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Analgesic efficacy of pre-emptive ultrasound-guided mid-point transverse process to pleura block for patients undergoing posterolateral thoracotomy incisions: Randomized controlled trial

Heba Abdelhamid Mohammed, Aliaa Muhammad Belal, Rehab Said Elkalla and Sohair Mostafa Soliman

Anesthesiology, Surgical Intensive Care and Pain Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt

ABSTRACT

Background: For anesthesiologists, managing pain during and after thoracic surgery remains a significant challenge. This research aims to assess the safety and efficacy of ultrasound (US)-guided pre-emptive mid-point transverse process to pleura (MTP) block for posterolateral thoracotomy.

Methods: This prospective randomized, double-blind clinical trial was conducted on 70 patients scheduled for a posterolateral thoracotomy operation under general anesthesia (GA). Patients were classified randomly and equally into Group I (MTP group) received MTP blocks, and Group II (sham block) received 2 ml of saline solution. The blocks were done after induction of GA but before the skin incision.

Results: Numerical rating scale (NRS) at rest and cough, total morphine consumption, the incidence of chronic pain at 3 months, and undesirable side effects (nausea, vomiting, respiratory depression) were significantly lower in MTP block than in sham block. Oxygen saturation and SpO_2/FiO_2 raised significantly in the MTP block than in the sham block ($P < 0.001$).

Conclusions: The US-guided MTP block provided effective analgesia with a lower pain score, lesser rescue analgesics consumption, and reduced risk of developing chronic pain posterolateral thoracotomy.

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Mid-Point transverse process to pleura; acute pain, chronic pain efficacy; thoracotomy; pre-emptive

1. Introduction

For anesthesiologists, managing pain during and after thoracic surgery remains a significant challenge. Comprehensive pain management during surgery, including cutting-edge peripheral nerve-blocking techniques, may reduce the significant risk of post-thoracotomy pain syndrome [1].

A thoracotomy, and more specifically, a posterolateral thoracotomy enable for safe control of pulmonary blood vessels during pulmonary resection, in addition to providing excellent access to the lung, middle and posterior mediastinum, hilum, endo thoracic trachea, and endo thoracic esophagus. The posterolateral thoracotomy has two possible drawbacks. It can cause problems with breathing by tightening chest muscles and making it harder to expand and contract the lungs [2].

A large number of patients may develop postoperative thoracotomy pain syndrome (PTPS), defined as "pain that recurs or continues along a thoracotomy scar at least 2 months after the surgery" as a result of insufficient postoperative pain treatment [3,4].

Postoperative pain can be better managed with multimodal analgesia, and combining different pain relief medication decreases the risk of side effects, such as those caused by opioids (such as nausea, pruritus, and vomiting) and respiratory depression [5].

Preemptive preoperative analgesia has evolved over the years since it was first proposed to be recognized as an intervention administered before the incision that facilitates postoperative mobilization and functional rehabilitation through reduced postoperative opioid consumption, reduced risk of complications, and increased patient satisfaction [6,7].

Costach et al. marked the introduction of the mid-point transverse process to pleura (MTP) block as a modified paravertebral block in 2017 [8]. Injections of LAs are made between the transverse process and the pleura. The LA travels via the fenestrations in the superior costotransverse ligament at the injection level and frequently to adjacent levels, reaching the dorsal and ventral rami in the paravertebral region [9].

This research aims to evaluate the analgesic efficacy and safety of ultrasound (US)-guided MTP block before posterolateral thoracotomy in cardiothoracic procedures.

CONTACT Heba Abdelhamid Mohammed heba.abdelhamid@med.tanta.edu.eg Demonstrator of Anesthesiology, Surgical Intensive Care and Pain Medicine, Faculty of Medicine, Tanta University, El-Gash Street, Medical Campus, The Faculty of Medicine, Tanta, El-Gharbia Governorate, Egypt

2. Patients and methods

This current randomized, double-blind study was conducted on 70 patients aged 21 to 65, male and female, American Society of Anesthesiologists (ASA) class II and III, and scheduled for a posterolateral thoracotomy for lobectomy, pneumonectomy, and decortication under general anesthesia (GA) at Tanta University Hospital in Cardiothoracic theatres from June 2021 to June 2022 after approval from our ethical committee of the faculty of Medicine of Tanta University with approval code 34,646/4/21. The study was registered at Clinical Trials Registry with the "NCT 05044858" registration number.

