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COMPARATIVE STUDY OF TRIAMCINOLONE VERSUS MORPHINE EFFECTIVENESS IN THORACIC EPIDURAL ANALGESIA FOR RIB FRACTURE PAIN

Ahmed Nabil Malek[1*], Ahmed Omar Mahmoud[2], Mohammed Farouk Abdel Hafez[1], Ahmed Ibrahim Ismail[1]

[1*] Department of Cardiothoracic Surgery, Faculty of Medicine, Assiut University Hospitals, Assiut, Egypt.
[2] Department of Anesthesia, Faculty of Medicine, New Valley University, Egypt.

***Corresponding Author:** Ahmed Nabil Malek
[*] Department of Cardiothoracic Surgery, Faculty of Medicine, Assiut University Hospitals, Assiut, Egypt.

Abstract
Background: Thoracic epidural analgesia continues to be an indispensable element of acute pain management that are predicated by anesthesia. It is employed to alleviate acute pain following rib fractures and thoracic and abdominal surgeries. The objective of this research was to evaluate the analgesic efficacy of morphine and thoracic epidural triamcinolone acetonide in the context of fractured chest.**Methods:** This prospective randomized comparative study involved 40 adults suffering from multiple fractured ribs among those presenting to Trauma Unit in Assiut University Hospital. Two equal groups of patients were randomly designated: Group (M) (Morphine group): was administered a combination of 9 ml of bupivacaine 0.25 % and 0.1mg/kg morphine, and group (S) (Steroid group): was administered a combination of 9 ml of bupivacaine 0.25 % and 80 mg of triamcinolone acetonide. All patients underwent routine investigations including coagulation studies and computed tomography and chest x-ray.
Results: There was a significantly higher visual analogue scale coughing scale in the steroid group during the follow-up starting from the 6th hour up to the 42nd hour. Group M had signifcinatly higher prevalence of nausea and vomiting than group S. The need for nonsteroidal anti-inflammatory drugs (NSAIDs) was significantly higher in the steroid group.
Conclusions: Epidural morphine can afford a better quality of pain alleviation than triamcinolone acetonide; however, it is not devoid of some respiratory complications in traumatic rib(s) fracture.

Keywords: Thoracic Epidural, Morphine, Triamcinolone Acetonide, Analgesia, Fracture Ribs.

Background

One of the most prevalent causes of trauma disabilities in a variety of situations, including traffic accidents, falls, occupational events, and intentional traumas, is rib fracture [1]. These patients experience a wide range of outcomes, from transient pain management to long-term substantial disability [1]. Previous research has demonstrated that the prevalence of protracted pain in the chest wall assossiated with rib fractures is higher than previously believed. Consequently, approximately 60% of these patients experience long-term disability and pain [2, 3].

During coughing, speaking, breathing, and even body movements, patients with rib fractures experience intense pain [4]. One of the primary objectives of chest injury treatment is to achieve effective pain control [4]. Pain can impede the efficacy of coughing and the secretions clearance, which may result in reduction of functional residual capacity (FRC), progressive atelectasis, a ends by respiratory distress. Respiratory complications can be prevented, and ventilatory function can be enhanced through pain control [5]. By proper understanding of the efficiency and safety of different analgesic methods can substantially improve the association between rib fractures and pulmonary morbidity and mortality in patients with rib fractures [5]. There are numerous treatment options available to alleviate the pain associated with chest injuries. Epidural analgesia is recommended by guidelines as an alternative to nonregional pain control methods; however, the evidence supporting this recommendation is extremely limited [6].

As an essential element of anesthesia-based acute pain management, thoracic epidural analgesia (TEA) is frequently employed to alleviate acute pain following thoracic and abdominal surgeries and rib fractures [7]. TEA is recommended when a moderate-to-large thoracic or upper abdominal incision is designed. Through optimization of the pain alleviation, surgical stress response attenuation and enabling the early mobilization, in fast-track surgery, TEA can be regarded a valuable adjunct. TEA does not have a unique contraindication that is not applicable to all neuraxial procedures [8].

Duch et al. [9] meta-analysis and systematic review revealed that compared to the paravertebral or intercostal modality, there is a substantially greater intervention effect for the pain reduction in favor of epidural analgesia.

This research aimed to evaluate the analgesic efficacy of morphine versus thoracic epidural triamcinolone acetonide in a flail chest.

Methods

This prospective randomized double blinded comparative study was conducted on forty adult patients aged 18-70 years, of both gender and mentally competent patients, suffering from multiple rib fractures, who were presented to Trauma Unit in Assiut University Hospital from December 2016 to December 2018. All the recruited patients had provided an informed written consent prior participation. After obtaining the the Ethics Committee approval of the Faculty of Medicine at Assiut University Hospital (NCT03413059), the study was performed.

Exclusion criteria were refusal to participate, uncooperative patients, contraindication to neuroaxial blockade, the need for invasive ventilation, renal dysfunction, head trauma, patients with persistent opioid use and chronic pain syndromes, body mass index (BMI) of 40 or more and those with psychiatric illnesses that would interfere with perception and assessment of pain.

Randomization and blindness:

Two equal groups of patients were randomly designated using a computer-generated random table:

Group (M) (Morphine group n=20): Upon admission to the trauma unit, patients were administered 0.1 mg/kg morphine and 9 ml of 0.25 % bupivacaine via an epidural catheter.

Group (S) (Steroid group n=20): Upon admission to the trauma unit, via an epidural catheter, cases were given a total of 10 ml of a mixture of 80 mg of triamcinolone acetonide and 9 ml of bupivacaine 0.25 %.

