes parameters were almost similar within two groups. Mean time to achieve adequate Aldrete recovery score after extubation was almost similar between two groups. Postoperative sedation level was also similar between two groups. Majorty of the surgeon were satisfied about anaesthesia technique in both group A and group B. Mean time of rescue analgesic requirement in postoperative period was satisfically significant (p<0.05) between two group but it was clinically less significant (group A = 112 minutes and group B = 141 minutes.

Conclusion: Intravenous dexmedetomidine may be an alternative to intercostal nerve blocks in patients undergoing simple mastectomy with axillary dissection under general anaesthesia as it provided stable intraoperative haemodynamics, reduced blood loss and analgesic requirement, smooth recovery, postoperative sedation level and surgeon satisfaction as well as intercostal nerve blocks.

Keywords: Intravenous dexmedetomidine, Intercostal nerve blocks, General anaesthesia, Rescue analgesia, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial pressure.

(JBSA 2021; 34 (2): 24-35)

Introduction:

The technique of anaesthesia normally used for breast cancer surgery is general anaesthesia, which almost always combining intravenous and inhalational agents. The downside of general anaesthesia includes inadequate pain control due to a lack of analgesia, and a high incidence of nausea and vomiting; increasing the length of hospitalization. Other controversial effects of general anaesthesia in oncologic patients are related with depression of the immune system.

Breast cancer is the most common cancer in women worldwide, with more than one million new cases diagnosed every year.3 The incidence of breast malignant neoplasia, as well as the need of surgical treatment, has increased probably due to prevention campaigns and diagnostic modalities. Nowadays, modern surgical intervention is more conservative but in most cases partial or total mastectomy associated with axillary exploration to remove lymph nodes for staging or immune-chemical testing is still necessary.4 Simple mastectomy with axillary dissection is the most common surgery for breast cancer patients in our country. This procedure is frequently associated with peroperative bleeding, unstable haemodynamics, postoperative pain, nausea and vomiting, which lead not only to increased patients suffering, but also to a prolongation of hospital stays and related Intraoperative costs. stable haemodynamics and optimum treatment for postoperative pain has been of fundamental importance in surgical patient care.

Acute postoperative pain is an integral risk factor in the development of chronic pain after breast cancer surgery. 40 % of women will have severe acute postoperative pain after breast cancer surgery, potentially disrupting the quality of postoperative recovery. Hazards of postoperative pain including unstable haemodynamics, nausea and vomiting, which lead not only to increased patients suffering, but also to a prolongation of hospital stays and related costs.

Adequate postoperative pain management is possible, if it is initiated from premedication, maintained intraoperatively and continued during the entire recovery period.⁶ Different

management strategies and interventions during perioperative period are available and continue to evolve in this regard. Traditionally, narcotics have been used for analgesia after breast surgery. However, these agents have unpleasant side effects like nausea, vomiting, sedation, pruritus, constipation and respiratory depression specially in case of elderly and obese patients. These adverse effects can be avoided by reducing the dose of opioid despite maintaining the analgesia and ensuring patient satisfaction. Many local anaesthetics and other adjuvant drugs are being investigated for use in this technique, in order to improve the quality of analgesia and reduce adverse effects. Intercostal nerve blockade (INB) is an alternative technique to improve postoperative pain.7

INB achieved can be intermittently, continuously, or permanently, depending on the technique used. It may provide relatively well-defined anatomical coverage, making them both an excellent diagnostic tool and a reliable therapeutic procedure.8 It may inhibit the post-operative stress response, reduce opioid consumption, promote early tracheal extubation, shorten duration of hospital stay, attenuate postoperative pain and contribute postoperative recovery in patients. Apart from the beneficial effects of intercostal nerve blocks, there are some disadvantages of this invasive procedure. Prolonged blockade requires either multiple reinsertions with the attendant risk of pneumothorax, placement of a catheter for bolus dosing or continuous infusion 9, injection with a neurolytic agent¹⁰ or cryoablation.¹¹ Another important risk to keep in mind is local anaesthetic toxicity. Blood levels of local anaesthetic after intercostal blockade and interpleural analgesia are significantly greater than after any other frequently performed regional anaesthetic techniques.12 There are sporadic case reports of other types of complications. Haematoma has occurred in a heparinized patient. 13 Bilateral intercostal nerve blocks have resulted in postoperative respiratory failure in patients with preoperative pulmonary compromise.14 Motor blockade and the loss of accessory respiratory muscle function were the hypothesized etiologic mechanisms. In a study looking at the efficacy of continuous epidural

versus intercostal analgesia, one intercostal catheter led to rib osteomyelitis which had to be treated surgically. Intraoperative intercostal nerve block performed by the surgical team has resulted in total spinal anaesthesia. Presumably, this serious complication occurred because of the proximity of the injections to spinal nerve roots. ¹⁵

Paravertebral neural block has also occurred with attempted intercostal nerve block during surgery.¹⁶