Our study excluded patients with a history of chronic pain or drug abuse, an allergy to local anesthetics, or a local infection at the procedure site. The reasoning behind the procedure was explained to each patient, benefits and potential risks of the study. Written informed consent was obtained from all patients.

2.1. Study design and sample size calculation

Our study's sample size was derived using formulas derived from existing research [6,7], which investigated the efficacy of MTP block (by Numerical Rating Scale (NRS)) as a primary outcome. There needed to be at least 30 participants in each group for a statistically significant difference of at least one to be seen in the postoperative NRS at 0.05 alpha error and 80% power of the study. To compensate for possible dropouts, we increased the sample size to 35 patients in each group.

Two groups of patients were randomly selected (35 participants each). Group 1 (MTP block): MTP blocks were administered. Group 2 (sham block): The similar procedures were performed but with injection of 20 ml saline solution. The blocks were performed after induction of GA but before skin incision.

2.2. Preoperative preparation

History taking, a clinical examination, and standard laboratory tests were performed before the operation. Gabapentin was prescribed to be started 1 week before the surgery at a dose of 300 mg/day at bedtime to be continued along the course of healing.

During the pre-anesthetic assessment (in the holding area), all patients were familiarized with NRS [9]. Every patient received midazolam at a dose of 0.02 mg/kg as premedication.

2.3. Intraoperative

Heart rate, non-invasive blood pressure, oxygen saturation, and temperature were all monitored in both groups using standard equipment (Datex Ohmeda). Later 3 min of pre-oxygenation, GA was induced with fentanyl 2 mic/kg, propofol 2 mg/kg, and tracheal intubation was aided by 0.5 mg/kg of atracurium. Anesthesia has been maintained with O_2 60% and isoflurane (one MAC), and the dial system was operated up and down according to patients' awareness which was monitored by a Bispectral Index between (40–60) and a change of hemodynamics. Mechanical ventilation was performed with end-tidal CO_2 around (30–40) mmHg.

2.4. For group 1 (MTP block)

The patient was seated in a lateral position, the incision site (usually T5-T6) was marked and the block region was sanitized with povidone-iodine. MTP block was performed at T5 level which was determined by counting from the twelfth rib. A high-frequency linear US probe (Philips CX50) was positioned 3-cm lateral to the spinous process in a sagittal manner. An echogenic needle with a short bevel was inserted in-plane in a cranial-caudal plane using a 22-gauge, 100-mm needle. The ultrasonic probe's customization targeted the transverse process, the costotransverse ligament, the pleura, the lung tissues, and the paraspinal muscles (erector spinae, trapezius, rhomboid). Following negative blood aspiration, a titrated bolus of 20 ml of 0.25% bupivacaine and dexamethasone 8 mg was injected superficially into the costotransverse ligament, and 15 min later, an incision was made to perform the surgical procedure. The location where the needle was supposed to stop was directly in the middle of the line connecting the transverse process's end to the pleura along its posterior border. Figure (1)

2.5. For group 2 (Sham block)

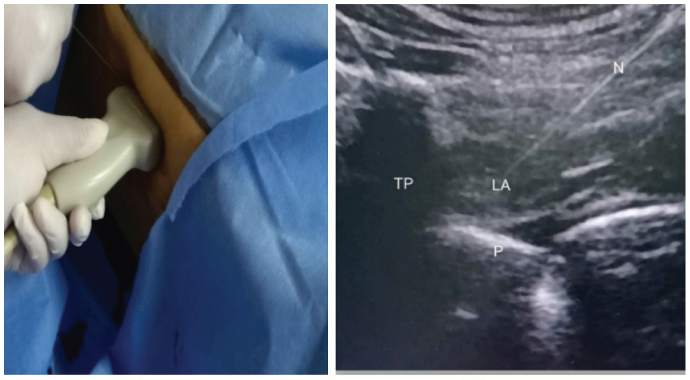
Using a similar procedure and MTP block approach but injecting a placebo (20 ml of normal saline) instead of local anesthetic.

