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ORIGINAL ARTICLE

Ultrasound Guided Pecs Ii Block Using Bupivacaine Versus Bupivacaine / Dexmedetomidine Mixture For Perioperative Analgesia In Modified Radical Mastectomy.

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ABSTRACT

Background: Pectoral nerve block (PECS block) is an evolving regional anesthetic technique for breast cancer surgery. Addition of dexmedetomidine may prolong the duration of analgesia of sensory blocks.

This study aimed to compare the effects of Ultrasound-guided PECS II block by either bupivacaine or bupivacaine/dexmedetomidine mixture for perioperative analgesia in modified radical mastectomy (MRM).

Patients and Methods: Forty five female patients undergoing elective unilateral MRM were randomly assigned into 3 equal groups; general anesthesia (GA) group: received conventional GA alone, GA/PECS-B group: received conventional GA plus PECS II block by bupivacaine, and GA/PECS-BD group: received conventional GA and PECS II block by bupivacaine/dexmedetomidine mixture. Intraoperative fentanyl, standard postoperative paracetamol and rescue morphine were given when required. Intra, postoperative opioids consumptions, time to first rescue analgesia, visual analogue scale (VAS), incidence of postoperative nausea and vomiting (PONV), incidence of patient and surgeon satisfaction, and hospital length of stay (LOS) were recorded.

Results: Intraoperative fentanyl, postoperative VAS and morphine consumption were significantly lower, time to first rescue analgesia was significantly longer (p=0.001) and hospital LOS were significantly shorter in GA/PECS-BD group than GA/PECS-B and GA groups and in GA/PECS-B group than GA group. Incidences of PONV and patient and surgeon satisfaction in GA/PECS-B and GA/PECS-BD groups were comparable and significantly lower (p= 0.022) than GA group.

Conclusion: PECS II block produces excellent analgesia in modified radical mastectomy demonstrated by diminished intra- and postoperative opioid requirements, delayed rescue analgesia and lower pain score. Addition of dexmedetomidine can improve the quality of PECS block.

Keywords: Ultrasound; PECS; Dexmedetomidine; Modified radical mastectomy

INTRODUCTION

Acute postoperative pain is an important risk factor in occurrence of chronic pain after breast cancer surgery (BCS). Inadequate pain control can affect patient recovery, impair pulmonary and immune function, and increase the incidence of thromboembolism and myocardial infarction **[1-4]**.

Regional anesthesia for BCS can offer superior acute pain control with chronic pain inhibition while reducing opioid use and its associated side effects. Thoracic epidural and thoracic paravertebral blocks (TPVB) were the gold standard procedures in BCS. While, these procedures are generally invasive, mostly accompanied by sympathetic block. As an alternative to these techniques, Pectoral nerve block

(PECS block) has been described as a hopeful technique during BCS **[4-7]**.

PECS block is interfacial plane block. The original block is PECS I, in which local anesthetic (LA) is deposited between pectoralis major (PMM) and pectoralis minor muscles (pmm) to block the lateral pectoral nerve (C5, 6, 7) and medial pectoral nerve (C8, T1) providing analgesia to the anterior thoracic wall **[8]**.

PECS II block is a modified PECS I block in which LA is injected in 2 planes. The first plane is between PMM and pmm and the second plane is between pmm and serratus anterior muscle (SAM) to block the 2nd to 6th intercostal nerves, including intercostobrachial nerve and the long thoracic nerves (C5-C7). This modification intended to extend analgesia to axilla **[7].**

Dexmedetomidine is highly selective potent α2-adrenoceptor agonist. It has sedative, analgesic, anxiolytic, sympatholytic and analgesic-sparing effects with minimal respiratory depression **[9, 10]**. Dexmedetomidine when added to bupivacaine can significantly shorten the onset time and prolong duration of analgesia of sensory blocks without serious side effects **[10-13]**.

The aim of this study was to compare the effects of Ultrasound-guided PECS II block by either bupivacaine or bupivacaine/dexmedetomidine mixture for perioperative analgesia in modified radical mastectomy (MRM).