In both groups, the patient was then given bupivacaine 0.125% (0.1 mg/kg/h) as a continuous thoracic epidural infusion for the 1st 72 hours. Both outcome assessor and pharmacist who prepared the drug were blinded to the group aalocation.

Preinterventionl evaluation:

All patients underwent thorough history taking including personal data (sex, age, weight & height), course, duration and severity of pain, associated comorbidities, prior interventional procedures, and

medications with significant side effects, routine investigations including coagulation studies and radiological studied (chest x ray and computed tomography (CT)).

Procedure and monitoring:
All blocks were performed in the intensive care unit (ICU) under complete aseptic conditions, as per the standard monitoring protocol of the American Society of Anesthesiologists (ASA). Before and during the intervention, an anesthesiologist monitored the blood pressure, peripheral oxygen saturation, and electrocardiogram of each patient. The patient was placed with fully extended head and flexed neck. During the proedcure, cases were sedated with a mixture of 50-100 mcg of fentanyl and 1-2 mg of midazolam. 2% lidocaine was infiltrated into the skin site of puncture after the area of injection was sterilized and a complete aseptic technique was employed. The epidural catheter were placed mid-level of fraction at the inter-vertebral thoracic space corresponding to the rib fractures. The optimal level of the catheter were confirmed by chest x ray and test dose of 3 ml lidocaine 2% with adrenaline (dilution 1:200000). Patients were followed up for analgesia, efficacy, side effects, and complications for the first 72 hrs.

Chest trauma score (CTS):
The thoracic trauma score was determined upon the patient's admission to the trauma unit.The CTS is comprised of 4 distinct components, each of which is assigned a point system: age (1=<45 years, 2=45-65, 3=>65); number of rib fractures (1=<3, 2=3-5, 3= >5 and the presence of bilateral rib fracture =2); pulmonary contusion (0=none, 1= unilateral minor, 2= bilateral minor, 3= unilateral major, 4= bilateral major) [14].

Pain assessment:
Pain evaluation was conducted by using visual analogue scale (VAS) at rest and on induced cough (asking patients to cough were done). It is composed of a 10-cm line that is accompanied by a label, such as "no pain," at one end and a label, such as "the worst pain imaginable" or "pain as bad as can be," at the other end." VAS scores was recorded at rest and on cough before injection and immediately post procedure and at 30 min, 2, 4, 6, 12, 24, 36, 48 & 72 h in trauma unit. The rescue analgesia: Parental ketorolac: maximally 30 mg were given when VAS score at rest is above 6 [11].

Respiratory parameters:
The respiratory parameters were assessed including respiratory rate, PaO_2/FiO_2 which was evaluated before and after administration of block at regular intervals, chest –X ray / 48 h and spirometry (FVC, forced expiratory volume (FEV) and FEV1/ forced vital capacity (FVC)) which was evaluated pre and after 24 h.

Laboratory work:
Serum cortisol level before procedure and 24, 48 hours post procedure. Three blood samples were obtained from each patient for determination of cortisol level in plasma tubes containing ethylenediaminetetraacectic (EDTA), centrifuged and stored at 20º C until assayed. Plasma concentrations of cortisol were measured by electrochemiluminescence immunoassay on an elecsys E-170 analyser. Serum blood glucose every 6 hours for the 1st 48 hours.

Other mesuaremnets:
The complications of the technique and the length of ICU and hospital stay were recorded. We also specifically evaluated potential adverse events, involving nausea, vomiting, and respiratory depression. metoclopramide 10 mg IV was given as rescue antiemetic when patients complained of nausea (score 2) or vomiting. Patients were also evaluated for hypotension, bradycardia and arrhythmia as a side effect of local anesthetic agent. Morphine side effects as postoperative nausea and vomiting, itching and bladder distension were evaluated.

Outcome:
The primary outcome was to measure the stress response to fracture ribs in morphine versus triamcinolone acetonide groups. The secondary outcome was to compare the quality of healing, pain relief, pulmonary complication & ICU stay in both groups.

Sample size:
G.power (Universitat Kiel, Germany) was employed to calculate the sample size. 18 patients were assigned to each cohort in 3.1.9.2. The sample size was determined to be N = 38 in each category based on the following factors: To assume a pooled standard deviation of 2 units of VAS, the research must have a power of 80% and a 0.05 α error. In order to compansate dropout rates, each cohort was supplemented with two additional cases.

Statistical analysis:
For the statistical analysis, SPSS v28 (IBM©, Armonk, NY, USA) was used. Histograms and Shapiro-Wilks test were utilized to determine the normality of the data distribution. Data that were not parametric and were given as a numerical median and interquartile range (IQR) were analyzed using the Mann Whitney-test. The numerical parametric variables were reported as mean (± SD) and were tested by the unpaired student t-test was used. We used the Chi-square test to assess categorical data or Fisher's exact test when necessary, which were then shown as percentages and frequencies. Statistical significance was defined as a two-tailed P value lower than 0.05.