At the end of the procedure, the patient was brought out of GA by administering neostigmine (0.05 mg/kg) to reverse the effects of the anesthetic on the muscles.

After recovery from anesthesia and on arrival to the recovery room, evaluation of pain intensity by postoperative (NRS) at rest and coughing was recorded, and paracetamol 1 g every 8 h would be administrated as analgesia at a regular base and required additional rescue analgesia was given if the (NRS) is four or more by IV morphine 3 mg was titrated at any time, and the total dose was calculated.

2.6. Measurement

NRS for pain was measured at rest and coughing at 0, 4, 8, 12, and 18 h. When NRS was four or above,



(A) (B)

Figure 1. (a): Identification of insertion point 3 cm lateral to the spinous process of (T5-T6). (b): Ultrasound-guided mid-point transverse process to pleura. The local anesthetic injection was made at the midpoint between the posterior border of the transverse process and the pleura (LA; local anesthetic, N; needle).

morphine of 3 mg was administered and increased as needed; 24-h postoperative morphine use and time until first rescue analgesia is given.

O_2 saturation and O_2 saturation/fraction of inspired oxygen (SpO_2/FiO_2) proportion were measured at 6, 8, 12, and 24 h postoperatively.

Development of chronic post-thoracotomy pain was investigated through regular pain clinic visits, and we telephoned our patients in between their regular visits for 3 months after surgery and asked them about pain, either recurring or persisting along of chest tube, pain characteristics either burning, shocking, or aching sensation. Also, we asked about the pain severity, physical and functional impairment, and the received treatment prescribed to control this pain, and

Undesirable side effects experienced within the 1st 24 h were recorded (nausea, vomiting, pruritus, and local anesthetic toxicity), and any technique-related complication was recorded.

The NRS pain score is the primary outcome. The secondary outcomes are adverse events and post-thoracotomy pain over 3 months of follow-up.

2.7. Statistical analysis

IBM's SPSS software (Armonk, New York: IBM Corp) version 20.0 was used for data entry and analysis. Normal distribution was confirmed using the Shapiro–Wilk test. Non-parametric data were characterized using the median and interquartile range, while parametric data were presented with range, mean, and standard deviation. The tests used were: The Chi-square test analyzed two categories or groups. Monte Carlo correction: To adjust the chi-square test. Student's t-test: When comparing two groups using quantitative variables with a normal distribution. ANOVA with repeated measures: When comparing quantitative variables over more than two time periods, assuming they are normally distributed, and Post Hoc test (Bonferroni adjusted) for pairwise comparisons as heart rate and mean arterial blood pressure. Mann Whitney test for improperly distributed quantitative data that cannot be directly compared between the two categories. A P value < 0.05 was considered to be significant.

3. Results

There were 85 patients assessed, and 15 were ruled out because they did not match the inclusion criteria (three patients had bleeding disorders, four were drug abused, two had skin infections at the block site, and two had a history of local anesthetic allergy). Also, four patients declined to take part in the research. Finally, 70 patients were included in the research. Seventy participants were divided into groups with equal numbers (35 patients each) by random selection of envelopes, prepared in advance and containing a computer-generated random number: US-guided MTP and sham block. There was no dropout in the follow-up periods; finally, 35 patients were analyzed in each group (Figure (2)).

Age, gender, and ASA physical status did not differ significantly between the two groups (Table 1).