PATIENTS AND METHODS

This study was a prospective double-blinded randomized controlled clinical trial. It was conducted at Zagazig University Hospitals (Zagazig, Egypt) from June, 2017 to December, 2019 after obtaining the approval from Institutional Review Board (IRB) and the patient's informed consent. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. Forty five female patients were enrolled in this study. Inclusion criteria were female patients of American Society of Anesthesiology (ASA) physical status II, aged between 21 and 65 years, with body mass index (BMI) between 18.5 and 32 kg/m² and undergoing elective unilateral modified radical mastectomy (MRM). The exclusion criteria were patient refusal, patients with coagulopathy or anticoagulant therapy, local infection at site of injection, advanced liver, renal and cardiac diseases, allergy to local anesthetic and studied drugs and pregnancy or breast feeding besides prior breast surgery except diagnostic biopsies. Randomization was performed using computer generated number tables and concealed using sealed opaque envelopes. Once enrolled in the study, patients were randomly assigned into 3 equal groups: General anesthesia (GA) group which received conventional GA alone, GA/PECS-B group which received conventional GA plus single injection Ultrasound-guided PECS II block by bupivacaine, and GA/PECS-BD group which received conventional GA plus single injection Ultrasound-guided PECS II block by bupivacaine/dexmedetomidine mixture. Data collectors and patients were blind to group allocation.

Preoperative management:

All patients were subjected to preoperative evaluation by history taking, general examination and laboratory investigation. The day before surgery, the study protocol were illustrated to all patients. Patients were kept fasting for about 6-8 hours. Patients were accustomed to the use of ten centimeters visual analogue scale (VAS) identifying (0 as no pain and 10 as worst imaginable pain) **[14].**

Intraoperative management:

In the operating room, intravenous access was secured in contralateral side of surgery and lactated ringer (8-10 ml/kg) was infused. Standard monitoring was applied comprising (pulse oximetry, non-invasive arterial blood pressure cuff and ECG). No premedication was given to prevent factors that may potentiate the effects of tested drugs. Adequate resuscitation equipment, all emergency drugs and lipid emulsion were prepared near the patients.

Conventional GA was induced via intravenous administration of propofol (2-3 mg/kg), fentanyl (l μg/kg) and cisatracurium (0.15 mg/kg) to facilitate endotracheal intubation by cuffed endotracheal tube. Anesthesia was maintained by 1-2 % isoflurane and IV administration of 0.04 mg/kg/20 min of cisatracurium. Patients were ventilated mechanically using volume controlled mode. The minute volume was adjusted to achieve normocapnia (38-42 mmHg). Supplemental intraoperative fentanyl (0.5 μg/kg) was given if there were signs of intraoperative inadequate analgesia such as increased heart rate (HR) and/or mean arterial blood pressure (MAP) by 20% above baseline (after exclusion of other causes of tachycardia or hypertension such as hypovolemia). At the end of surgery, inhalational agent was discontinued and the effect of cisatracurium was reversed with IV administration of 0.05 mg/kg of neostigmine plus 0.02 mg/kg of atropine. Patients were extubated after fulfilling the criteria of extubation then the patients transferred to the post anesthesia care unit (PACU). Standard postoperative paracetamol and rescue morphine were given when required.

Technique of establishment of single injection Ultrasound-guided PECS II block:

Under complete aseptic conditions, the patient was positioned supine with the ultrasound machine on the opposite side to the operator. The linear multi-frequency probe (6-13 MHz) of ultrasound SonoSite M-Turbo (USA) was used.

The probe was positioned under the lateral third of the clavicle transverse to the body axis **[15]**, after recognition of the appropriate anatomical structures under ultrasound guidance; (subcutaneous tissue, PMM, pmm and pleura) from superficial to deep. In between PMM and pmm, there were thoracoacromial artery and lateral pectoral nerve**.** Spinal needle (22 gauge) was inserted in-plane and carefully advanced until it reached the plane between PMM and pmm (**PECS I block)**,then either 10 ml of 0.5% bupivacaine only in GA/PECS-B group or mixed with 1 µg/kg dexmedetomidine in GA/PECS-BD group was slowly injected after frequent negative aspiration with direct visualization of its spread between the two muscles, then the probe moved laterally and distally to reach the level of 2nd, 3 rd and 4th ribs at which the lateral border of the pmm was present. At the 3 rd rib, the serratus anterior muscle (SAM) covering the 2 nd , 3 rd, and 4th ribs, and Parietal pleura were identified. Spinal needle (22 gauge) was advanced in-plane, medially to laterally between pmm and SAM at the level of the 3 rd rib (**PECS II block**); Then either 20 ml of 0.5% bupivacaine only in GA/PECS-B group or mixed with 1 µg/kg dexmedetomidine in GA/PECS-BD group was slowly injected after frequent negative aspiration with direct visualization of its spread between the two muscles as described by Blanco et al [**4, 7, 8]**.