Results
69 patients were evaluated for eligibility in this study; 18 patients failed to fulfill the criteria, and 11 patients declined to participate. The remaining 40 patients were randomly assigned to two equal groups. The statistical analysis and follow-up of all allocated patients was done. **Fig. 1**
There was no signifcnat difference between both groups regarding the demographic data (age, BMI, and gender, comorbidities) and clinical data (CTS, the number of fractured ribs, the site and type of injury and baseline chest x-ray) were insignificantly different betwrrn both groups. **Table 1**
There was no significant different between both groups at all time meausrements regarding the resting VAS. There was a significantly higher VAS coughing scale in the steroid group starting from the 6th hours up to the 42nd hours of follow up; otherwise, there was no significant difference. **Table 2; Fig. 2**
FVC, FEV_1, FEV_1/FVC, and RR were insignificantly different between both groups at each pre and post-intervention. **Table 3**
Regarding blood sugar, there was an insignificant difference between both groups during the early 6 hours. There was a highly significant differences during the 18th and 24th hours ($P< 0.001$). Regarding serum cortisol level, there was a highly significant difference between both groups in serum cortisol at the 48th hours, but there was an insignificant difference at other times. **Table 4**
Table 5 shows that the need for rescue analgesia (1st request, NSAID requirement) was signifcnatly lower in group M compared to group S (10% vs, 40%, P=0.032), with no signifcnat difference between both groups regarding the ICU stay, need for mechanical ventilation and length of hospital stay.
Regarding the adverse effects of studied groups, the incidence of nausea and vomiting were signifcnatly higher in group M compared to group S ($P<0.001$, 0.001), with no significant difference between both groups regarding the incidence of pneumonia, hypotension, bradycardia, respiratory failure and dural puncture. **Table 6**

Discussion
Representing about 10% of trauma, fractured ribs are the most prevalent type of chest injury. For patients with multiple fractured ribs, invasive mechanical ventilation (IMV) was the conventional management in the past. Over time, the IMV need has declined; however, mortality rates have remained exceptionally consistent in recent years. Elevated mortality rates were recorded in patients

who sustain severe trauma, particularly those who also suffer extrathoracic injuries [16]. These patients are typically intubated prior to their ICU admission. The primary documented risk factors for complications include older age, increased number of fractured ribs, concomitant injuries, and chronic pulmonary disease [12].

Patients with fractured ribs must incorporate pain control as a critical component of their treatment regimen. Multiple fractured ribs elicit severe pain, which significantly increases the risk of secretion accumulation and respiratory failure by impeding the ability to cough and breathe. EA is the preferable method of pain control in adults with blunt chest trauma, as opposed to nonregional pain-control modalities (e.g., enteral or intravenous analgesics as NSAIDs, opioids & acetaminophen) [13].

As regards the study primary outcome (the VAS pain score), the VAS score during rest was comparable between both studied groups at all time measurements, while had improved (decreased) significantly over time in both groups. As regard pain score during cough, VAS score was significantly lower over time in both groups. However, the morphine group was significantly lower during the first 42 hours than the steroid group.

Our study agrees with Wu et. al. [14] who reported that the pain scores were found to be substantially decreased with epidural analgesia. The incidence of organ failure or pulmonary complications, as well as the durations of ICU or hospital stays, were not different between the groups.

It is noteworthy that the literature generally lacks information regarding the use of epidural steroid injections in acute pain management contexts, such as traumatic rib fractures, regardless of the duration from the initial injury to the initiation of management [15]. Steroids upregulate the C-fos gene and maintain the nerve membrane potentials, meanwhile opioids operate at the substantial gelatinosa of the spinal cord to determine the extent of the opioid half-life, hence steroids may be a more effective treatment option for specific patients [16].

As regard spirometry, a significant rise in FEV_1 was found in both groups, with no significant difference between both groups at all time measurements. FEV_1/FVC ratio was insignificantly different at all time measurements within groups and between groups. It is widely recognized that optimal epidural analgesia can enhance vital capacity, dynamic lung compliance, and functional residual capacity by reducing airway resistance and substantially increasing PaO_2 [17].

Our results agree with Mackersie et al. [18] determined that recieving lumbar epidural fentanyl had a significant enhancement in spirometry data as vital capacity and maximal inspiratory pressure. Jarvis et al. [19], meta-analysis, showed that despite the presence of a higher number of rib fractures, a more severe injury, and a higher level of physiologic acuity in patients who received epidural analgesia, the use of this therapy results in greater improvement in tidal ventilator volumes during the first 24 hours of therapy, shorter MV duration, and also lower incidence of pulmonary complications and pneumonia.

The evidence suggests that patients who received epidural analgesia had shorter MV duration and higher tidal volumes. Compared to patients who received patient-controlled analgesia, those who received epidural analgesia exhibited superior analgesia and pulmonary function, as well as a reduced level of circulatory inflammatory mediators associated with acute lung injury, as demonstrated by Moon et al. [20] Regarding the postoperative cortisol level, the overall comparison between the two groups shows a higher cortisol level in the steroid group than the morphine group at 48 hr which delineates less pain and stress in patients receiving morphine infusion.

In a previous study, glucose and cortisol levels were monitored for a period of three weeks following epidural or shoulder intra-articular injections. Their conclusion was that diabetic patients continued to experience a substantial decrease in cortisol levels after receiving an epidural steroid injection 21 days after the injection [21].

Blood sugar level was statistically significantly lower in the morphine group than the steroid group. However, when our study compared the same group, either the morphine or steroid groups regarding the testing time effect on blood sugar level, found a statistically significant drop of sugar level within the group I .Meanwhile, testing time effect on sugar level in group II shows a

significant rise from pre status at first, 6 h, 12 h, and 18 h respectively; however, in both groups at 48 h the blood sugar decrease to reach a value that is close to the initial sugar baseline but was not significantly different from it respectively which implicates the powerful analgesic and anti-stressful effect of morphine over steroid on patients of the study.

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As regard rescue analgesia, the steroid group showed signifcnatly higher need for ketorolac rescue analgesia in comparison with the morphine group (40% vs. 10.0%), which reflects the weak direct analgesic effect of the triamcinolone acetonide.