Many other drugs, have been investigated with different doses and routes to perioperative haemodynamic stability analgesia. These include oral acetaminophen, NSAIDs, gabapentinoids, tramadol, clonidine epidural administration of opioids and local anaesthetics and multimodal combinations. The above mentioned drugs and routes are associated with some unwanted effects. So, it is logical to investigate newer agents with different approaches to achieve the best possible outcome. The dexmedetomidine is a potent and highly selective a-2 adrenoceptor agonist with some special characteristics. It has sedative, analgesic, amnestic, anxiolytic, sympatholytic, anti-shivering and antisialogogue activities.¹⁷ Intraoperative administration of intravenous dexmedetomidine produces an anestheticsparing effect.¹⁸ It is approved by the USA Food and Drug Administration (FDA) for sedation in the intensive care unit (ICU). The analgesic action of dexmedetomidine are proposed to involve both spinal and supraspinal mechanisms. Regarding the spinal mechanism, alpha-2 receptors are also located in the α-2C and α-2A receptors, situated in the neurons of dorsal horn especially lamina II(substantiagelatinosa) of the spinal cord and it act on both pre and postsynaptic mechanisms to produce antinociception

This hyperpolarized state makes the generation of new action potentials virtually impossible, and refractory to further stimulation.²¹

Suggested supraspinal mechanism is activation of α -2A receptors at the locus coeruleus in the brain stem causing decrease in nor epinephrine release from pre-synaptic neurons with inhibition of postsynaptic activation.²²

of Intraoperative administration dexmedetomidine maintained hemodynamic stability by attenuating the stress induced sympathoadrenal responses to intubation, surgery and also emergence from anesthesia.²³ It reduces nociceptive input, increases the nociception threshold, and reduces activation of nociceptive receptors prior to the surgical incision.24 The haemodynamic effects of dexmedetomidine is dose related and biphasic (low, then high) for mean arterial pressure, pulmonary arterial pressure, and vascular resistances.²⁵ At lower doses, its dominant action is hypotension and bradycardia due to α-2A receptor mediated sympatholysis located at locus coeruleus.²⁶ At higher doses, the hypertensive action dominates via the activation of alpha-2B adrenoceptors located on the smooth muscle cells in the resistance vessels.27 Dexmedetomidine causes a mild increase in PaCO2 and a decrease in minute ventilation with a minimal change in respiratory rate which is not clinically significant.²⁸ In addition, it does not cause respiratory depression or decrease arterial oxygen saturation. Dexmedetomidine can potentially offer a superior analgesic effect compared to clonidine.29

In our country, few articles published on dexmedetomidine and intravenous dexmedetomidine not yet done on simple mastectomy with axillary dissection Bangladesh. Ιt was assumed that dexmedetomidine may be an alternative to intercostal nerve blocks for patients undergoing simple mastectomy with axillary dissection under general anaesthesia.

This study evaluate the effectiveness of intravenous dexmedetomidine compared to intercostal nerve blocks in patients undergoing simple mastectomy with axillary dissection under General anaesthesia.

Methodology

It was a single-blindedprospectiverandomized comparative study. The study was conducted at BSMMU after permission from the Institutional Review Board. 60 female patients aged between 30 and 50 years were enrolled in this study, who were suffering from breast cancer and selected

for simple mastectomy with axillary dissection. Informed consent was taken from the patient. Assessment of physical status of the patient were done following American Society of Anaesthesiology (ASA) physical status and ASA I or ASA II only were included in the study.

The study was single-blinded; therefore the patients were unaware of the study group allocation. However, the investigator was aware of the type of the drugs/techniques used in the investigation. Patients were interviewed for a detailed medical and drug history underwent physical examinations the day before surgery to verify whether she fulfilled the inclusions criteria. All the investigations were reviewed. Before the surgery, the patients were instructed clearly about the use of the visual analogue scale (VAS- 0 no pain, and 10 worst pain possible) and the other procedure in details. All patients were under routine preoperative fasting for 6 hours and were not permitted to drink for 2 hours.

The patients were randomly allocated into two equal groups using a sealed envelope technique by supervisor. Group A received general anaesthesia with intravenous dexmedetomidine and Group B received general anaesthesia with intercostal nerve blocks.

Preoperative heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded 20 minutes before the induction of anaesthesia in both group A and group B by the investigator.

General anaesthesia induced in both group A and B using 1.5 μg/kg fentanyl, 1.5 mg/kg propofol and 1.5-2 mg/kg suxamethonium. Appropriate size of endotracheal tube used for tracheal intubation and the correct position of the tube determined by auscultation of breath sounds. Mechanical ventilation and tidal volume (8-10 ml/kg) was regulated under a maintained respiratory rate and end tidal CO2 (35±5 mmHg). After confirmation and fixation of the endotracheal tube, 0.1mg/kg vecuronium was given to the patients when respiration restarted. To maintain anaesthesia and analgesia, halothane 0.6%, N2O 66%, O2 33% and 0.04 mg/kg vecuronium was given according to the anaesthesia status and muscle relaxation in both groups.