Postoperative management:

In PACU, patients were monitored with standard ASA monitors (pulse oximetry, NIBP device and ECG). Patients scored ≥ 9 in the modified Aldrete scoring system were considered eligible for discharge to surgical ward **[16]**. All patients received paracetamol (1gm IV infusion/ 8 hours) as a standard analgesia. VAS pain score was monitored at (0, 2, 4, 6, 9, 12, and 24 hours postoperatively), when VAS score was ≥ 3, incremental doses of 2-3 mg of morphine (slow IV) was administered.

The following data were detected and recorded:

Patients' demographic data: Age, body weight (Wt), height (Ht) and BMI. **Duration of operation** (calculated from the moment of surgical incision till the moment of adhesive tape application on the wound). **Duration of GA** was calculated from the moment of induction of GA till the moment of withdrawal of inhalational anesthesia at the end of operation. **MAP and HR** were measured at baseline (before induction of GA), at intubation, at surgical incision, at 20 minutes (min) and then every 10 min till the end of operation. **Intraoperative total fentanyl dose**. **VAS score** at 0 (immediately), 2, 4, 6, 9, 12 and 24 hours (h) postoperatively. **Time to first rescue analgesia** (morphine) which is the time from the moment of the end of surgery till VAS score becomes ≥ 3. **Total postoperative morphine consumption** during first 24 h. **Incidence of PONV. Postoperative hospital LOS** (till the patient discharge). **Incidence of patients and surgeon satisfaction** (satisfied /unsatisfied).

Sample size: Sample size was calculated assuming that, number of morphine demands (patient controlled analgesia) in PECS group was (2.5±1.2) and in GA group was (4.3±1.8) **[17]**. So sample size was calculated by Open Epi program to be 45 patients (15 patients in each group) with confidence level 95% and power of test 80%.

Statistical analysis: Collected data were statistically analyzed using Statistical Package for Social Science software (version 20, SPSS Inc., Chicago, IL). Continuous variables that normally distributed were described as mean ± SD. Categorical variables were summarized as frequencies and percentages. Quantitative data was evaluated using Analysis of variance (ANOVA), while qualitative data was evaluated by Chi square test ($\chi 2$). P values <0.05* was considered statistically significant.

RESULTS

All the 45 patients participated in the study completed the study as shown in the CONSORT flow diagram **(Fig.1-suppl)** demographic data including age, Wt, Ht, BMI and duration of surgery did not show any statistical significant differences **(p > 0.05)** between the three groups **(Tab. 1).**

MAP and HR were comparable at baseline readings and at intubation in the three studied groups. Immediately after surgical incision, MAP and HR in GA group were significantly increased **(p = 0.001 and 0.002 respectively)** than in GA/PECS-B and GA/PECS-BD groups and in GA/PECS-B group than in GA/PECS-BD group. Also intraoperative hemodynamics (MAP and HR) in GA/PECS-BD group were better than in the other two groups **(Fig.1&2)**.

The total intraoperative fentanyl dose was statistically significant lower in GA/PECS-BD group (100.0 ± 0.17 µg) than GA/PECS-B group (110.3 ± 0.41 µg) and GA group (150.89 ± 0.22 µg) **(p=0.001)**. Also it was statistically significant lower in GA/PECS-B group compared to GA group **(p=0.009) (Tab. 2)**.

The total postoperative morphine requirement in the first 24 hours was statistically significant lower in GA/PECS-BD group (3.36 ± 0.121 mg) than GA/PECS-B group (5.57 ± 0.23 mg) and GA group (11.07± 0.42) **(p=0.001).** Also it was statistically significant lower in GA/PECS-B group compared to GA group **(p=0.003) (Tab. 2).**

Time to first rescue analgesia was statistically significant longer in GA/PECS-BD group (244.79 ± 0.41 min) than in GA/PECS-B group (164.67 ± 0.49 min) and GA group (91.7 ± 0.13 min) **(P =0.000)**. Also it was statistically significant longer in GA/PECS-B group compared to GA group **(p=0.000) (Tab. 2)**.