By increasing the patient's tolerance for deep breathing and sneezing, adequate pain management enhances lung volume and effectively clears secretions. Therefore, the need for MV and the earlier return of gastrointestinal function are encouraged, the infection rates and neuroendocrine stress responses are reduced and the complication risk is diminished [22].

ICU stay was insignificantly different between both groups. Bulger et al., [22] reported that following rib fractures, epidural analgesia is linked to a reduction in both the duration of MV and the incidence of nosocomial pneumonia.

On the other hand, Kieninger et al. [23] concluded that in cases, mainly those with less significant injuries, epidural analgesia is linked with a longer period of stay and increased complications, irrespective of cardiopulmonary comorbidities.

Patients with one or more fractured ribs who received epidural analgesia experienced higher rates of respiratory complications and a prolonged hospital stay in comparison to those who received other analgesic interventions, according to a recent matched-cohort study conducted by McKendy et al. [24]

In a previous systematic review and meta-analysis, the effects of epidural analgesia were compared to those of other analgesic modalities in patients with one or more traumatic rib fractures and had demonstrated that epidural analgesia did not have any beneficial effects on the outcome measures of respiratory complications, ICU length of stay, hospitalization, duration of MV, and death [25].

It is evident from our data that the prevalence of pulmonary complications is high such as pneumonia was higher, representing about 20 % of all patients with most patients in the morphine group. The need for mechanical ventilation, hypotension, and Dural puncture presented an insignificant difference between the two studied groups. Our study reported that nausea, vomiting, and respiratory depression were higher and statistically significant in patients of the morphine group.

In the current study, the need for mechanical ventilation was insignificant different between the two groups.

Bachoumas et al. [26] found that epidural analgesia did not correlate with a reduced incidence of IMV in chest trauma patients. They suggest that additional research be conducted to determine the

most effective pain control strategy for these patients, particularly those with severe pain or high opioid requirements..

Regarding nausea and vomiting, use of epidural morphine was associated with a significant difference in both groups, Lourens [27] demonstrated that the complications reported ranged from severe neurologic injury to medication adverse reactions. Reduced consciousness, pruritus, vertigo, and vomiting are among the adverse reactions that are linked to opioids. Hypotension, marked bradycardia, sensory and motor paralysis, and urinary retention are among the adverse reactions to local anesthetics. Postdural puncture headache is one example of catheter-associated complications. We found that , the time of hospital discharge was longer and statistically insignificant in patients of the steroid group.

Carrier et al. [28] meta-analysis found that the implementation of epidural analgesia in adult patients with traumatic rib fractures, as well as other analgesic options, did not offer a substantial advantage in terms of mortality, reduction in ICU length of stay, and hospital length of stay. However, its effects on patient-reported pain were variable. Nevertheless, the duration of mechanical ventilation may be reduced by combining TEA with local anesthetics.The limitations of the study were the small sample size of our study, the short period of follow-up, which did not allow us to look for the development of chronic pain after an injury.

Conclusions:

Epidural morphine can afford a better quality of pain alleviation than triamcinolone acetonide; however, it is not devoid of some respiratory complications in traumatic rib(s) fracture. Triamcinolone as an adjunct to a local anesthetic agent in thoracic epidural blockade may provide comparable analgesia as well as patient satisfaction to the epidural opioid regimen but with fewer side effects and pulmonary complications. It could be an effective alternative strategy for patients who are exceedingly sensitive to opioids. VAS score and postoperative analgesic requirements of patients with multiple fracture ribs were substantially reduced by the addition of Triamcinolone to bupivacaine, without any serious side effects. It also has an anti-inflammatory effect, which makes him superior to morphine in asthmatic patients due to the histaminic effect of opioids, but it elevates blood cortisol & glucose levels as a side effect of corticosteroids, so that, not suitable in diabetic patients.

Therefore, studies with a larger sample size to make an evidence-based conclusion about the triamcinolone effects in acute pain management are recommended. Follow up on the occurrence of chronic pain after 3 months, and the comparison between the groups is recommended.

List of abbreviations:

CT: Computed tomography, FEV: Forced Expiratory Volume, FVC: forced vital capacity, ICU: Intensive care unit, TEA: Thoracic epidural analgesia, VAS: Visual Analogue Scale

Declarations

Ethics approval and consent to participate:

After obtaining the the Ethics Committee approval of the Faculty of Medicine at Assiut University Hospital (NCT03413059), the study was performed. All the recruited patients had provided an informed written consent prior participation.

Consent for publication: Not applicable.

Availability of data and material:

The data supporting the present findings are contained within the manuscript.

Competing interests: The authors declare no conflict of interest.