There was a statistically significant increase of pain intensity measured by NRS at rest and with coughing in the Sham group as compared to the MTP group at 0, 4, 8, 12, and 18 h postoperatively with (P less than 0.001), indicating superiority of analgesia in the MTP group over the sham group. At the same time, there was no significant difference at any other time studied. Figure 3(a,b)

There was a statistically significant decrease of oxygen saturation in the Sham group compared to the MTP group at six, eight, 12, and 24 h after surgery with (P less than 0.001). Figure 4(a)

There was a statistically significant decrease of SpO_2/FiO_2 in the Sham group compared to the MTP group (P less than 0.001) after surgery 6, 8, 12 and 24 h after surgery (Figure 4(b)).

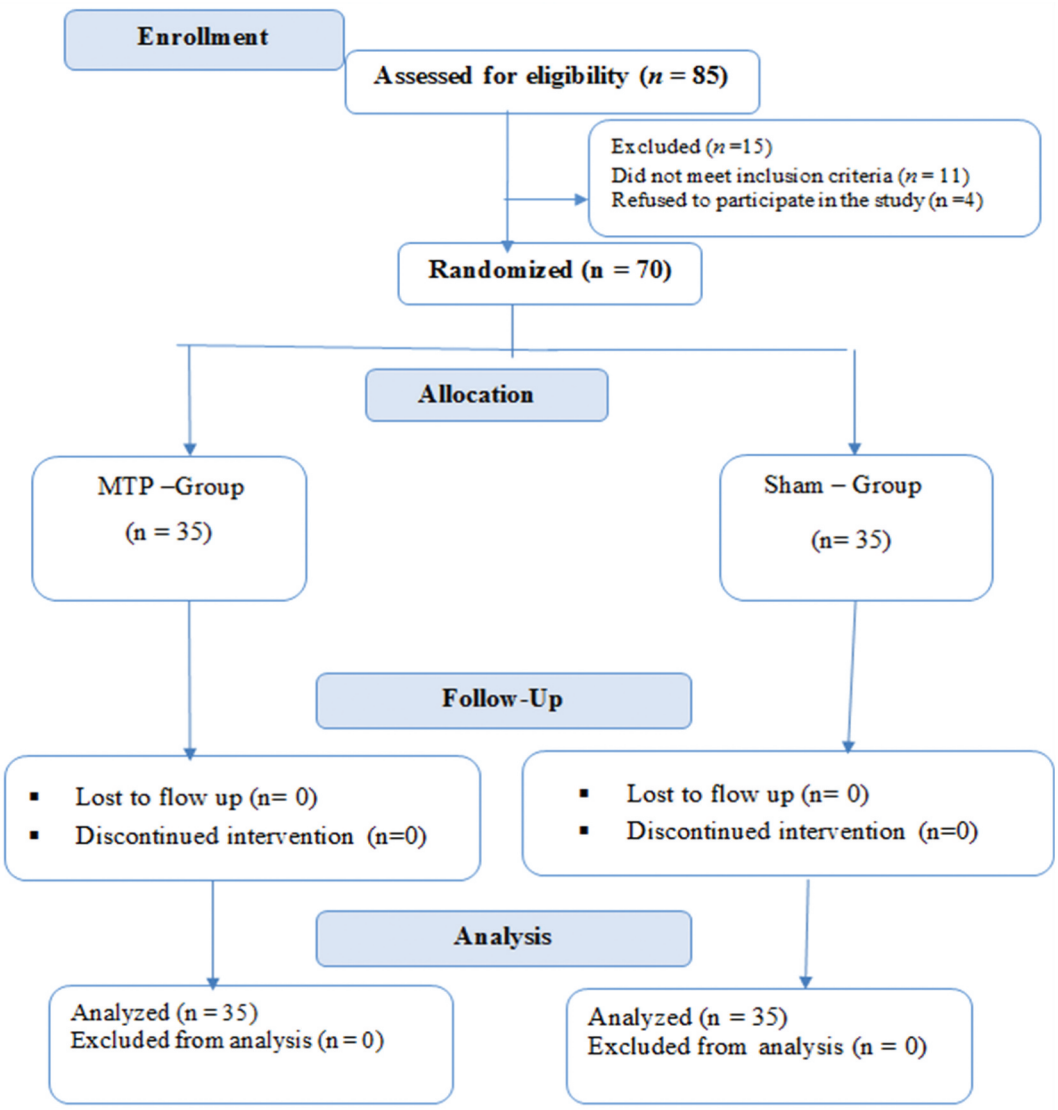


Figure 2. CONSORT flow diagram.