In group A, dexmedetomidine (vial contains 200 μ g/2ml) one vial had been diluted in 0.9% normal saline and 50 ml solution were made containing dexmedetomidine 4 μ g/ml. The total volume infused to the patient by investigator was 0.25 ml/kg of solution, which started 20 minutes before induction of anaesthesia at the rate of 1 ml (15 drops) per minute.

In group B, after general anaesthesia, intercostal nerve blocks were given by the investigator 3rd to 6th intercostal space in the midaxillary line at the same side of the operation. With all aseptic precaution and after proper cleaning 3rd rib in the midaxillary line was identified. The skin was drawn cephalad with the palpating hand by about 1 cm. A 4 to 5 cm, 22 gauge needle was introduced through the chosen entry site at a 20 degree cephalad angle with the bevel facing cephalad. The needle was advanced until it contacted the rib. With the palpating hand holding the needle firmly and resting securely on the patient's skin, the injecting hand gently "walks" the needle caudally while the skin was allowed to move back over the rib. The needle was then advanced further a few mm, while maintaining the 20 degree tilt angle cephalad. After negative aspiration for blood, 4ml 0.25% of bupivacaine was injected. The 4th, 5th and 6th intercostal nerve blocks had been induced by the same procedure. During surgery, patient's haemodynamic status (pulse, blood pressure) were carefully recorded in every patients at different time intervals (during induction, 15 minutes interval upto 30 minutes and 30 minutes interval uptoextubation). Patient was reversed with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg and extubation was done adequate spontaneous ventilation when resumed. Following surgery, time to achieve adequate recovery (ModifiedAldrete Score 9-10) was recorded in every patients. Pain intensity was recorded using a Visual Analog Scale (VAS) score in recovery room and postoperative ward for 6 hours: just after induction, 15 minutes interval upto 30 minutes, 30 minutes interval upto 2 hours then 1 hour interval upto 4 hours and 2 hours interval upto 6 hours. Patient was also be observed for the time of rescue analgesic requirement (time from extubation to the time postoperatively, when pain reported by patient \geq

5 on Visual Analogue Scale, injection pethidine 1.5mg/kg I/M administered).After was completion of the surgery level of sedation was assessed by using Ramsay Sedation Score; just after induction, 15 minutes interval upto 30 minutes, 30 minutes interval upto 2 hours then1 hour interval upto 4 hours and 2 hours interval upto 6 hours.Surgeon satisfaction was also assessed using a 5 point Likert Scale on the basis of anaesthetic techniques where 1 equals to very dissatisfied, 2 equals to dissatisfied, 3 equals to neutral, 4 equals to satisfied and 5 equals to very satisfied. Any adverse events like hypotension, bradvcardia. hypertension, tachycardia, respiratory depression, nausea, vomiting or allergic manifestations if occurred was recorded and treated accordingly.

Results

Table I shows mean age, height, weight and ASA Grade almost similar in two groups. The difference was statistically not significant (p>0.05) between two groups.

Mean age (years) of the patient was 38.9 ± 5.7 in group-A and 41.0 ± 4.8 in group-B.

Among them maximum and minimum age was 50 years and 30 years in group-A and 50 years and 34 years in group-B.

Mean weight (kg) of the patient was 55.9±10.1 in group-A and 60.5±10.4 in group-B and maximum and minimum weight was 70kg and 48 kg in group-A and 80 kg and 43 kg in groupB.Mean height (cm) of the patient was 157.9±4.1 in group-A and 159.1±3.2 in group-B andamong them maximum and minimum height was 165 cm and 145 cm in group-A and 168 cm and 145 cm in group-B.Out of 30 patients 18 (60%) patients was ASA grade I and 12 (40%) patients was ASA grade II in group-A and 16 (55%) patients was ASA grade I and 14 (45%) patients was ASA grade II in group-B.Table II shows mean duration of anaesthesia and surgery of the study patients, it was observed that the mean duration of anaesthesia and surgery was statistically not significant (p>0.05) between two groups.

Maximum and minimum duration of anaesthesia was 148 minutes and 112 minutes in

group-A and 149 minutes and 130 minutes in group-B. Duration of surgery was maximum 120 minutes and minimum 90 minutes in group-A and 120 minutes and 95 minutes in group-B.

Table I: Demography of patients between two groups.

Demographic variable	Group-A	Group-B	P value
	(n=30)	(n=30)	
	Mean±SD	Mean±SD	
Age (in years)	38.9±5.7	41.0±4.8	a0.128ns
Height (cm)	157.9± 4.1	159.1±3.2	a0.211ns
Weight (kg)	55.9±10.1	60.5±10.4	a0.087ns
ASA grade	n (%)	n (%)	
Grade I	18(60.0%)	16 (55.0%)	ho goons
Grade II	12(40.0%)	14(45.0%)	^b 0.602 ^{ns}

Unpaired t-test were performed for age, height and weight, p value < 0.05 was considered as significant. Chi-Square test was performed for ASA grade, p value < 0.05 was considered as significant.