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References

1. Dogrul BN, Kiliccalan I, Asci ES, Peker SC. Blunt trauma related chest wall and pulmonary injuries: An overview. Chin J Traumatol. 2020;23:125-38.
2. Prins JTH, Van Lieshout EMM, Overtoom HCG, Tekin YS, Verhofstad MHJ, Wijffels MME. Long-term pulmonary function, thoracic pain, and quality of life in patients with one or more rib fractures. J Trauma Acute Care Surg. 2021;91:923-31.
3. Kahloul M, Kacem I, Sboui MM, El Maalel O, Daami H, Hafsia M, et al. Chronic Pain following Chest Trauma: Prevalence, Associated Factors, and Psychosocial Impact. Pain Res Manag. 2020;2020:1030463.
4. Peek J, Kremo V, Beks R, van Veelen N, Leiser A, Link BC, et al. Long-term quality of life and functional outcome after rib fracture fixation. Eur J Trauma Emerg Surg. 2022;48:255-64.
5. Liu SS, Wu CL. Effect of postoperative analgesia on major postoperative complications: a systematic update of the evidence. Anesth Analg. 2007;104:689-99.
6. Bachoumas K, Levrat A, Le Thuaut A, Rouleau S, Groyer S, Dupont H, et al. Epidural analgesia in ICU chest trauma patients with fractured ribs: retrospective study of pain control and intubation requirements. Ann Intensive Care. 2020;10:116.
7. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan Jr JA, Wu CL. Efficacy of postoperative epidural analgesia: a meta-analysis. JAMA. 2003;290:2455-63.
8. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg. 2008;248:189-98.
9. Duch P, Møller M. Epidural analgesia in patients with traumatic rib fractures: a systematic review of randomised controlled trials. Acta Anaesthesiologica Scandinavica. 2015;59:695-9.
10. Chen J, Jeremitsky E, Philp F, Fry W, Smith RS. A chest trauma scoring system to predict outcomes. Surgery. 2014;156:988-93.
11. Birkner DR, Halvachizadeh S, Pape HC, Pfeifer R. Mortality of Adult Respiratory Distress Syndrome in Trauma Patients: A Systematic Review over a Period of Four Decades. World J Surg. 2020;44:2243-54.
12. Papazian L, Aubron C, Brochard L, Chiche JD, Combes A, Dreyfuss D, et al. Formal guidelines: management of acute respiratory distress syndrome. Ann Intensive Care. 2019;9:69.
13. Galvagno SM, Jr., Smith CE, Varon AJ, Hasenboehler EA, Sultan S, Shaefer G, et al. Pain management for blunt thoracic trauma: A joint practice management guideline from the Eastern Association for the Surgery of Trauma and Trauma Anesthesiology Society. J Trauma Acute Care Surg. 2016;81:936-51.
14. Wu CL, Jani ND, Perkins FM, Barquist E. Thoracic epidural analgesia versus intravenous patient-controlled analgesia for the treatment of rib fracture pain after motor vehicle crash. J Trauma Acute Care Surg. 1999;47:564-7.
15. Rauchwerger JJ, Candido KD, Deer TR, Frogel JK, Iadevaio R, Kirschen NB. Thoracic epidural steroid injection for rib fracture pain. Pain Pract. 2013;13:416-21.
16. Guay J, Nishimori M, Kopp S. Epidural local anaesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting and pain after abdominal surgery. Cochrane Database Syst Rev. 2016;7:Cd001893.
17. Auroy Y, Narchi P, Messiah A, Litt L, Rouvier B, Samii K. Serious complications related to regional anesthesia: results of a prospective survey in France. Anesthesiology. 1997;87:479-86.
18. Wijayasinghe N, Andersen KG, Kehlet H. Neural Blockade for Persistent Pain After Breast Cancer Surgery. Reg Anesth Pain Med. 2014;39:272-95.
19. Mohta M, Verma P, Saxena AK, Sethi AK, Tyagi A, Girotra G. Prospective, randomized comparison of continuous thoracic epidural and thoracic paravertebral infusion in patients with unilateral multiple fractured ribs—a pilot study. J Trauma Acute Care Surg. 2009;66:1096-9.

20. Kumar R, Sharma A, Bansal R, Kamal M, Sharma L. Ultrasound-Guided Continuous Erector Spinae Plane Block in a Patient with Multiple Rib Fractures. Turk J Anaesthesiol Reanim. 2019;47:235-70.
21. Moon HJ, Choi KH, Lee SI, Lee OJ, Shin JW, Kim TW. Changes in blood glucose and cortisol levels after epidural or shoulder intra-articular glucocorticoid injections in diabetic or nondiabetic patients. Am J Phys Med Rehabil. 2014;93:372-8.
22. Bulger EM, Edwards T, Klotz P, Jurkovich GJ. Epidural analgesia improves outcome after multiple rib fractures. Surgery. 2004;136:426-30.
23. Kieninger AN, Bair HA, Bendick PJ, Howells GA. Epidural versus intravenous pain control in elderly patients with rib fractures. Am J Surg. 2005;189:327-30.
24. McKendy KM, Lee LF, Boulva K, Deckelbaum DL, Mulder DS, Razek TS, et al. Epidural analgesia for traumatic rib fractures is associated with worse outcomes: a matched analysis. J Surg Res. 2017;214:117-23.
25. Peek J, Smeeing DP, Hietbrink F, Houwert RM, Marsman M, de Jong MB. Comparison of analgesic interventions for traumatic rib fractures: a systematic review and meta-analysis. Eur J Trauma Emerg Surg. 2019;45:597-9.
26. Bachoumas K, Levrat A, Le Thuaut A, Rouleau S, Groyer S, Dupont H, et al. Epidural analgesia in ICU chest trauma patients with fractured ribs: retrospective study of pain control and intubation requirements. Ann Intensive Care. 2020;10:1-12.
27. Lourens GB. Complications associated with epidural catheter analgesia. The Nurse Practitioner. 2016;41:12-6.
28. Truitt MS, Murry J, Amos J, Lorenzo M, Mangram A, Dunn E, et al. Continuous intercostal nerve blockade for rib fractures: ready for primetime? J Trauma Acute Care Surg. 2011;71:1548-52.