Table 1. Comparison of the two study groups based on demographic information.

	Group I (*n* = 35)		Group II (*n* = 35)			
	No.	%	No.	%	Test of Sig.	P
Sex						
Male	21	6.0	22	62.9	χ2=	0.806
Female	14	4.0	13	37.1	0.060	
Age (years)						
Min. – Max.	23.0–63.0		23.0–6.0		t=	.716
Mean ± SD.	43.31 ± 11.45		44.26 ± 1.10		0.365	
ASA						
II	20	57.1	22	62.9	χ2=	0.626
III	15	42.9	13	37.1	0.238	

SD: **Standard deviation, t: Student t-test**, χ2: **Chi-square test**, p: p-value for comparing between the two studied groups.

There was a statistically significant increase in the time of first rescue analgesia in the MTP group as IQR (18.0–18.0) compared to the sham group as IQR (4.0–18.0) (*P* values = 0.001). There was a statistically significant increase in total morphine consumption in the sham group as IQR (1.50–9.0) as compared to the MTP group as IQR (0.0–1.50) (*P* value < 0.001). Table 2

In the MTP group, there were six patients developed post-thoracotomy pain (2 stabbings while 4 tinglings), mostly along the scar incision, and two patients extended to the chest tube site, all patients suffered from mild-to-moderate pain, three patients developed persistent pain after the surgery. In comparison, other three patients developed recurrent pain within 1 month, five patients responded to NSAID and one