The mean postoperative VAS at 0 (immediately), 2, 4, 6, 9, 12, and 24 h after surgery was statistically significant lower in GA/PECS-BD group than GA/PECS-B and GA groups **(p ≤ 0.001).** Also it was statistically significant lower in GA/PECS-B group when compared to GA group. The peak of mean postoperative VAS score was at 2 and 12 h in GA group **(Tab. 3)**.

There was statistically significant increase in patient **satisfaction (p=0.008)** and surgeon satisfaction **(p=0.030)** in GA/PECS-BD and GA/PECS-B groups compared to GA group, with no significant difference between GA/PECS-BD and GA/PECS-B groups **(P > 0.05) (Tab. 4)**.

PONV was statistically significant lower in GA/PECS-BD and GA/PECS-B groups than GA group **(p =0.022)** with no statistically significant difference between GA/PECS-BD and GA/PECS-B groups **(p > 0.05)**. The number of cases was 1(6.7%) in GA/PECS-BD group vs. 1(6.7%) in GA/PECS-B group vs. 6 (40%) in GA group **(Tab. 4).**

Hospital LOS was statistically significant shorter in GA/PECS-BD (1.45 ± 0.05 days) than in GA/PECS-B (1.87 ± 0.05 days) and GA groups (1.98± 0.09 days) **(P =0.001)**. Also it was significantly shorter in GA/PECS-B group than in GA group **(p=0.000) (Tab. 5)**

Table (1): Patients' demographic data and duration of operation in the three studied groups.

Patients demographic data	GA group (n=15)	GA/PECS-B group (n=15)	GA/PECS-BD group (n=15)	P value (ANOVA) Test
Age (years)	41.6±7.16	39.33±7.59	38.66±4.32	0.44
Height (m)	1.61±0.037	1.60±0.029	1.62±0.032	0.79
Weight (Kg)	78.83±5.52	78.16±5.92	78.23±5.41	0.93
BMI (kg/m^2)	30.43±1.39	30.26±1.70	29.20±1.97	0.11
Duration of operation (min)	100.00±7.26	101.33±7.93	100.13±9.56	0.89
Duration of GA (min)	128.53±8.10	129.33±7.76	133.33±9.38	0.26

Data are expressed as mean ± standard deviation (SD).
P* value < 0.05: Significant.
P value > 0.05: Not significant.

Table (2): Intraoperative total fentanyl doses, postoperative total morphine requirement in the first 24 h and the time to first rescue analgesia in the studied groups.

Item	GA group (n=15)	GA/PECS-B group (n=15)	GA/PECS-BD group (n=15)	P-value (ANOVA) Test
Total fentanyl doses (µg)	150.89 ± 0.22	110.3 ± 0.41	100.0 ± 0.17	0.001
p-value of post Hoc	----	0.009*[a]	0.000*[b]	
	----	-----	0.000*[c]	
Total morphine requirement in the first 24 h (mg)	11.07± 0.42	5.57 ± 0.23	3.36 ± 0.121	0.001
p-value of post Hoc	----	0.003*[a]	0.000*[b]	
	----	----	0.009*[c]	
Time to first rescue analgesia (min)	91.7 ± 0.13	164.67 ± 0.49	244.79 ± 0.41	0.000
p-value of post Hoc	----	0.000*[a]	0.000*[b]	
	----	-----	0.000*[c]	

Data are expressed as mean ± SD.
P* value < 0.05: Significant.

P value > 0.05: Not significant.
[a]; comparison between GA and GA/PECS-B groups.
b; comparison between GA and GA/PECS-BD groups.
c; comparison between GA/PECS-B and GA/PECS-BD groups.

Table (3): Mean postoperative VAS scores at various times of measurement in the three studied groups.

VAS	GA group (n=15)	GA/PECS-B group (n=15)	GA/PECS-BD group (n=15)	P-value (ANOVA) Test
Immediate postoperative	2.1±0.42	1.8±0.33	1.4±0.32	**<0.001**
2 h	3.4±0.56	2.7±0.42	2.3±0.36	**<0.001**
4 h	3.2±0.33	2.9±0.3	2.5±0.41	**<0.001**
6 h	3.3±0.35	3.0±0.33	2.7±0.32	**0.001**
9 h	3.2±0.4	2.88±0.34	2.3±0.38	**<0.001**
12 h	3.4±0.34	3.0±0.32	2.7±0.31	**<0.001**
24 h	2.8±0.32	2.5±0.36	2.1±0.3	**0.001**

Data are expressed as mean ± SD.
P* value < 0.05: Significant.
P value > 0.05: Not significant.