Table 1: Demographic and clinical data of the study groups

		Group M (n=20)	Group S (n=20)	p-value
Demographic data	**Age (years)**	44.6 ± 8.2	43.6 ± 10.16	0.73
	Male/female	17/3	18/2	1
	BMI	27.78 ± 3.39	28.43 ± 3.52	0.579
	Comorbid conditions			
	Diabetic	4 (20%)	6 (30%)	0.76
	Hypertensive	4 (20%)	4 (20%)	
	More than one comorbid	3 (15%)	4 (20%)	
	History of chronic lung disease			
	COPD	1 (5%)	1 (5%)	0.834
	Bronchial Asthma	2 (10%)	1 (5%)	
Clinical data	**Chest trauma score**	7.5 (5)	7.5 (4.25)	0.92
	Site of injury			
	Right	5 (25%)	6 (30%)	0.924
	Left	7 (35%)	7 (35%)	
	Bilateral	8 (40%)	7 (35%)	
	Pulmonary contusion	2 (10%)	2 (10%)	---
	Number of fractured ribs	5 (3)	5 (1.25)	0.71
	Type of injury			
	Multiple fracture ribs with pulmonary contusion	9 (45%)	10 (50%)	0.831
	Multiple fracture ribs	6 (30%)	5 (25%)	
	Chest wall bruise with pulmonary contusion	3 (15%)	3 (15%)	
	Flail injury	1 (5%)	0 (0%)	

	Flail injury with pulmonary contusion	1 (5%)	2 (10%)	
	Chest X-ray baseline			
	Free	10 (50%)	12 (60%)	0.99
	Contusion of lung	3 (15%)	2 (10%)	
	Hemothorax	3 (15%)	2 (10%)	
	Hemopneumothorax	2 (10%)	2 (10%)	
	Pneumothorax	2 (10%)	2 (10%)	

Data are presented as mean± Standard deviation, frequency (%) or median (IQR), BMI: body mass index

Table 2: VAS during resting and coughing of the study groups

Variables		**Group M (n=20)**	**Group S (n=20)**	**p-value**
Resting VAS	**Baseline**	8 (6.75-8.75)	7 (6-8)	0.09
	After 6 hrs.	4 (3-5)	4 (4-5)	0.15
	After 12 hrs.	3 (1.75-3.75)	2.5 (1.75-3)	0.13
	After 18 hrs.	1 (0-2)	1 (0-2)	1
	After 24 hrs.	1 (0-2)	2 (1-2)	1
	After 30 hrs.	2 (1-3)	1 (1-2)	1
	After 36 hrs.	1 (1-1.75)	1 (0-2)	1
	After 42 hrs.-	1 (0-1.75)	1.5 (0-2)	1
	After 48 hrs.	1 (0-1.75)	1 (0-2)	1
	After 54 hrs.	1 (1-2)	1 (0-1)	0.32
	After 60 hrs.	1 (0-1)	1 (0-1)	1
	After 66 hrs.	0 (0-1)	0 (0-1)	0.47
	After 72 hrs.	0 (0-1)	0 (0-0.75)	1
VAS coughing	**Baseline**	6.5 (6-8)	8 (6.75-9)	0.32
	After 6 hrs.	7 (6.75-8)	7 (6-8)	**0.001***
	After 12 hrs.	5.5 (4.75-7)	7 (5.75-7)	**0.02***
	After 18 hrs.	6 (4.75-6)	6 (5.75-7)	**0.001***
	After 24 hrs.	6 (4-6)	6 (5.75-6)	**0.001***
	After 30 hrs.	5 (3.75-6)	6 (5-6)	**0.002***
	After 36 hrs.	4.5 (3.75-5)	5.5 (5-7)	**0.02***
	After 42 hrs.	4 (4-5)	5 (4.75-6)	**0.001***
	After 48 hrs.	4 (3-4.75)	5 (3-5)	0.12
	After 54 hrs.	3 (2-4)	2.5 (2-3)	0.67
	After 60 hrs.	2 (1.75-3)	2 (1-3)	0.56
	After 66 hrs.	1.5 (1-2)	2 (2-3)	0.20
	After 72 hrs.	1 (1-2.5)	2 (1-2)	0.21
PO_2/FiO_2	**Baseline**	150.09±2.75	151.24±4.41	0.329
	After 6 hrs.	154.16±2.67	152.58±2.32	0.084
	After 12 hrs.	232.37±3.48	229.87±3.92	**<0.04***
	After 24 hrs.	234.00±3.18	231.75±3.72	**<0.04***
	After 36 hrs.	234.50±3.94	235.50±3.85	0.422
	After 48 hrs.	313.49±4.52	317.49±6.19	**<0.02***
	After 60 hrs.	315.33±4.51	318.50±5.01	**<0.04***
	After 48 hrs.	317.50±4.17	317.83±4.86	0.818

Data are presented as mean± SD, , PO_2/FiO_2: partial pressure of oxygen in arterial blood/the fraction of inspiratory oxygen concentration, VAS visual analogue scale ,*: statistically significant as p-value ≤ 0.05.

Table 3: Spirometry data and respiratory rate of the study groups

		Group M (n=20)	Group S (n=20)	p-value
FVC	**Pre**	2.51±0.68	2.53±0.49	0.914
	24 hrs.	3.26±0.86	3.19±0.52	0.771
FEV_1	**Pre**	2.22±0.62	2.29±0.39	0.624
	24 hrs.	2.91±0.62	2.92±0.52	0.958
FEV_1/FVC	**Pre**	0.88±0.05	0.92±0.05	0.082
	24 hrs.	0.92±0.07	0.92±0.05	0.451
RR (breath/min)	**Pre**	16.9± 3.43	15.75± 2.73	0.248
	24 hrs.	14.85± 1.93	14.6± 2.16	0.702

Data are presented as mean± SD. FEV forced expiratory volume in the 1st second, FVC: forced vital capacity, RR: respiratory rate, *: statistically significant as p-value ≤ 0.05.

