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Impact of Thoracic Epidural Analgesia on Major Adverse Cardiac Events (Maces) Following Major Gastrointestinal Cancer Surgeries

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Abstract

Background and Objectives: *Major gastrointestinal cancer surgeries are associated with significant perioperative mortality and morbidity due to increased incidence of major perioperative cardiovascular event (MACEs). This study examined the effect of perioperative patient controlled epidural analgesia (PCEA) on reduction of MACEs in cardiac risky patients undergoing major gastrointestinal cancer surgery.*

Methods: *60 patients (ASA II and III) of either sex were scheduled for elective Upper gastrointestinal cancer surgeries. Patients were allocated randomly into two groups (30 patients each) to receive, beside GA: continuous intra and post -operative intravenous infusion with fentanyl for 72 hours post-operatively (control group) or continuous intra and post -operative epidural infusion with bupivacaine 0.125% and fentanyl (TEA group) for 72 hours post-operatively*

Intra-operative and post operative (HR and MAP) were recorded. Postoperative pain was assessed over 72 h using numerical rating scale (NRS). All patients were screened for occurrence of MACEs by ECG and echocardiography. And other postoperative complications and duration of ICU stay were recorded.

Results: *There was a significant decrease in the incidence of MACEs with less pain scores in patients of TEA group in comparison to control group. Postoperative complications were comparable in both groups.*

Conclusion: *Perioperative PCEA in cardiac risky patients subjected to major gastrointestinal cancer surgery reduced significantly postoperative major adverse cardiac events with better pain control in comparison with perioperative PCIA analgesia.*

Keywords: *major perioperative cardiovascular event (MACEs), thoracic epidural analgesia, PCA, NRS.*

Introduction

About 200 million surgeries were performed per year worldwide and the number is increasing. Of these patients, millions of major surgical procedures are performed each year and major gastrointestinal cancer surgery are typical representatives of such high-risk patients [1].

The high risk non-cardiac surgical population represents a major global healthcare challenge. And about 10 million patients suffer a major perioperative cardiovascular event (MACEs) within 30 days of perioperative period. [2] This is because elective major gastrointestinal urgery associated with severe postoperative morbidity (including cardiac ischemic

events) may not able to undergo subjective measures of cardiorespiratory reserve, such as metabolic equivalency tests (METs) [3].

Major adverse cardiac events (MACEs) as (non-fatal cardiac arrest, non-fatal myocardial infarction, heart failure, and clinically relevant arrhythmias), represent the most common cause of perioperative morbidity and mortality, with incidence rates ranging between 1% and 7%. Despite decades of research into event prediction and prevention, the incidence of the events has remained largely unchanged [4].

Underlying cardiovascular disease significantly contributes to perioperative morbidity and mortality, and type of surgery, age of patients, cerebrovascular disease or diabetes mellitus increase overall prevalence of MACEs in non cardiac surgery being highest in patients older than 70 yr undergoing major vascular surgery [5].

Moreover, anticancer chemotherapy is known to be cardiotoxic and it appears that chemotherapy increases the postoperative cardiac risk after major cancer surgery. The most frequent cytotoxic agents used in treatment are cisplatin and 5-fluorouracil which have nephrotoxic and cardiotoxic effects, respectively. Additionally, combined use of chemotherapy and radiation is associated with higher treatment-related toxicities than use of radiation alone [6].

Cardiac Risk Index (RCRI) is one of the most widely used cardiac event risk stratification system and a lot of literature addressing the impact of intraoperative anesthetic hemodynamic management on perioperative cardiac events. [7-8].

Epidural analgesia is effectively applied in these surgeries to improve perioperative pain; epidural analgesia is coupled with improved analgesia, earlier extubation time, better haemodynamics, less respiratory complications, and superior left ventricular function [9-11].

The aim of this study was to evaluate the effect of perioperative patient controlled epidural analgesia (PCEA) on reduction of (MACEs) in comparison to patient controlled intravenous analgesia (PCA) in risky cardiac patients who were undergone major upper gastrointestinal cancer surgeries.

Patients and Methods

This prospective randomized study was approved by the local ethics committee of the South Egypt Cancer Institute, Assiut University, Egypt. In the duration from October 2017 till October 2018, after written informed consent, ASA (II-III) 66 ischemic cardiac adult patients were randomly allocated for elective major gastrointestinal cancer but 60 patients of them were finally analyzed.

Exclusion criteria were the following: contraindications to epidural catheter insertion (coagulopathy, recent -less than 1 week-treatment with thrombolytic or potent anti platelet drugs as clopidogrel, and local infection), allergy to local anesthetic medications or opioids. Patient whose ability to use PCEA pump or who cannot be taught how to evaluate their own pain intensity were also excluded from the study.