Table II: Duration of anaesthesia and surgery in both groups (N=60)

Duration of anaesthesia	Group-A	P value	
and surgery	(n=30)	(n=30)	
	Mean±S D	Mean±SD	_
Duration of anaesthesia (mins)	132.8 ±16.9	138.1±11.3	0.138 ^{ns}
Range (min, max)	112-148	130-149	
Duration of surgery (mins)	103.8±15	5. 106.4±10.3	0.451 ^{ns}
Range (min, max)	90-120	95-120	

ns= not significant

Unpaired t-test were performed for duration of anaesthesia and surgery, p value < 0.05 was considered as significant.

Figure 1 showing the mean HR, SBP, DBP and induction of the study patients. It was observed that relatively higher in group B than group A.

But significant (p>0.05) between two groups.

MAP starting at 20 minutes before mean HR, SBP, DBP and MAP was the difference was statistically n

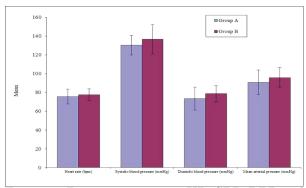


Figure 1 : Preoperative mean HR, SBP, DBP and MAP of the study groups

Unpaired t-test were performed to measure HR, SBP, DBP and MAP, p value < 0.05 was considered as significant.

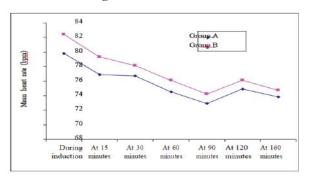


Figure 2: Intraoperative mean heart rate in different follow up

Unpaired t-test was performed to measure intraoperative HR, p value < 0.05 was considered as significant.

Figure 3 shows intraoperative systolic blood pressure in different follow up of the study patients. It was observed that mean systolic blood pressure was relatively higher in group B than group A. But the difference was statistically not significant (p>0.05) between two groups.

Figure 4 shows intraoperative diastolic blood pressure in different follow up of the study patients. It was observed that mean diastolic blood pressure was slight higher in group B than group A. But the difference was statistically not significant (p>0.05) between two groups.

Figure 5 shows mean arterial pressure in different follow up of the study patients. It was

observed that mean arterial pressure was relatively higher in group B than group A. But the difference was statistically not significant (p>0.05) between two groups.

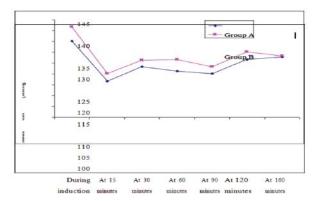


Figure 3: Intraoperative mean systolic blood pressure in different follow up

Unpaired t-test was performed to measure intraoperative SBP, p value < 0.05 was considered as significant.

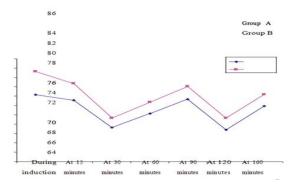


Figure 4: Intraoperative mean diastolic blood pressure in different follow up

Unpaired t-test was performed to measure intraoperative DBP, p value < 0.05 was considered as significant.

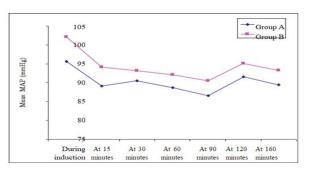


Figure 5 : Intraoperative mean arterial pressure in different follow up

Unpaired t-test was performed to measure intraoperative MAP, p value < 0.05 was considered as significant.

Figure 6 shows postoperative visual analogue scale score in different follow up of the study patients. It was observed that mean VAS score was higher in group A than group B in every follow up. But the difference was statistically not significant (p>0.05) between two groups.

Table III shows the time of rescue analgesic requirement in postoperative period of the study patients, it was observed that mean time of analgesic requirement was earlier in group A than group B. The difference was statistically significant (p<0.05) between two groups

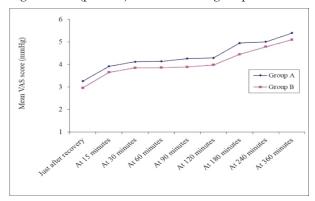


Figure 6: Postoperative visual analog scale scores of the study groups in different follow up Unpaired t-test was performed to measure postoperative VAS, p value < 0.05 was considered as significant.

Table III: Time of rescue analgesic requirement in postoperative period (N=60)

Analgesic requirement	Group-A (n=30)	Group-B (n=30)	P value
•	Mean±SD	Mean±SD	_
Time of analgesic			
Requirement (minutes)	112±80.6	141.1±90.	4 0.012 ^s

postoperative mean time of rescue analgesic requirement, p value < 0.05 was considered as significant.

Unpaired t-test was performed to measure

Figure 7 shows Ramsay Sedation Score at different follow up of the study patients in the postoperative period. It was observed that sedation score was higher in group A than group B in every follow up. But the difference was statistically not significant (p>0.05) between two groups.

Table IV shows time to achieve adequate recovery, score 9-10 by Modified Aldrete Recovery score after extubation. It was observed that Modified Aldrete Recovery score fulfilled (9-10) earlier by group B patients than group A. But the difference was statistically not significant (p>0.05) between two groups.