Table (4): The incidences of patient and surgeon satisfaction and postoperative nausea &vomiting (PONV) in the studied groups.

Item	GA Group (n=15)		GA/PECS-B group (n=15)		GA/PECS-BD group (n=15)		P-value (chi – square test)
	N	**%**	**N**	**%**	**N**	**%**	
patient satisfaction							
▪ Unsatisfied	11	73.3%	5	33.3%	3	20.0%	0.008
▪ Satisfied	4	26.7%	10	66.7%	12	80.0%	
P-value of chi –square test	----		0.028*[a]		0.003*[b]		
	----		----		0.681*[c]		
Surgeon satisfaction							
▪ Unsatisfied	11	73.3%	6	40.0%	4	26.7%	0.030
▪ Satisfied	4	26.7%	9	60.0%	11	73.3%	
P-value of chi –square test	----		0.050*[a]		0.010*[b]		
	----		----		0.438*[c]		
Postoperative nausea & vomiting							
▪ No	9	60%	14	93.3%	14	93.3%	0.022
▪ Yes	6	40%	1	6.7 %	1	6.7%	
P-value of Chi –square test	----		0.030*[a]		0.030*[b]		
	----		----		1.00*[c]		

Data are expressed as numbers and percentages.
P* value < 0.05: Significant.
P value > 0.05: Not significant.
[a]; comparison between GA and GA/PECS-B groups.
b; comparison between GA and GA/PECS-BD groups.
c; comparison between GA/PECS-B and GA/PECS-BD groups.

Table (5): postoperative hospital length of stay (LOS) in the three studied groups.

Item	GA Group (n=15)	GA/PECS-B group (n=15)	GA/PECS-BD Group (n=15)	P-value (ANOVA) Test
Hospital length of stay (days)	1.98± 0.09	1.87 ± 0.05	1.45 ± 0.05	0.001
p-value of post Hoc	----	0.000*[a]	0.000*[b]	
	----	-----	0.000*[c]	

Data are expressed as mean ± SD.
P* value < 0.05: Significant.
P value > 0.05: Not significant.
[a]; comparison between GA and GA/PECS-B groups.
[b]; comparison between GA and GA/PECS-BD groups.
[c]; comparison between GA/PECS-B and GA/PECS-BD groups.