All patients were evaluated preoperatively by a cardiologist and anesthesiologist according to the revised cardiac risk index –Lee RCRI index -. That was calculated as one point was assigned to each of the following factors: a history of CAD, a history of cerebrovascular disease, history of heart failure, insulin-dependent diabetes mellitus, impaired renal function, and high-risk type of surgery. ECG and echocardiography were recorded and analyzed.

Preoperative data were taken within two days before surgery as; demographic data, medical, surgical history, physical examination and routine laboratory investigations. One day before surgery, all patients were taught how to evaluate their own pain intensity using the Numerical Rating Scale (NRS), scored from 0-10 (where 0= no pain and 10=worst pain imaginable).and how to use the PCA device (Abbott Pain Management Provider. S. No: 96450292. Abbott Laboratory, North Chicago. IL: 60064, USA) ®.

The Patients were randomly assigned into two groups (30 patients each) by using opaque sealed envelopes containing computer generated randomization schedule, the opaque sealed envelopes are sequentially numbered that were open before application of anesthetic plan.

Patients of both groups were premedicated with midazolam 0.05 mg/kg and ranitidine 50 mg. After shifting the patient to the induction room , ECG, pulse oximeter, non-invasive blood pressure and invasive

blood pressure monitors were attached. Peripheral Venous line and an infusion of lactated ringers' solution was started.

Control group (No. =30)

-Surgery was performed under **standard general anesthesia.**

-Postoperative analgesia was provided through patient Intravenous -controlled analgesia (PICA) for 72 hours postoperatively.

TEA group (No. =30)

-Surgery was done under standard general anesthesia. And additionally Thoracic Epidural catheter was inserted prior induction of GA.

Postoperative analgesia will provided through Patient-Controlled Epidural Analgesia (PCEA) using TEA for 72 hours postoperatively.

Standard General Anesthesia

After pre-oxygenation for 3 minutes, intravenous anesthesia (propofol 1.5 mg/kg) induced with fentanyl 1-2 μg/kg administered over min. Tracheal intubation will be performed after adequate neuromuscular blockade with cisatracurium 0.5 mg/kg. Anesthesia was maintained by isoflurane 1-1.5 MAC, cisatracurium 0.03 mg/kg given when indicated. Patients were mechanically ventilated to maintain ETCO2 between 35-40 mmHg. The inspired oxygen fraction (FIO2) was 0.5 using oxygen-and-air mixtures. At the end of surgery neuromuscular block was antagonized in all patients with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg and trachea was extubated in the operating room. Tracheal extubation were performed when patients meet the following criteria: hemodynamic stability, adequate muscle strength, full consciousness, and adequate ventilation breathing rate: 10 to 30 breaths/min, PaO2/IFO2 ≥80/0.4, PaCO2, 30 to 45 mmHg).

Intra operative analgesia in control group: - by continuous intravenous fentanyl infusion 2 μg g/kg/hr intra operatively to maintain heart rate (HR) and blood pressure within 20% of the basal value. Rescue analgesia of 0.5 μg /kg was given. Fentanyl infusion was continued until shifting the patient to ICU.

Intraoperative analgesia in TEA group: by epidural bolus dose of 0.1 ml/kg of a mixture (0.125% bupivacaine/Fentanyl 10 μg/ml) After a negative response to test dose-was administered, epidural were considered to be adequately working if there is decreased pin prick sensation at the expected dermatomal level, decreased blood pressure from its basal level and absence of stress response to surgical incision. Then, the bolus dose was followed by continuous infusion of 0.1 ml/kg of the same mixture.

Thoracic Epidural catheter

Under strict aseptic precautions thoracic epidural was performed using a 16 gauge Tuhy epidural needle by a paramedian approach. T8-T9 interspace was chosen for the injection (with air) after skin wheal of lidocaine local anesthetic 2%. The catheter was introduced approximately 4 cm into the epidural space. The epidural space was identified by the loss of resistance technique. A 3ml test dose of 2% Lidocaine with 1: 200,000 Adrenaline was given after the placement of the epidural catheter.

Post operative analgesia in control group; using PCA Fentanyl 10 μg /ml solutions through PCA device that programmed to give a bolus dose 2 ml/dose with a minimal lockout interval of 10 min with no background infusion. Post operative analgesia in TEA group using PCEA; background epidural infusion of 0.1 ml / kg/h of the mixture of (1.25 mg/ml bupivacaine plus 10 μg /ml Fentanyl) and 3 ml as top up dose of this mixture with lockout interval of 20 min. The analgesic regimen in both groups was adjusted to achieve a NRS< 3.

Data collected Intra operatively include (MAP, HR, colloid, and blood transfusion,) and duration of anesthesia and surgery.