Table V shows surgeon satisfaction after operation, it was observed that majority of the surgeon satisfied in both group A and in group B. The difference was statistically not significant (p>0.05) between two groups.

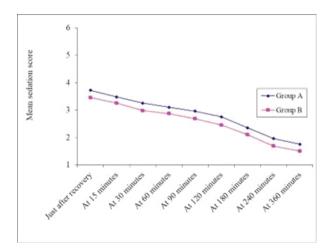


Figure 7: Postoperative mean sedation score at different intervals of the study group

Unpaired t-test was performed to measure postoperative mean sedation score, p value < 0.05 was considered as significant.

s=significant

Table IV : Time to achieve adequate recovery (Modified Aldrete Recovery score,

N=60)

Groups	(1-5) minutes (5-8)		(8-10)	Above10	bР	
		Minutes	minutes	minutes	value	
GroupA(n=3	30)60%(18)	30%(9)	10% (3)	0%	0.06^{ns}	
GroupB(n=3	30)73.3%(22)	16.7%(5)	7%(2)	0%		

ns=not significant

Chi-Square test was performed for recovery score, p value < 0.05 was considered as significant.

Table V: Surgeon satisfaction of the study patients using Likert Scale (N=60)

Surgeon satisfaction	Group- A		Group-B		P value
(Likert Scale)	(n=30)		(n=30)		
	n	%	n	%	
1-2	0	0.0	0	0.0	
3-4	0	0.0	0	0.0	
5-6	0	0.0	1	3.3	$0.528^{ m ns}$
7-8	2	6.7	3	10	
9-10	28	93.3	26	86.7	

ns=not significant

Chi-Square test was performed for surgeon satisfaction score, p value < 0.05 was considered as significant.

Discussion:

This single-blinded randomized comparative study was carried out with an aim to

effectiveness of intravenous dexmedetomidine compared to intercostal nerve blocks in patients undergoing simple mastectomy with axillary dissection under general anaesthesia regarding haemodynamic intraoperative status, postoperative intensity of pain, time of postoperative rescue analgesic requirement, recovery condition, sedation level and surgeon satisfaction. A total of 60 patients with carcinoma of breast scheduled for unilateral simple mastectomy with axillary dissection, aged 30-50 years and ASA grade I and II were enrolled in the study and they were randomly allocated into two equal groups.

In this present study, mean age, height and weight was almost similar in group A and in group B. Although, all above parameters were slightly higher in group B than group A but the difference was statistically not significant between the two groups. About 60% patients had ASA Grade I and 40% patients had ASA Grade II in group A and 55% patients had ASA Grade I and 45% patients had ASA Grade II in group B. The difference was statistically not significant between these two groups. Beegum et al. (2015) in their study observed that, "Postoperative Analgesic Requirements in Patients Receiving Intra-operative dexmedetomidine Infusion" had no significant differences in comparability between either groups with regard to age, weight and ASA grades.30

Barletta et al. (2009); Arain et al. (2004); Gurbet et al. (2006) also found no significant differences between patient groups in their age, weight, height and ASA physical status.^{31,32}

In this present study, it was observed that the mean duration of anaesthesia and surgery were relatively higher in group B than group A. It was may be due to extra time required to give intercostal nerve blocks in group B patients after anaesthesia. But the difference was statistically not significant between two groups. However, Syal and Chandel (2017) compared the post-operative analgesic effect of paravertebral block, pectoral nerve block and local infiltration in patients undergoing modified radical

mastectomy and found no significant difference in mean duration of surgery in all groups.³³

Abdelmageed et al. (2011); Gurbet et al. (2006) also found no significant differences between patient groups in their durations of anesthesia and surgery. But they did not compare the intravenous dexmedetomidine with INB, which was different from this study. 34,35

In the study, preoperative haemodynamics were measured at 20 minutes before induction and it was not statistically significant may be due to patients were either normotensive or well controlled hypertension in both groups. During induction mean HR, SBP, DBP and MAP was relatively higher in group B than group A possibly due to intubation reflex which was attenuated by intravenous dexmedetomidine in group A (Scheinin et al. 1992.).³⁶

 $_{
m the}$ difference was statistically not significant between two groups. Moreover, it was observed HR, SBP, DBP and MAP after 15 minutes, 30 minutes, 60 minutes, 90 minutes, 120 minutes and 160 minutes in group A and in group B. All the times HR, SBP, DBP and MAP were almost similar in both groups. The difference was statistically not significant. Sarkar et al. (2018) observed in their study compared epidural bupivacaine and dexmedetomidine with bupivacaine and fentanyl for postoperative pain relief in lower limb orthopedic surgery and found that at baseline (immediately after epidural block) heart rate of group II was higher than that of group I.37 Between-group difference in heart rate was not found to be statistically significant at any of the periods of their observation. Between-group differences of SBP was not found to be statistically significant at any of the periods of observation of their study population except at 120 min and 180 min. DBP of group I was found to be higher than that of group II. At all time periods of observation except at 2 min, 3 min, 4 min, 75 min, 90 min, and 4 h, DBP of group I was found to be higher than that of group II. Difference in diastolic blood pressure of above two groups was not found to be statistically

significant at any of the periods of observation. The observation time and pattern were not similar to this study. These findings were also supported by other studies (Arain et al. 2004; Gurbet et al. 2006; Mandal et al. 2011; Martin et al. 2003). 35,38,39,40