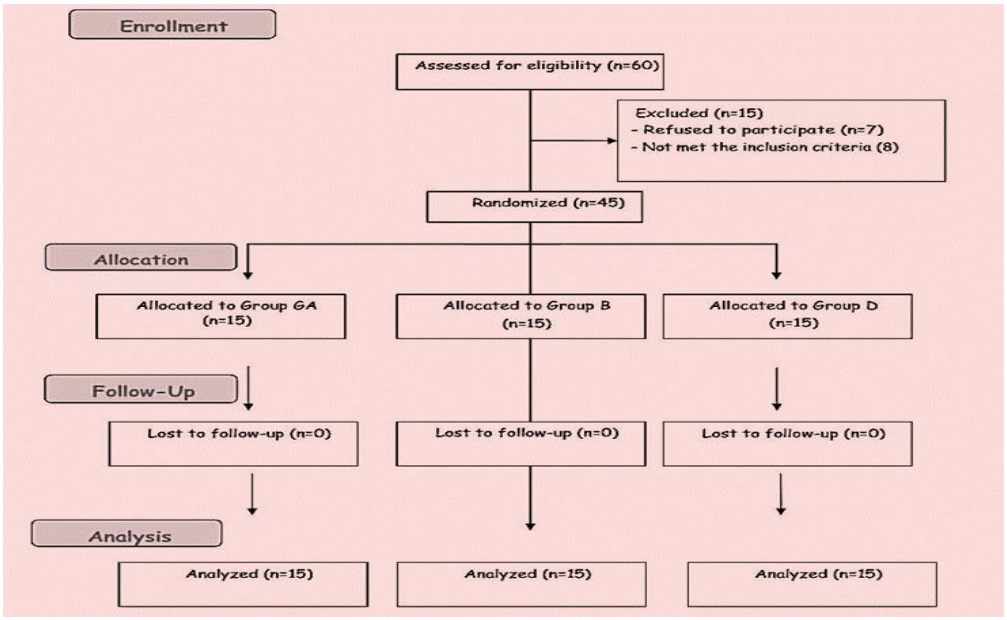

Fig. 1-suppl): CONSORT flow diagram

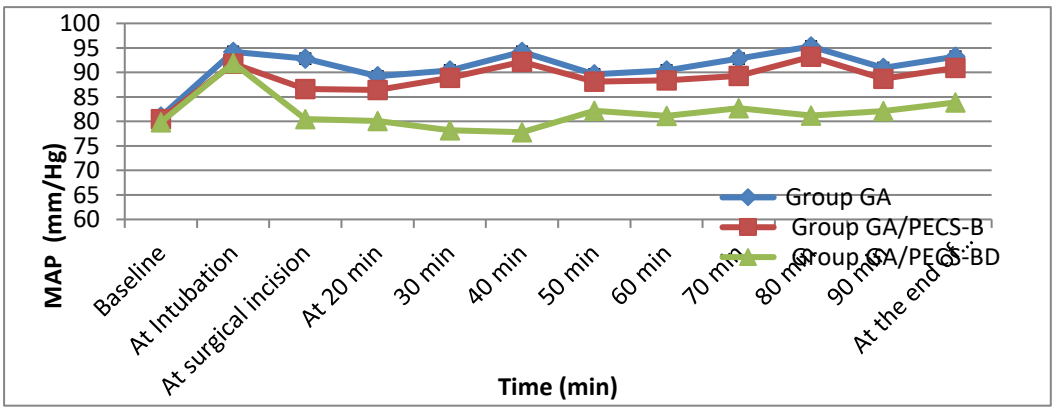

Fig. (1): Intraoperative changes in the mean arterial pressure (MAP) among the three studied groups.
- Data are expressed as (Mean ± SD).
- Baseline= just before induction of general anesthesia.

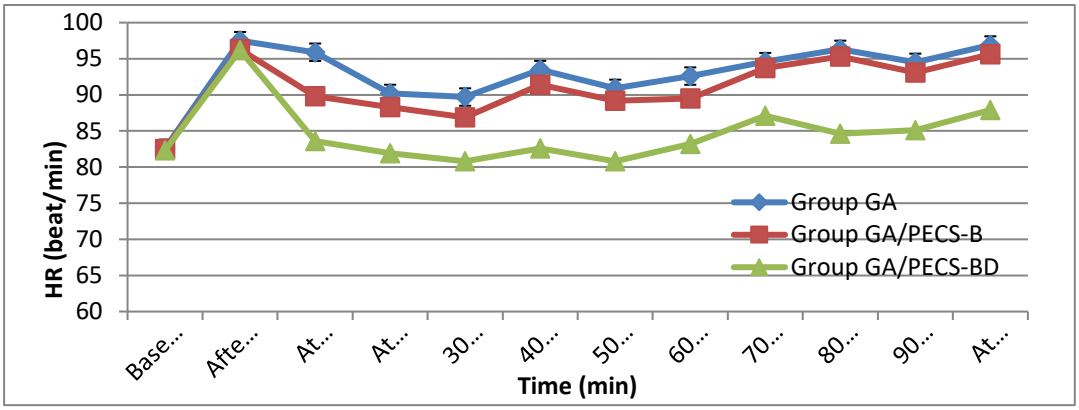

Fig. (2): Intraoperative heart rate (HR) changes among the three studied groups.

- Data are expressed as (Mean ±SD).
- Baseline= just before induction of general anesthesia.

DISCUSSION

In the current study, intraoperative hemodynamics (MAP and HR) were more stable in GA/PECS-BD group than in the other two groups. This finding may be attributed to the analgesic and sympatholytic activity of dexmedetomidine. Total intraoperative fentanyl and postoperative morphine consumptions were statistically lower in GA/PECS-BD group than in GA/PECS-B and GA groups. The time to first rescue analgesia was statistically significant longer in GA/PECS-BD group than in GA/PECS-B and GA groups. The mean VAS scores at 0, 2, 4, 6, 9, 12 and 24 h postoperatively in GA/PECS-BD group were statistically significant lower than those in GA/PECS-B and GA groups. Also, the incidences of patient and surgeon satisfactions in GA/PECS-BD and GA/PECS-B groups were statistically comparable and significantly lower than that in GA group. PONV was statistically significant lower in GA/PECS-BD and GA/PECS-B groups than GA group with no statistically significant difference between GA/PECS-BD and GA/PECS-B groups. Additionally, hospital LOS was statistically significant shorter in GA/PECS-BD group than in GA/PECS-B and GA groups.