Post operative all patients were admitted to surgical ICU and were followed-up by an investigator who was blinded to the study and findings on ECG. And beside the routine follow up, the following were recorded:

-Daily 12-lead ECG for 3days,

-Vital signs (HR, MAP and CVP) were recorded every one hour in ICU.

-Echocardiography to evaluate cardiac function.

-NRS- every 4 hours for 3 days-for pain measurement. And total fentanyl consumption was calculated.

-Any concomitant events like nausea; vomiting, pruritus or respiratory depression (decrease oxygen

saturation ≥90%) were recorded postoperatively.

-Duration of hospital and ICU stay and patients outcome (living or dead).

Study end-points:-Occurrence one or more of MACE (major advanced cardiac events) such as myocardial ischemia, myocardial infarction [MI], pulmonary edema, Non-fatal cardiac arrest, primary cardiac arrest, and malignant arrhythmia throughout 72 hours after surgery.

Non-fatal cardiac arrest: An absence of cardiac rhythm or presence of chaotic rhythm requiring any component of basic or advanced cardiac life support.

Acute myocardial infarction and ischaemia were replaced by terminology of myocardial injury which is more sensitive to evidence of myocardial cell necrosis. And also infarction and ischaemia are difficult to define in this setting because patients often do not have the classical symptoms or ECG changes of myocardial infarction.

We defined myocardial injury as (new ECG findings suggestive of ischemia, new ST segment changes, new pathologic Q wave or new T wave inversion) or New echocardiographic findings suggestive of ischemia (new regional wall motion abnormalities).

Congestive heart failure was defined as new in-hospital signs or symptoms of dyspnoea or fatigue, orthopnoea, paroxysmal nocturnal dyspnoea, increased jugular venous pressure, pulmonary rales on physical examination, cardiomegaly, or pulmonary vascular engorgement. The decision cut-point for the diagnosis of heart failure is identical to that of 100 pg/ml.

Malignant arrhythmia was defined as ECG evidence of atrial flutter, atrial fibrillation, or second- or third-degree atrioventricular conduction Block.

All ECGs and Echocardiography were analyzed by a consultant cardiologist who was responsible for the patients' management.

Statistical analysis

The required sample size was calculated using Epi Info software version 7 (CDC, 2012) ®. Using post hoc power analysis with accuracy mode calculations with incidence of MACEs as the primary objective and therefore, it was estimated that minimum sample size of 29 patients in each study group would a chive a power of 80% to detect an effect size of 0.8 in the outcome measures of interest, assuming a type I error of 0.05

All analyses were performed with the SPSS 21.0 ® software. Categorical variables were described by number and percent (N, %), where continuous variables described by mean and standard deviation (Mean, SD). And Mann–Whitney test were used to compare between two groups while Chi square test was used for qualitative data. Where compare between continuous variables by t-test. P was considered significant if 60.05 at confidence interval 95%.

Results

66 ischemic cardiac adult patients were randomly allocated for elective major abdominal cancer but 60 patients of them were finally analyzed (Figure 1) with no statistical differences in demographic data (table1) nor pre-operative morbid conditions (table 2) and echo findings (table 3& Figure 2).

In our study, the main finding was decreased of perioperative MACEs in patients of the TEA group in comparison to patients of control group (Figure 4).

In patients of the TEA group the quality of postoperative analgesia was better especially during first 24 hour postoperative period in comparison to control group (table 6), with comparable other postoperative side effects as (nausea, vomiting and pruritus) between two groups during 72 hours (Figure 5).

HR and MAP also was optimized significantly both intra and post operatively in TEA group instead of being elevated (not markedly but significantly) in control group (table 4, 5). Significant increase in ICU and hospital stay, in patients of control group who also showed increased consumption fentanyl in post operative period in comparison to patients of TEA group (table 7).

There were no cases of serious epidural catheter-related complications, such as respiratory depression, epidural hematoma or abscess, local inflammation, or permanent neurologic damage in our study.