In this study shows visual analogue scale score after operation was almost similar between two groups. Mean VAS at 15 minutes was 3.92±0.50 in group A and 3.65±0.66 in group B and at 360 minutes was 5.40±0.67 in group A and 5.10±0.72 in group B. The difference was statistically not significant between two groups. There was also no significant difference between the two group mean VAS scores at each time point assessed in the PACU and on the ward after surgery, and the same was true for the mean VAS scores in the postoperative period (Gurbet et al. 2006).35Abdelmageed et al. (2011) study found VAS scores of the two groups during the first 12 hours after surgery. VAS scores were similar in the two groups thereafter.34 The mean VAS scores were never >5 in the dexmedetomidine group during the first 2 hours after surgery.

Mean time of rescue analgesic requirement of the study patients in this study was observed postoperatively. It was observed that mean time of rescue analgesic requirement was earlier in group A than group B. This may be due to intercostal nerve blocks provide more analgesia dexmedetomidine. than intravenous difference was statistically significant between two groups. Sarkar et al. (2018) study found the first analgesic requirement in (Dexmedetomidine group) was earlier compared to group I (Fentanyl group). Difference in time of first analgesic requirement between the above two groups was found to be statistically significant.³⁷ The period between extubation and the first analgesic request in the PACU was significantly longer in the dexmedetomidine group as compared to the placebo group (Abdelmageed et al. 2011). Beegum et al. (2015) also found time of first analgesic administration was significantly delayed by 3.9 hours in the intervention group compared to control group (t=9.68, p<0.001). 34,30

In this present study, Aldrete Recovery Score fulfilled earlier by group B patients than group A and Ramsay Sedation Score was higher in group A than group B in every follow up. This was due to sedative effects of intravenous dexmedetomidine (Carollo et al. 2008 and Venn et al. 1999). But the difference was statistically not significant between two groups.^{41,42}

Arain et al. (2004) observed that sedation scores were changed from pre surgery baseline during recovery periods was significantly slower in the PACU in the dexmedetomidine-treated patients.³⁸ All these patients recovered without any specific treatment. The sedation scores did not differ significantly between the two groups during the 48 hours after surgery (Abdelmageed et al. 2011). Gurbet et al. (2006) study also found sedation scores were also similar between two group at all corresponding times throughout the 48-hr period of observation.^{34,35}

In this study, Surgeon Satisfaction was assessed using a 5 point Likert Scale on the basis of anaesthetic technique where 1 equals to very dissatisfied, 2 equals to dissatisfied, 3 equals to neutral, 4 equals to satisfied and 5 equals to very satisfied, it was observed that majority of the surgeon were very satisfied in group A (93.3%) and in group B (86.7%). The difference was statistically not significant (p>0.05) between two groups. Alhashemi (2006) observed that forty-four patients undergoing cataract surgery under peribulbaranaesthesia randomly received either iv dexmedetomidine 1 µg kg-1 over 10 min followed by 0.1-0.7 µg kg-1 h-1 iv infusion (Group D) or midazolam 20 µg kg-1 iv followed by 0.5 mg iv boluses as required (Group M). Surgeon satisfaction was comparable in both groups.43It was observed that 6.67% patient had bradycardia and 3.33% patient had hypotension in group A and 6.67% patient had hypertension and 3.33% patient had tachycardia in group B. Dexmedetomidine provide postsynaptic activation of central α2A receptors results in sympatholytic effect leading to hypotension and bradycardia in group A. In group B both hypertension and tachycardia may be due to pain and the possible cause of pain was inadequate intercostal nerve blocks. Demographic variables, duration of anaesthesia and surgery, preoperative and intraoperative haemodynamics, postoperative VAS, sedation score, time to achieve adequate recovery and surgeon satisfaction score was statistically not significant between two groups in this study. Only time of rescue analgesic requirement in postoperative period statistically significant but clinically it was less significant. Adverse events that occurs intraoperatively were managed without any complications.

Conclusion:

Intravenous dexmedetomidine may be an alternative to intercostal nerve blocks in patients undergoing simple mastectomy with axillary dissection under general anaesthesia as it provided stable intraoperative haemodynamics, reduced blood loss and analgesic requirement, smooth recovery, postoperative sedation level and surgeon satisfaction as well as intercostal nerve blocks.