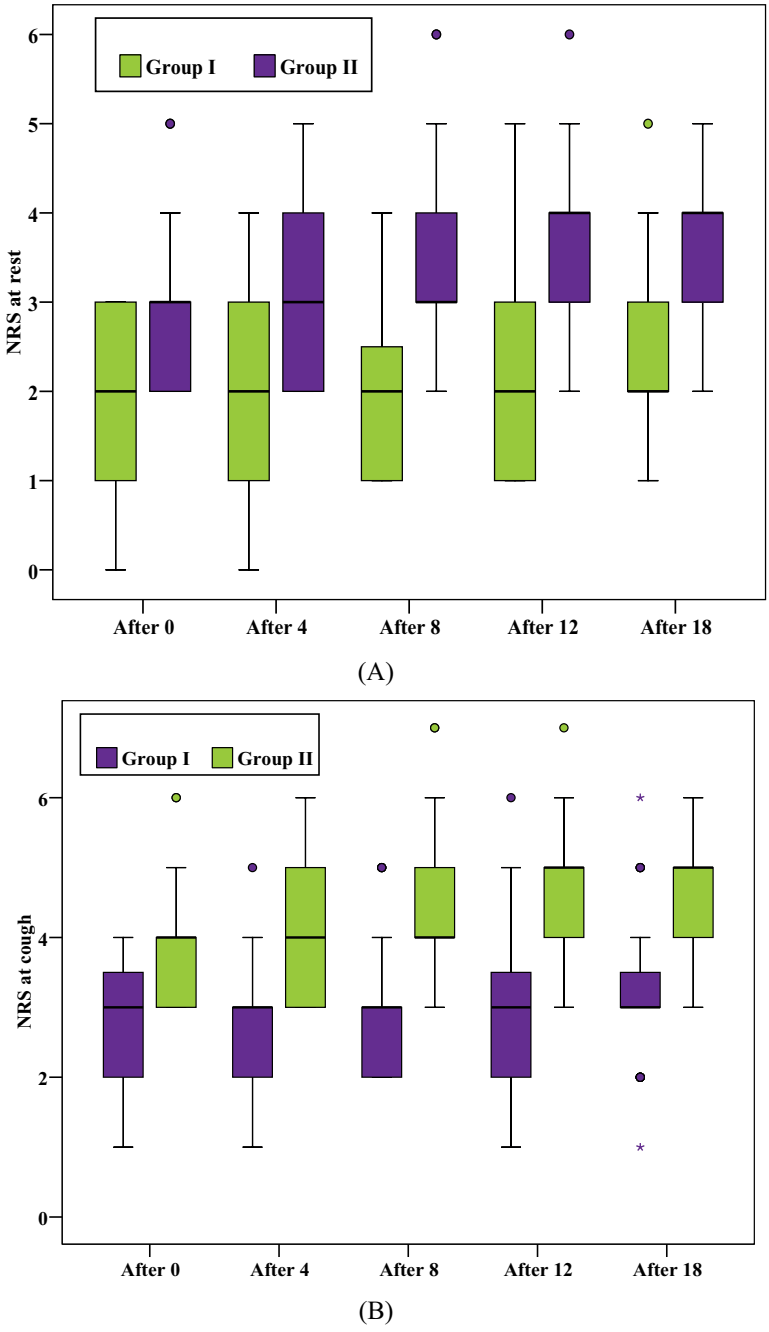


Figure 3. Comparison between the two groups regarding resting NRS (A) and during coughing (B).

patient needed an increased dose of gabapentin, and one patient developed physical and emotional impairment. While in the sham group there were 15 patients developed post-thoracotomy pain (10 stabbing while 5 tingling), mostly along the scar incision, and 4 patients extended to the chest tube site, 9 patients suffered from mild-to-moderate pain while 6 suffered from severe pain, 7 patients developed persistent pain after the surgery. In comparison, eight other patients developed recurrent pain within 1 month, 10 responded to NSAID, 5 needed increased gabapentin, and 5 developed physical and emotional impairment (Table 2)

There was a significant increase in the incidence of undesirable side effects (nausea, vomiting, respiratory depression) in the sham group versus the MTP group ($p < 0.001$). Table 3

4. Discussion

The MTP block has the advantage over the standard PVB in that visibility of the SCTL is unnecessary, which may be challenging in obese patients. The second advantage of this block is that the needle's target point is rather superficial and not close to tissues like the pleura or neurovascular bundles [9].

In our study, there was a significant increase of NRS in the Sham group as compared to the MTP group at 0, 4, 8, 12 and 18 h postoperatively at rest and with cough with ($P < 0.001$), indicating effective