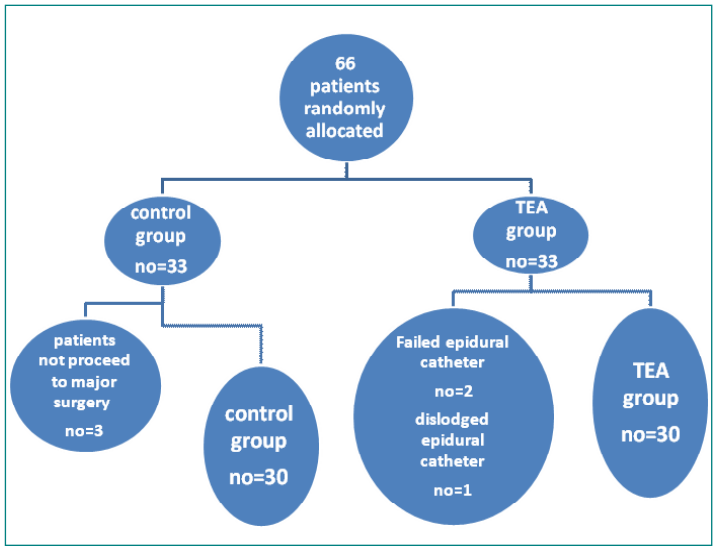

Figure 1. *Flow diagram of patients*

Table 1. Demographic data and patient's characteristics

	Control group (n=30)	TEA group (n=30)	P. value
Age: mean±SD	63.73 ± 5.61 (55-74)	61.73 ± 6.07 (5574)	0.191
Gender, M/F	18/20	12/10	0.592
BMI, kg/m 2: mean±SD	22.1 ±3.3	23.9 ±1.5	0.066
ASA (n and %)			
II	14 (46.7)	12 (40.0)	0.501
III	16 (53.3)	9 (60.0)	
Operative duration (hours), mean±SD	5.64 ± 0.7(4.4 - 7)	5.41 ± 0.68(4.3 - 7)	0.196
Type of Surgery:			
- Whipple's surgery	17(56.7%)	15(50.0%)	0.795
- Gastrectomy	7(23.3%)	8(26.7%)	0.998
- Oesophagectomy	6(20.0%)	7(23.3%)	0.976

Data were expressed as mean ± SD., TEA =thoracic epidural group. P. value < 0.05 considered statistically significant. Between two groups no significant difference found regarding patient's characteristics.

Table 2. *Patient's pre-operative morbid conditions*

	Control group (n=30)	TEA group (n=30)	P. value
ECG finding:			
Atrial fibrillation	10 (33.3%)	11(36.7%)	0.782
Pre mature atrial ectopics	4(13.3%)	4(13.3%)	1.000
Bundle branch block	4(13.3%)	2(6.7%)	0.394
Ventricular Hypertrophy	10(33.3%)	11(36.7%)	0.782
Site of Ischemic Heart Disease (IHD)			
Inferior IHD	14(46.7%)	14(46.7%)	1.000
Anterior IHD	2(6.7%)	0(0%)	0.374

Lateral IHD	8(26.7%)	4(13.3%)	0.194
Mixed IHD	6(20%)	12(40%)	0.091
Risky diseases :			
Hypertension	15(50%)	16(53.3%)	0.798
Diabetes Mellitus	16(53.3%)	15(50%)	0.798
Renal Failure	4(13.3%)	5(16.7%)	0.712
COPD	2(6.7%)	3(10%)	0.644
Hyper lipedemia	14(46.7%)	12(40%)	0.601
RCSI, mean±SD (range)	**3.07 ± 0.78 (2 - 4)**	**3.07 ± 0.58 (2-4)**	0.782

Data were expressed as mean ± SD., TEA =thoracic epidural group. P. value < 0.05 considered statistically significant. Between the two groups no significant difference found regarding patient's characteristics.

Table 3. *patient's pre-operative Echo findings*

	Control group (n=30)	TEA group (n=30)	P. value
Diastolic dysfunction			
Grade 1(G1)	22(73.3%)	24(80%)	0.834
Grade 2 (G2)	8(26.7%)	6(20%)	0.705
VALVE LESION			
No valve lesion	7(23.3%)	7(23.3%)	1.000
Mild valve lesion	10(33.3%)	9(30%)	0.783
Moderate lesion	12(40%)	13(43.3%)	0.795
Sever valve regurge	1(3.3%)	1(3.3%)	1.000
Other ECHO findings			
SWMA	8(26.7%)	9(30%)	0.777
Dilated atrium or ventricle	14(46.7%)	13(43.3%)	0.791
Pulmonary hypertension	9(30%)	11(36.7%)	0.582
Hyper trophic ventricle	10(33.3%)	8(26.7%)	0.577
EF, mean±SD (range)	**49.8 ± 5.99(41-60)**	**48.4 ± 5.52 (39-59)**	0.789

Data were expressed as mean ± SD. SWMA =segmental wall motion abnormality, TEA =thoracic epidural group. EF=ejection fraction, between two groups no significant difference was found