References:

- Oddby-Muhrbeck, E., Jakobsson, J., Andersson, L. and Askergren, J.Postoperative nausea and vomiting-A comparison between intravenous and inhalation anaesthesia in breast surgery. Actaanaesthesiologic ascandinavica. 1994;(1):52-56.
- Stevenson, G.W., Hall, S.C., Rudnick, S., Seleny, F.L. and Stevenson, H.C. The effect of anesthetic agents on the human immune response. Anesthesiology: The Journal of the American Society of Anesthesiologists.1990;72(3):542-552.
- Cronin-Fenton, D.P., Nørgaard, M., Jacobsen, J., Garne, J.P., Ewertz, M., Lash, T.L. and Sørensen, H.T. Comorbidity and survival of Danish breast cancer patients from 1995 to 2005. British journal of cancer.2007; 96(9):1462.
- Belzarena, S.D.,2008. Comparative Study between thoracic epidural block and general anesthesia for oncologic mastectomy. Rev Bras Anestesio. 2008;58:561–568.
- Gärtner, R., Jensen, M.B., Nielsen, J., Ewertz, M.,Kroman, N. and Kehlet, H. Prevalence of and factors associated with persistent pain following breast cancer surgery. Journal of American Medical Association. 2009; 302(18):985-1992.
- Woolf, C.J. and Chong, M.S. Preemptive analgesia—treating postoperative pain by preventing

- the establishment of central sensitization. Anesthesia & Analgesia.1993; 77(2):362-379.
- Shah, A., Rowlands, M., Krishnan, N., Patel, A. and Ott-Young, A. Thoracic intercostal nerve blocks reduce opioid consumption and length of stay in patients undergoing implant-based breast reconstruction. Plastic and reconstructive surgery.2015;136(5):584e-591.
- 8. Detterbeck, F.C. Efficacy of methods of intercostal nerve blockade for pain relief after thoracotomy. The Annals of thoracic surgery. 2005;80(4):1550-1559.
- Debreceni, G., Molnar, Z., Szelig, L. and Molnar, T.F. Continuous epidural or intercostal analgesia following thoracotomy: a prospective randomized double-blind clinical trial. Actaanaesthesiologicascandinavica.2003;47(9):1091-1 095.
- 10. Roviaro, G.C, Federico V., Fascianella, A., Mariani, C., Ramella, G., Ceccopieri, M., and Pezzuoli, G. Intrathoracic intercostal nerve block with phenol in open chest surgery. A randomized Study with statistical evaluation of respiratory parameter. 1986; 90(1):64-67.
- 11. Maiwand, M.O., Makey, A.R. and Rees, A. Cryoanalgesia after thoracotomy. Improvement of technique and review of 600 cases. The Journal of thoracic and cardiovascular surgery. 1986; 92(2):291-295.
- Tucker, Geoffrey T., Daniel C. Moore, Phillip O. Bridenbaugh, L. Donald Bridenbaugh, and Gale E. Thompson. "Systemic absorption of mepivacaine in commonly used regional block procedures. Anesthesiology.1972; 37(3): 277-287.
- 13. Nielsen, C.H., 1989. Bleeding after intercostal nerve block in a patient anticoagulated with heparin. Anesthesiology: The Journal of the American Society of Anesthesiologists, 71(1), pp.162-14. Cory, P.C. and Mulroy, M.F. Postoperative respiratory failure following intercostal block Anesthesiology: The Journal of the American Society of Anesthesiologists.1981;54(5):418-418.
- 15. Gallo, J.A., Lebowitz, P.W., Battit, G.E. and Bruner, J.M. Complications of intercostal nerve blocks performed under direct vision during thoracotomy: a report of two cases. The Journal of thoracic and cardiovascular surgery.1983; 86(4):628-630.
- 16. Berrisford, R.G. and Sabanathan, S.S. Direct access to the paravertebral space at thoracotomy. The Annals of thoracic surgery.1990;49(5):854.
- 17. Carollo, D.S., Nossaman, B.D. and Ramadhyani, U. Dexmedetomidine: a review of clinical applications. Current Opinion in Anesthesiology.2008;21(4):457-461.
- 18. Aantaa, R., Kanto, J. and Scheinin, M. Intramuscular dexmedetomidine, a novel alpha2-adrenoceptor agonist, as premedication for minor gynaecological surgery. Acta anaesthesiologic ascandinavica.1991;35(4):283-288.