Table 4: Blood sugar and serum cortisol in study groups

		Group M (n=20)	Group S (n=20)	p-value
Blood sugar (mg/dL)	**Baseline**	197.15 ± 90.08	151.4 ± 80.22	0.09
	After 6 hrs.	183.15 ± 79.44	196.5 ± 67.14	0.5
	After 12 hrs.	167.3 ± 63.27	191 ± 20.75	0.12
	After 18 hrs.	159.25 ± 74.31	199.75 ± 13.52	**0.02***
	After 24 hrs.	147.9 ± 65.61	188.75 ± 13.66	**0.01***
	After 30 hrs.	140.6 ± 54.91	161.25 ± 13.07	0.11
	After 36 hrs.	135.25 ± 44.94	142.5 ± 21.67	0.52
	After 42 hrs.	127.25 ± 67.46	143.7 ± 22.76	0.31
	After 48 hrs.	122.05 ± 68.97	131 ± 21.58	0.58
Serum cortisol (microgram/dL)	**Baseline**	308 ± 109.33	319 ± 155.29	0.79
	After 24 hrs.	220.25 ± 99.11	280.5 ± 114.18	0.08
	After 36 hrs.	189.5 ± 99.23	213.1 ± 106.06	0.47
	After 48 hrs.	180.75 ± 46.35	224.9 ± 86.32	**0.05***
	After 72 hrs.	204.5 ± 14.32	199.5 ± 45.48	0.64

Data are presented as mean± SD or median (IQR), IQR interquartile range. *: statistically significant as p-value ≤ 0.05.

Table 5: Need for rescue analgesia, length of ICU, need for MV and hospital stay in study groups

	Group M (n=20)	Group S (n=20)	p-value
Need for rescue analgesia (1st request, NSAID requirement)	2 (10%)	8 (40%)	**0.032***
ICU stay	6.5 (2.5)	8 (3)	0.443
Need for mechanical ventilation	3(15%)	4 (20%)	1
Length of hospital (days)	12 (4)	14 (1.5)	0.09

Data are presented as median (IQR) or frequanct (%), IQR interquartile range., NSAID: non-steroidal anti-inflammatory drugs, ICU: Intensive care unit, *: statistically significant as p-value ≤ 0.05.

Table 6: Adverse effects of the study groups

Variables	Group M (n=20)	Group S (n=20)	p-value
Pneumonia	4 (20%)	5(25%)	0.191
Nausea	11 (55%)	0 (0%)	**<0.001***
Vomiting	16 (80%)	7 (35%)	**0.001***
Hypotension	6 (30%)	2 (10%)	0.235
Bradycardia	2 (10%)	3 (15%)	0.633
Respiratory failure	0 (0%)	0 (0%)	---
Dural puncture	2 (10%)	2 (10%)	1

Data are presented as frequency (%), *: statistically significant as p-value ≤ 0.05.