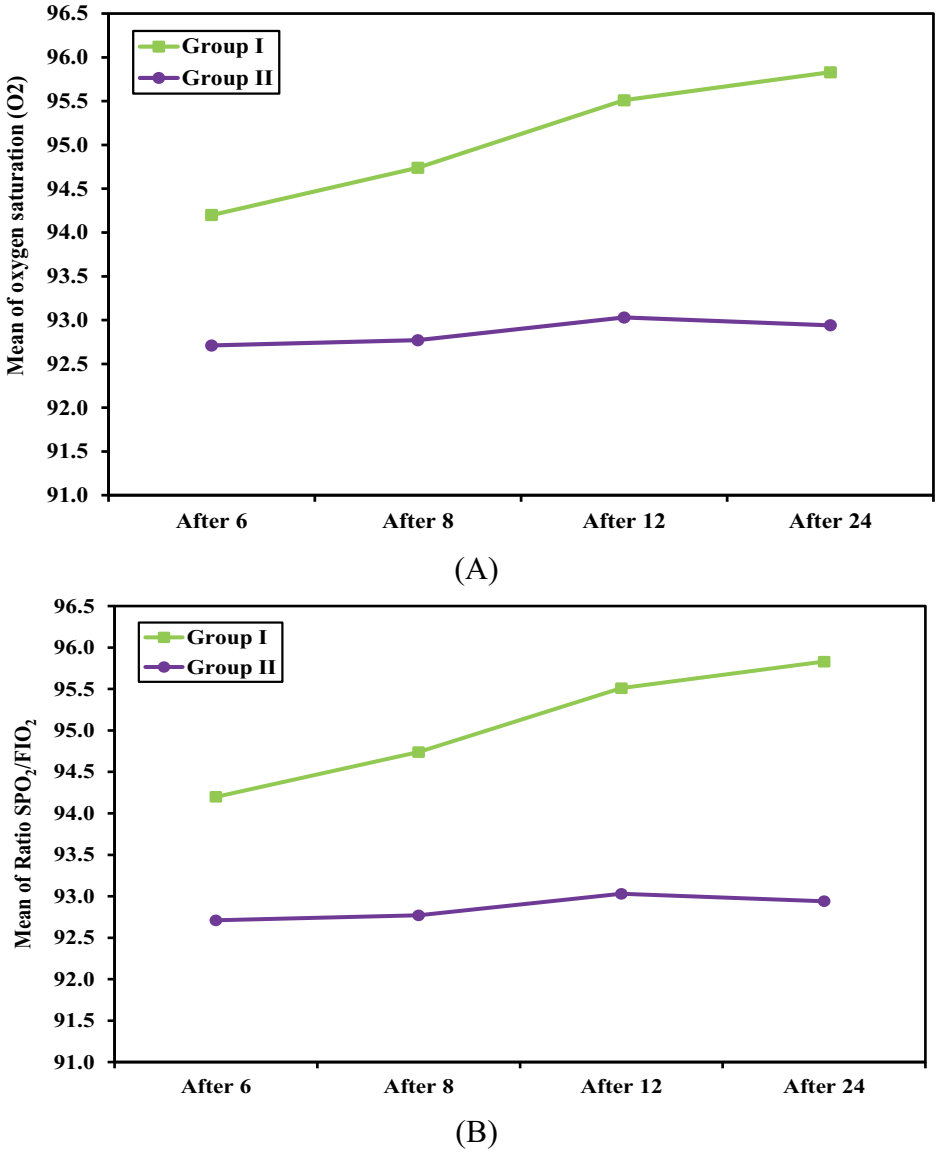


Figure 4. Comparison between the two studied groups according to oxygen saturation (%) (A) and SpO_2/FiO_2 (B).

Table 2. Comparison of the two groups concerning the time to first analgesic requirement and total morphine use and chronic pain at 3 months.

	Group I ($n = 35$)	Group II ($n = 35$)	Test of Sig.	P
Time of first rescue analgesia (h)				
Min. – Max.	4.0–18.0	0.0–18.0	U = 292.5*	0.001*
Median (IQR)	18.0 (18.0–18.0)	8.0 (4.0–18.0)		
Total morphine (mg)				
Min. – Max.	0.0–12.0	0.0–15.0	U = 268.0*	<0.001*
Median (IQR)	0.0 (0.0–1.50)	6.0 (1.50–9.0)		
Chronic pain at 3 months			**χ2**=5.510*	0.019*
Absent	29 (82.9)	20 (57.1)		
Present	6 (17.1)	15 (42.9)		

IQR: Inter quartile range, U: Mann Whitney test, χ2: Chi-square test, *: Statistically significant at $p \leq 0.05$.

and prolonged analgesia reaching 18 h postoperatively in the MTP group. This prolonged time of analgesia may be due to adding dexamethasone to bupivacaine.

In line with our results, Costache et al. [8] investigated a case of 77-year-old presented for right mastectomy and sentinel lymph node biopsy and received MTP block before induction of GA. They found that the patient's pain score was 0/10 on arrival to recovery and 1–2 at discharge from the recovery room.

Also, Bhoi et al. [10] investigated a case report of 61-year-old planned to undergo with right-breast lump excision and sampling of axillary node. The MTP block was conducted in the pre-anesthesia room at the T2, T3 and T5 levels (7 ml of 0.375% ropivacaine at each level). Pain score was zero (both

Table 3. Comparison of the two groups concerning undesirable side effects in both groups.