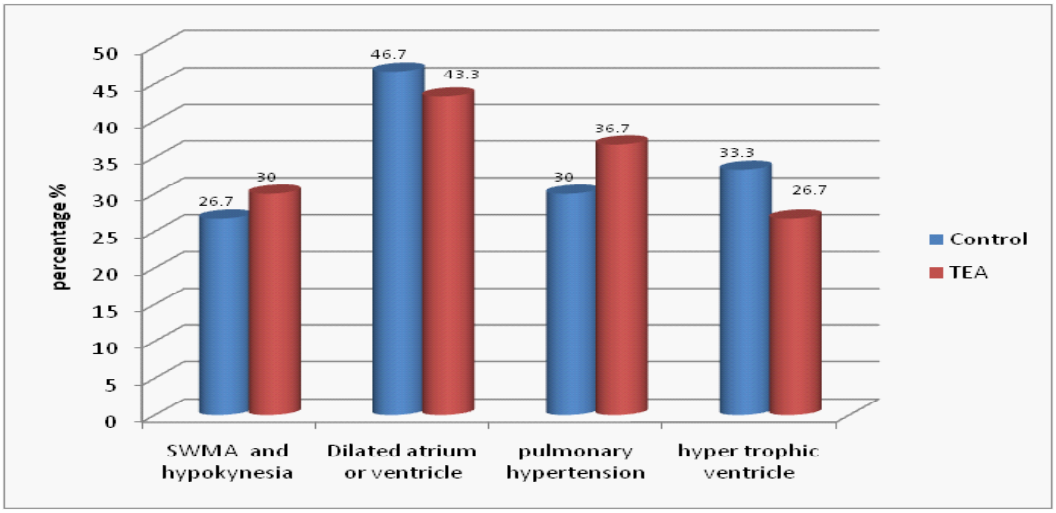

Figure 2. *pre-operative Other ECHO findings*

SWMA= segmental wall motion abnormality, TEA =thoracic epidural group. between two groups no significant difference found.

Table 4. *Intra-operative haemodynamics*

Intraoperative MAP (mmhg)	**Control group (n=30)**	**TEA group (n=30)**	**P. value**
Baseline reading	75.9±10.6(58 - 94)	80±9.3(68 - 95)	0.117
1h	82.47 ± 10.04(62 - 100)	73.53 ± 10.02(56 - 90)	0.002*
2h	79.67 ± 12.12(62 - 98)	65.07 ± 7(52 - 77)	0.001*
3h	75.73 ± 11.79(60 - 100)	69.67 ± 7.32(60 - 82)	0.120
4h	77.2 ± 13.43(62 - 108)	73.2 ± 8.35(59 - 86)	0.218
5h	73.13 ± 8.86(62 - 98)	72.93 ± 4.95(65 - 82)	0.914
6 h	75.73 ± 11.79(60 - 100)	69.67 ± 7.32(60 - 82)	0.120
Mean	**77.85 ± 9.02(63.8 - 98)**	**70.07 ± 5.65(62-81.8)**	**0.018***
Intraoperative HR (bpm)			
Baseline reading	72.8±11.0(56 - 94)	77.9±14.0(57 - 97)	0.126
1h	85.13 ± 10.37(65 - 98)	75.4 ± 7.16(65 - 89)	0.001*
2h	82.93 ± 18.02(56 - 120)	72.47 ± 14.43(57 - 110)	0.016*
3h	82.27 ± 13.96(58 - 110)	72.67 ± 11.81(56 - 108)	0.012*
4h	80.07 ± 14.14(59 - 108)	75.33 ± 11.57(50 - 98)	0.161
5h	72.93 ± 12.34(55 - 100)	72.73 ± 13.05(55 - 100)	0.952
6 h	80.07 ± 14.14(59 - 108)	76.33 ± 11.57(50 - 98)	0.168
Mean	**80.67 + 8.92(68.2 - 96.2)**	**73.72+8.47(66.2+101.0)**	**0.016***

Data are expressed as mean ± SD. At base line reading and 1, 2, 3, 4,5 and 6 hours MAP= mean arterial pressure (mmhg), HR=heart rate (beat per minutes).h=hour interval TEA =thoracic epidural group.between two groups there was significant difference in early post operative periods.being optemized in TEA group and elevated in control.

Table 5. *Post-operative haemodynamic variables (mean of readings/day)*

	Control group (n=30)		**TEA group (n=30)**		**P. value**
	Range	**Mean±SD**	**Range**	**Mean±SD**	
Post-operative HR (bpm)					
Day1	64.8 - 148.4	92.91±19.07	55 - 128	84.59 ± 21.78	0.003*
Day2	67.4 - 121.4	88.53 ± 15.1	63.6 - 112	80.6± 15.14	0.047*
Day3	68.8 - 83.6	85.11 ± 7.14	61.4 - 83.8	77.41± 4.63	0.247
Post-operative MAP (mmhg)					
Day1	68.8 - 83.6	77.21 ± 4.63	61.4 - 83.8	73.69 ± 7.14	0.031*
Day2	64.8 - 87.2	76.15 ± 7.94	62.6 - 89.2	73.75 ± 7.96	0.247
Day3	58.4 - 88.4	72.37 ± 9.72	59 - 87	71.2 ± 8.3	0.617
Post-operative CVP (cm H2O)					
Day1	5.2 - 19	8.89 ± 2.72	5.2 - 16	10.01 ± 3.7	0.187
Day2	4.2 - 19.8	8.47 ± 1.86	6.4 - 13.8	9.76 ± 3.89	0.106
Day3	7 - 15.6	8.13 ± 1.59	6.6 - 13.2	8.97 ± 2.13	0.093