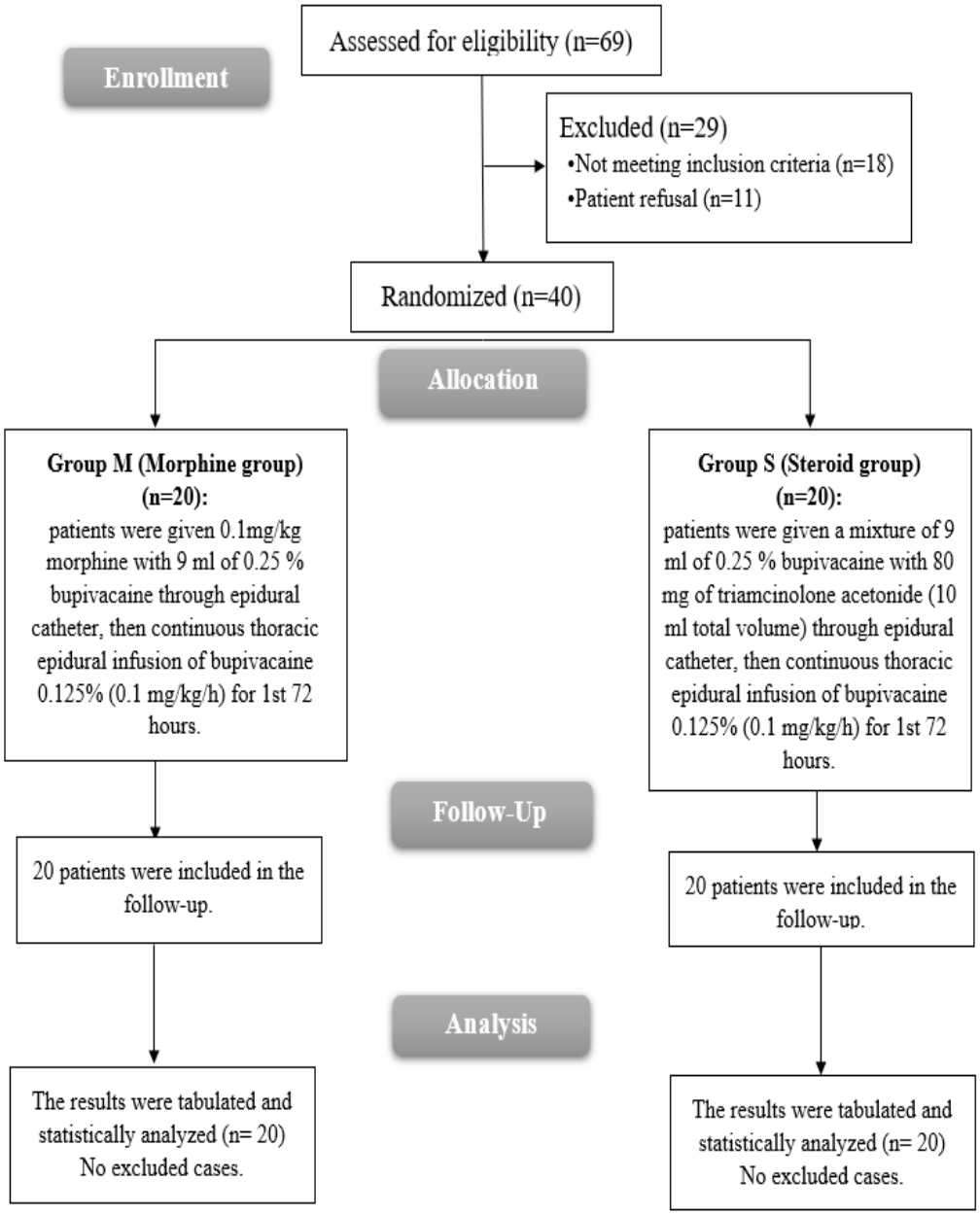
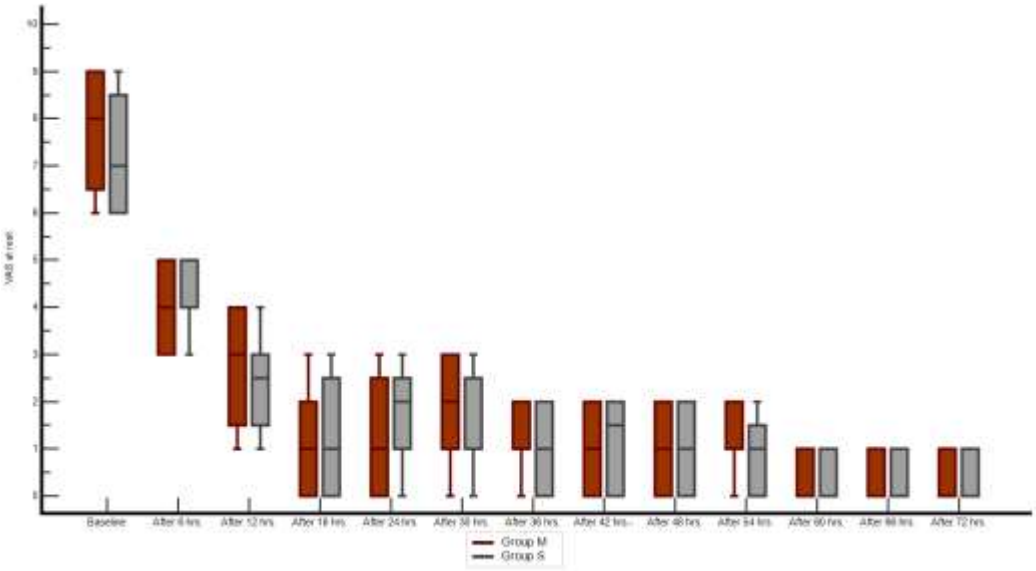
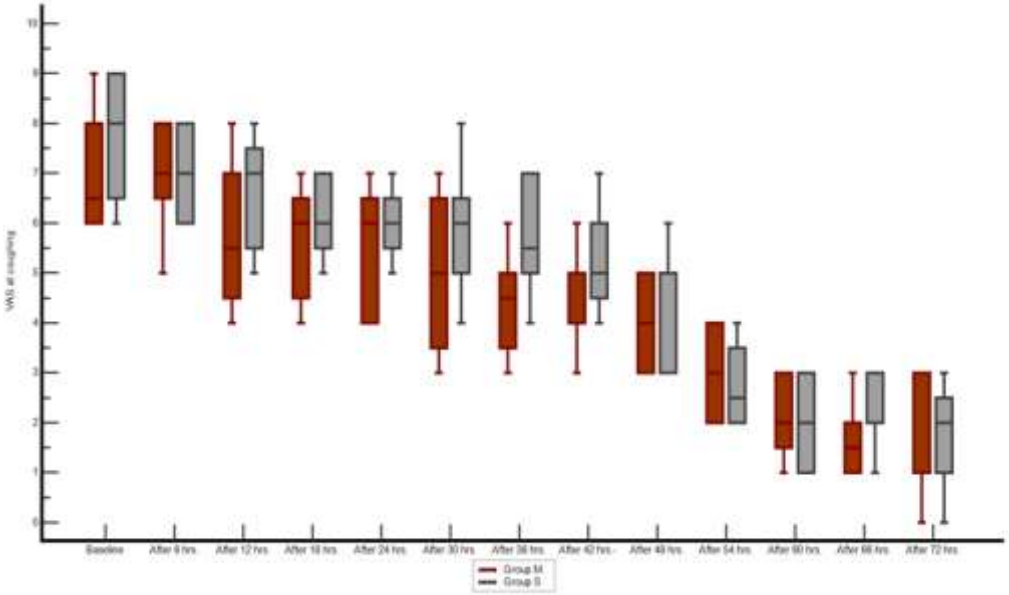


Figure 1: CONSORT flowchart of the enrolled patients



(A)



(B)

Figure 2: (A) VAS at rest, (B) VAS at coughing of the study groups