These findings agreed with **Kumar et al [18],** who reported that there was better intraoperative hemodynamic stability observed in PECS group compared to GA group, they also demonstrated that there was significant reduction **(P< 0.05)** in intraoperative fentanyl and postoperative morphine in PECS group compared to GA group in the first 12 hours. Also, there was delayed rescue analgesia in PECS group than in GA group with statistically significant difference **(P < 0.05)** between the two groups. Furthermore, they demonstrated significant reduction in VAS scores and PONV scores **(P <0. 05)** in PECS group than in GA group.

The same results were obtained by **Bashandy and Abbas [17]** who revealed significant reduction **(P< 0.05)** in intraoperative fentanyl, postoperative morphine, VAS scores, and PONV scores in the PECS group than in GA group. Also, there was delayed rescue analgesia in PECS group than in GA group with statistically significant difference **(P < 0.05)** between the two groups. Also they proposed that there was significant reduction **(P <0. 05)** in hospital LOS in PECS group than GA group.

The same results were obtained by **Hassn et al [19]** who found that there was significant reduction of hemodynamic response to intubation as well as surgical incision in PECS group using bupivacaine and dexmedetomidine compared to placebo (PECS using saline) group**.** Additionally they concluded that there was significant reduction in intraoperative opioid consumption, total postoperative analgesia, and hospital LOS **(P <0.05)** in PECS group using bupivacaine plus dexmedetomidine compared to placebo group.

Similar results were obtained by **Kim et al [20]** who reported that there was significant reduction in MAP and HR after surgical incision in PECS II group compared to GA group in BCS. Also **Senapathi et al [21]** concluded that there was significant reduction in intraoperative opioid consumption and total postoperative analgesia in PECS group compared to placebo group. Additionally, **Kulhari et al [22]** stated that there was reduction in 24 h morphine consumption in the PECS II group compared to TPVB group, also there was prolongation of the duration of analgesia in the PECS II group compared to TPVB group**.**

Also these results coincided with **Kaur et al [23]** and **Manzor et al [24]** who reported that postoperative pain scores numerical rating score (NRS) and VAS were significantly lower in PECS group using dexmedetomidine than PECS group using LA only.

The results of the present study were not in agreement with the results of **Cros et al [25],** who performed a placebo-controlled trial, multimodal analgesic regimen. They found that intraoperative

sufentanil and postoperative morphine consumption in the 1st 24 hours did not differ between the 2 groups (PECS I using saline and PECS I using bupivacaine), Also they revealed that there was no significant difference in NRS observed between PECS group using bupivacaine and placebo group during recovery. As they assumed that Pecs I block alone may not be necessary to reduce pain scores when postoperative analgesia is adjusted by dexamethasone, wound infiltration with a long-acting LA, acetaminophen, and NSAIDs ± morphine. Also this may be due to inability of PECS I to block the thoracic intercostal nerves (T2-T6) and long thoracic nerve which extend analgesia to axilla.

Additionally, the results of the current study were not in accordance with **Manzor et al [24]** who found that patient satisfaction was significantly better in dexmedetomidine group than bupivacaine group. Also, **Morioka et al [3]** reported that the incidence of PONV was not significantly different between total intravenous anesthesia (TIVA) group and TIVA plus PECS group. This may be due to lack of significant difference regarding postoperative opioids between two groups, which may attributed to inability of PECS to block the anterior cutaneous branches of the intercostal nerves. Increased postoperative opioids may be the cause of increased incidence of PONV.

This study has some limitations:

The present study has some limitations as small sample size with subsequent under power of the study and inability to assess the onset and the level of sensory block because the block was performed after induction of GA.

CONCLUSION:

PECS II block provides excellent analgesia in conjunction with general anesthesia in modified radical mastectomy, demonstrated by delayed first analgesic request, diminished analgesics needs, and lower pain score. It reduced Postoperative nausea and vomiting, hospital length of stay with better patient and surgeon satisfaction. Addition of dexmedetomidine improves the quality of PECS block and significantly prolongs the duration of analgesia without major side effects.

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