Data were expressed as mean ± SD. HR=heart rate (beat per minutes). TEA =thoracic epidural group. MAP= mean arterial pressure (mmhg), CVP=central venous pressure (cmH2o). between two groups there was ONLY significant difference in early post operative day regarding patient's H.R and MAP but not CVP. P. value < 0.05 considered statistically significant

Table 6. *Post-operative NRS (3 days readings)*

	Median (IQ range)		P. value
	Control group	TEA group	
NRS 0h	3(2:4)	2 (2:2)	0.007*
NRS 4 h	3(2:4)	2 (1:3)	0.018*
NRS 8 h	2 (2:3)	1 (1:2)	0.002*
NRS 12 h	2(2:3)	1 (1:2)	0.019*
NRS 16 h	2(2:3)	1(1:1)	0.013*
NRS 20 h	2(1:3)	2 (2:3)	0.193
NRS S 24 h	2(2:2)	2(2:3)	0.055
NRS 28 h	2(1:3)	2(2:3)	0.794
NRS 32 h	2(2:3)	2(2:3)	0.180
NRS 36 h	3(2:3)	3(2:3)	0.121
NRS 40 h	2(2:3)	2.5(1:3)	0.307
NRS 44 h	2.5(2:3)	2(2:2.8)	0.091
NRS 48 h	3(2:3)	2(2:3)	0.113
NRS 52 h	2(1:3)	2 (2:3)	0.194
NRS 56 h	2(2:2)	2(2:3)	0.057
NRS 60 h	2.5(2:3)	2(2:2.8)	0.091
NRS 64 h	3(2:3)	2(2:3)	0.113
NRS S 68 h	2(1:3)	1 (1:1)	0.194
NRS 72 h	2(2:2)	2(2:3)	0.057

Data were expressed as Median and (IQ range). VAS=visual analogue scale TEA =thoracic epidural group.0h=immediately after recovery, h=hour. between two groups there was significant difference in early post operative hours P. value < 0.05 considered statistically significant.

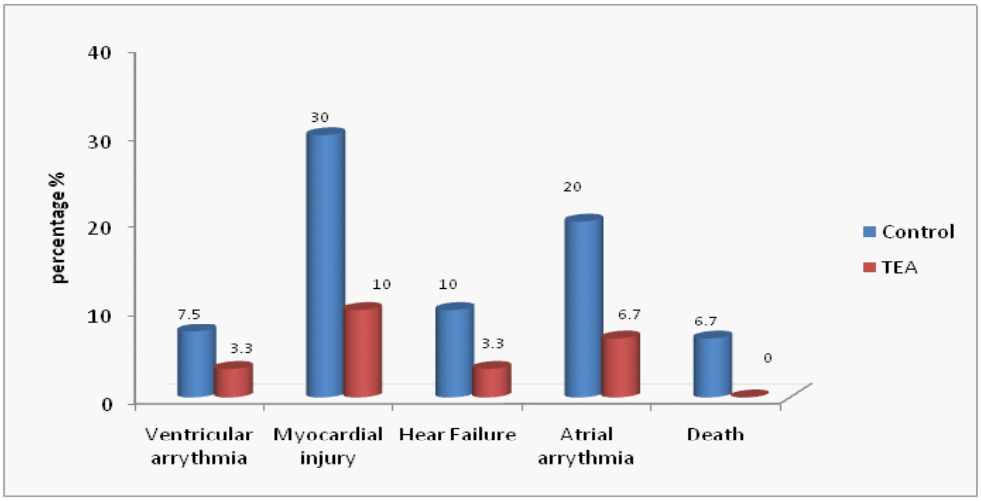

Figure 3. Post operative MACE

Data were expressed in number and percentage. TEA =thoracic epidural group ,MACE= major advanced cardiac events,HF= heart failure, EF = ejection fraction. in postoperative period in TEA group there was significant decreased of myocardial injury and postoperative arrhythmia (atrial and ventricular). compared to control group. Moreover, there were trends towards decreased other complications as Congestive heart failure but did not reach statistical significance