	Group I ($n = 35$)		Group II ($n = 35$)			
	No.	%	No.	%	χ^2	^{MC}p
No complications	28	8.0	10	28.6	18.655*	<0.001*
Nausea	3	8.6	9	25.7		
Respiratory depression	3	8.6	10	28.6		
Vomiting	1	2.9	6	17.1		

χ^2: Chi-square test, MC: Monte Carlo, *: Statistically significant at $p \leq 0.05$.

at rest and during movement) upon awakening. Within one hour, the patient was moved to a ward. 1 g of intravenous paracetamol is routinely administered every 6 h. At 12 h, the patient complained of mild pain with movement, which was alleviated by 75 mg of IV diclofenac.

Also, Syal et al. 2020 [11] studied a case report of 64-year-old woman with morbid obesity scheduled for modified radical mastectomy. They performed MTP block (20 ml of 0.5% ropivacaine) before surgery. They demonstrated that pain was mild at rest and on movement postoperatively.

In contrast to our findings, Eskin et al. [12] compared US-guided MTP block (20 mL of 0.25% bupivacaine) for postoperative pain management in patients undergoing elective lumbar decompression surgery for one or two vertebral levels. The results showed that MTP block effectively reduced postoperative pain compared to the control group.

In the present study, there was a significant decrease in 18 hr postoperative morphine consumption and prolonged time of first rescue analgesia in the MTP group as compared to the Sham group, indicating the adequate analgesic quality of the MTP block.

In agreement with our study, Syal et al. 2020 [11] found that the patient reported mild pain, and needed significantly fewer opioids.

Also, Eskin et al. [12] showed that the MTP group waited considerably longer than the control group before needing any rescue analgesia. The number of patients requiring rescue analgesia was significantly lower with MTP than with controls during the 1st 12 h after surgery.

There was a statistically significant decrease in oxygen saturation and SpO_2/FiO_2 in the Sham group compared to the MTP group at 6, 8, 12, and 24 h postoperatively. The difference in oxygen saturation can be explained by improving the respiratory mechanics due to good analgesia, even during a cough.

Pedoto et al. [13] reported a 55-year-old woman with metastatic breast requested thoracoscopy under sedation for the treatment of a recurrent, loculated, malignant right pleural effusion. The patient did not move, breathing on his own, and remained adequately oxygenated. At the same time, an MTP block was performed under US guidance using 30 mL of 0.25% bupivacaine hydrochloride, 10 mL of 2% lidocaine, 4 mg of dexamethasone, and 100 g of clonidine injected in 5 mL increments.

In the current study, there was a statistically significant increase in the incidence of undesirable side effects (nausea, vomiting, respiratory depression) in the Sham group versus the MTP group ($p < 0.001$). This may be explained by increased opioid consumption in the Sham group.

In addition to our study, Syal et al. 2020 [11] found that the patient reported a better recovery profile, with less postoperative nausea and vomiting, earlier ambulation, and less time spent in bed.

Moreover, Kahramanlar et al. [14] found that vascular injury, pneumothorax, hypotension, epidural or spinal injection, and nerve damage are less likely to occur with the MTP block in patients undergoing unilateral simple mastectomy.

In the present trial, there was a significant increase in the incidence of chronic post-thoracotomy pain in the Sham group compared to the MTP group. This lower incidence can be explained by the abortion of acute post-thoracotomy pain by MTP block, which prevents chronic pain development. Other researchers must investigate the effect of MTP block on chronic postoperative pain, as there are few studies about this effect.

One of the limitations of our study is the relatively small sample size to prove the secondary outcomes. Additional studies with a large number of patients are required for generalization of these results. Also, we recommend further studies to assess using different concentrations with different additives of bupivacaine in US-guided MTP block.

5. Conclusion

The US-guided MTP block provided effective analgesia with a lower pain score and less morphine consumption, and little postoperative pain with a lower incidence of pain that persists after a thoracotomy compared to sham block in patients undergoing posterolateral thoracotomy.

Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Heba Abdelhamid Mohammed http://orcid.org/0009-0000-7299-0961

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