- Calvillo, O. and Ghignone, M., 1986. Presynaptic effect of clonidine on unmyelinated afferent fibers in the spinal cord of the cat. Neuroscience letters, 64(3), pp. 335-339.
- Ono, H., Mishima, A., Ono, S., Fukuda, H. and Vasko, M.R., 1991. Inhibitory effects of clonidine and tizanidine on release of substance P from slices of rat spinal cord and antagonism by α-adrenergic receptor antagonists. Neuropharmacology, 30(6), pp.5859.
- Kuraishi, Y., Hirota, N., Sato, Y., Kaneko, S., Satoh, M. and Takagi, H. Noradrenergic inhibition of the release of substance P from the primary afferents in the rabbit spinal dorsal horn. Brain research1985;359(1):177-182.
- Yoshitomi, T., Kohjitani, A., Maeda, S., Higuchi, H., Shimada, M. and Miyawaki, T. Dexmedetomidine enhances the local anesthetic action of lidocaine via an α-2A adrenoceptor. Anesthesia & Analgesia.2008;107(1):96-101.
- Scheinin, B., Lindgren, L., Randell, T., Scheinin, H. and Scheinin, M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. British journal of anaesthesia.1992; 68(2):126-131.
- Kelly, D.J., Ahmad, M. and Brull, S.J. Preemptive analgesia II: recent advances and current trends. Canadian Journal of Anesthesia. 2001;48(11):1091.
- Ebert, T.J., Hall, J.E., Barney, J.A., Uhrich, T.D. and Colinco, M.D. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology: The Journal of the American Society of Anesthesiologists. 2000; 93(2):382-394.
- 26. Lakhlani, P.P., MacMillan, L.B., Guo, T.Z., McCool, B.A., Lovinger, D.M., Maze, M. and Limbird, L.E. Substitution of a mutant α2a-adrenergic receptor via "hit and run" gene targeting reveals the role of this subtype in sedative, analgesic, and anesthetic-sparing responses in vivo. Proceedings of the National Academy of Sciences.1997; 94(18):9950-9955.
- Makaritsis, K.P., Johns, C., Gavras, I. and Gavras, H., 2000. Role of α2-adrenergic receptor subtypes in the acute hypertensive response to hypertonic saline infusion in anephric mice. Hypertension.2000; 35(2):609-613.
- 28. Hsu, Y.W., Cortinez, L.I., Robertson, K.M., Keifer, J.C., Sum-Ping, S.T., Moretti, E.W., Young, C.C., Wright, D.R., MacLeod, D.B. and Somma, J., 2004. Dexmedetomidinepharmacodynamics: Part icrossover the comparison of respiratory effects dexmedetomidine and remifentanilinhealthy The Journal of the volunteers. Anesthesiology: American Society of Anesthesiologists.2004; 101(5):1066-1076.
- Grosu, I. and Lavand'homme, P. Use of dexmedetomidine for pain control. F1000 medicine reports, 2. 2010;17:90.

- 30. Beegum, T.S., Bindu, M., Lesna, M.P. and Suresh, V. Postoperative Analgesic Requirements in Patients Receiving Intra-operative Dexmedetomidine Infusion. International Journal of Health Sciences & Research.2015; 5(8): 145-154.
- 31. Barletta, J.F., Miedema, S.L., Wiseman, D., Heiser, J.C. and McAllen, K.J. Impact of dexmedetomidine on analgesic requirements in patients after cardiac surgery in a fast-track recovery room setting. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy.2009;29(12):1427-1432.
- 32. Gurbet, A., Basagan-Mogol, E., Turker, G., Ugun, F., Kaya, F.N. and Ozcan, B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Canadian Journal of Anesthesia.2006;53(7):646.
- 33. Syal, K. and Chandel, A. Comparison of the post-operative analgesic effect of paravertebral block, pectoral nerve block and local infiltration in patients undergoing modified radical mastectomy: A randomised double-blind trial. Indian journal of anaesthesia.2017; 61(8):643.
- 34. Abdelmageed, W.M., Elquesny, K.M., Shabana, R.I., Abushama, H.M. and Nassar, A.M., 2011.
- Gurbet, A., Basagan-Mogol, E., Turker, G., Ugun, F., Kaya, F.N. and Ozcan, B. Intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Canadian Journal of Anesthesia.2006;53(7):646.
- 36. Scheinin, B., Lindgren, L., Randell, T., Scheinin, H. and Scheinin, M.. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. British journal of anaesthesia.1992;68(2):126-131.

- 37. Sarkar, A., Bafila, N.S., Singh, R.B., Rasheed, M.A., Choubey, S. and Arora, V. Comparison of epidural bupivacaine and dexmedetomidine with bupivacaine and fentanyl for postoperative pain relief in lower limb orthopedic surgery. Anesthesia, essays and researches.2018;12(2):572.
- Arain, S.R., Ruehlow, R.M., Uhrich, T.D. and Ebert, T.J. The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. Anesthesia & Analgesia. 2004;98(1):153-158.
- 39. Mandal, M.C., Das, S., Gupta, S., Ghosh, T.R. and Basu, S.R. Paravertebral block can be an alternative to unilateral spinal anaesthesia for inguinal hernia repair. Indian journal of anaesthesia.2011; 55(6):584-589.
- Martin, E., Ramsay, G., Mantz, J. and Sum-Ping, S.J.
 The role of the α2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. Journal of Intensive Care Medicine. 2003; 18(1):29-41.
- Carollo, D.S., Nossaman, B.D. and Ramadhyani, U. Dexmedetomidine: a review of clinical applications. Current Opinion in Anesthesiology 2008;21(4):457-461.
- 42. Venn, R.M., Bradshaw, C.J., Spencer, R., Brealey, D., Caudwell, E., Naughton, C., Vedio, A., Singer, M., Feneck, R., Treacher, D. and Willatts, S.M. Preliminary UK experience of dexmedetomidine, a novel agent for postoperative sedation in the intensive care unit. Anaesthesia. 1999; 54(12):1136-1142.
- 43. Alhashemi, J.A., 2006. Dexmedetomidine vs midazolam for monitored anaesthesia care during cataract surgery, BJA: British Journal of Anaesthesia. 2006;96(6):722–726.