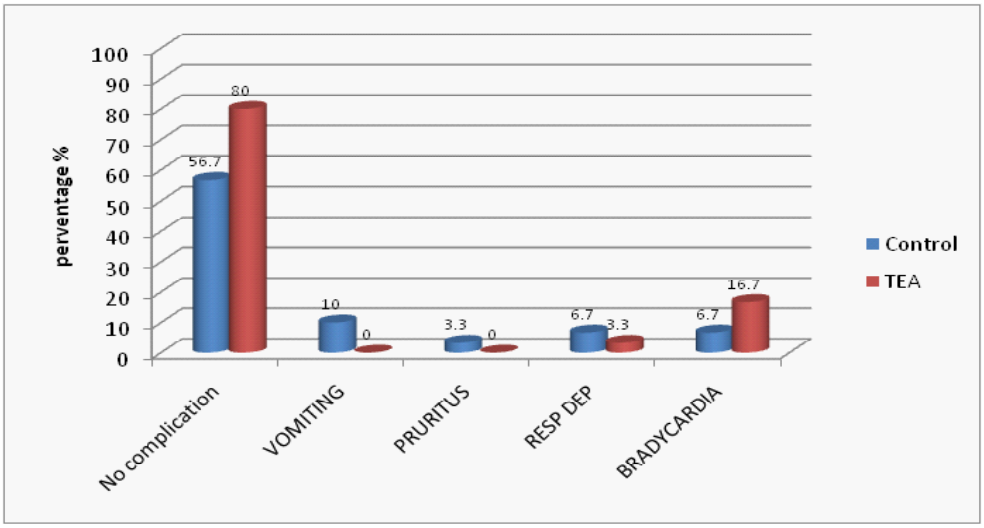

Figure 4. *Post-operative complications from the studied drugs*

TEA =thoracic epidural analgesia group, RESP DEP=respiratory depression There was no significant difference between two groups.

Table 7. *ICU, Hospital stay and Fentanyl consumption*

	Control group (n=30)		TEA group (n=30)		P. value
	Range	Mean±SD	Range	Mean±SD	
ICU stay(day)	3 - 11	7.47 ± 2.16	3 - 8	5.6 ± 1.57	0.00**
Hospital stay(day)	3 - 31	22.13 ± 7.62	10 - 25	18.13 ± 4.12	0.014*
Fentanyl (mic/72h) consumption	1200 - 2000	1646.67 ± 234.5	600 - 1000	753.33 ±122.43	0.000**

Data were expressed as mean ± SD, TEA =thoracic epidural analgesia group, ICU=intensive care unit P. value < 0.05 considered statistically significant. There was significant difference between two groups. Patients of TEA group stay less period in ICU and hospital and consumed less fentanyl.

Discussion

In patients of the TEA group the quality of postoperative analgesia was better especially during 72 hour postoperative period in comparison to control group. Our choice of 72 hours as period for PCA (either I.V. or epidural) because the large proportion of clinically unrecognized acute myocardial infarction (AMI) is related to the fact that most AMI occur during the early postoperative period [12].

In our study, the main finding was decreased of MACEs in patients of the TEA group in comparison to patients of control group.

Generally, major non-cardiac surgery is associated with Major advanced cardiac events which represent the most common cause of serious perioperative morbidity and mortality. One out of 10 patients who developed a MACE died during the hospital stay [13]. Most MACE-related death after major surgery arises from myocardial infarction and arrhythmias. [14].

MI is associated with poor prognosis. However, asymptomatic perioperative MI is as strongly associated as symptomatic MI with 30 day mortality. [15]. Other Authors observed low incidence of serious postoperative cardiac events in Major non-cardiac surgery as Mangano (3%) and Lee (2%) [16-17].

We can explain the high prevalence of cardiac complications in the major surgeries -like these selected for the study-is due to the fact that major surgery triggers an organism's response to stress, which is characterized by profound endocrine, metabolic, and hemodynamic alterations. The activation of the sympathetic system results in tachycardia and increases myocardial oxygen consumption. [18].

Also major surgeries especially that carried out in upper abdomen are procedures with intense pain that, if not properly treated, may cause deep physiological and hormonal alterations in the body [19]. More over severe abdominal pain causes shallow breathing, atelectasis, retention of secretions and lack of cooperation in physiotherapy followed by hypoxia and cardiac complication. This increases the incidence of post-operative morbidity and leads to delayed recovery. [20].

Cardiac sympathetic over activity can damage myocardial cells by causing a release of large amount of catecholamines and cytokines. Therefore, locally blocking cardiac sympathetic fibers could considerably protect the heart and reduce the secondary effects. [21]. Both TEA and intravenous analgesia were found to reduce pulmonary and cardiac complications, and improve tissue oxygenation and tissue reperfusion. [22].

TEA was heavily studied and the utility of peri-operative epidural analgesia in reducing postoperative cardiac morbidity has created much controversy since Yeager et al. [23]. Then many studies (agree with us) have shown that TEA together with general anaesthesia provided better myocardial protection than general anaesthesia alone [24-25] and many meta-analyses suggest that TEA may decrease cardiac morbidity and mortality after cardiac and major non-cardiac surgery. [26-27]. and in experimental myocardial ischaemia, TEA reduced infarct size.

Other study that confirm our results proved that cardiac morbidity was shown to be lower among patients undergoing major vascular surgery after the administration of general anesthesia combined with postoperative epidural analgesia compared to the administration of general anesthesia alone and postoperative systemic opioid analgesia [28].

TEA was found to decrease adverse perioperative cardiac events by its overall reduction of sympathetic tone and block of the cardiac accelerator fibers could reduce the risk of dysrhythmias and injury as observed during cardiac surgery and cardiopulmonary bypass. [29]. Better pain relief with concomitant reduction in the postoperative stress response and systemic sympathetic activity may contribute to this effect [30].

More over Blomberg et al found that large coronary epicardial arteries and coronary arterioles are densely innervated by sympathetic adrenergic nerve fibers. Coronary blood flow after TEA was investigated in patients with ischemic heart disease. Endocardial to epicardial blood flow was improved, so that regional distribution of perfusion is optimized. [31]

Also Schmidt et al approved that TEA improved diastolic function in patients with coronary artery disease undergoing operative revascularization. Diastolic dysfunction has been reported to be an early sign of cardiac ischaemia. [32].

On contrary of our results; clinical data on myocardial ischaemia and mortality are inconclusive as in a randomized trial that showed TEA did not reduce the 30 day complication rate and do not confirm that reduced morbidity such as respiratory or cardiac complication after cardiac surgery. [33]

Also against us a study conducted by Mohamed et al, in our institute they studied 60 ischemic patients underwent elective major abdominal cancer surgery assigned into 2 groups; 30 patients each to receive general anesthesia (G1) or combined general and epidural anesthesia (G2).they concluded that The LEA combined with general anesthesia in high risk patients with ischemic heart disease undergoing major abdominal cancer surgery provided better pain relief, and Ischemic cardiac events were similar in both groups. [34]

Regarding haemodynamic; Kessler et al. who compared the heart rate in patients between those who received general anaesthesia together with TEA(Group1) and those who received only general anaesthesia (Group2) during coronary artery bypass surgery performed on a beating heart and reported that the heart rate in the group 1 was lower than preoperative values ,during sternotomy and anastomosis compared to group 2. [35]

But both Berendes et al. and Fillinger et al. [36-37]. were against us as they did not observe a difference in hemodynamic findings between the control group and

the TEA treatment group who studied TEA in patients undergoing coronary artery bypass grafting.

Scott et al. presented the first randomized evaluation of the impact of perioperative TEA on outcome in a large series of 400 patients with normal ventricular function undergoing CABG in whom the epidural catheters were placed immediately before surgery. There was a reduction in the incidence of supra ventricular arrhythmias (SVA). [38]

According to Moltner, Dysrhythmias are common complications in immediate postoperative period even more common after upper abdominal and thoracic surgeries [39]. As conducted by Giroban et al who concluded that dysrhythmias in the postoperative period was 20% of 185 patients undergoing thoracobdominal surgeries. [40]

We can explain occurrence of arrhythmias by many factors as pre-existing cardiac pathology, intraoperative events, and arrhythmia triggers. Autonomic imbalance after operation has been implicated as a possible trigger, and is thought to be characterized by increased sympathetic tone and lower vagal tone.. Also Dysrhythmias may be associated with improper treatment of pain, and have the excess of circulating catecholamines as the most important physiopathological mechanism, producing an imbalance between oxygen offer and consumption by the myocardium. [41-42]

In our study, no patient developed significant hypotension. Similar findings were noted in studies done by Elzohry et al .In the study conducted by five episodes of postoperative hypotension occurred in the PCEA group versus none in the PCA group. The patients were treated by simple fluid loading. [43].

The explanation of this finding is in another study that applied the Apgar score during surgery, intraoperative hypotension (mean systolic arterial pressure, 40mm Hg) also predicted cardiovascular events and other postoperative complications as well. [44]

Decreasing MACEs in TEA group and decreased fentanyl consumption were reflected on ICU and hospital stay as proved by Bouman et al. who reported that the patients in the epidural PCA group were discharged earlier in one and half days on average than the PCIA group. Also, patients in the epidural PCA group started ambulation earlier than in the PCIA group [45].

Conclusion

Perioperative PCEA in cardiac risky patients subjected to major gastrointestinal cancer surgery reduced significantly postoperative major adverse cardiac events with better pain control in comparison with perioperative PCIA analgesia.

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