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RESEARCH ARTICLE

High Thoracic Epidural Analgesia as an Adjunct to General Anesthesia in Patients Undergoing Off-Pump Coronary Artery Bypass Grafting

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Abstract:

Aim:

To investigate the effect of high thoracic epidural analgesia combined with general anesthesia on pain management and postoperative outcomes in patients undergoing off-pump Coronary Artery Bypass Grafting (CABG).

Materials and Methods:

Patients were divided into two groups; Group 1 received general anesthesia and high thoracic epidural anesthesia whereas Group 2 received general anesthesia alone during off-pump coronary artery bypass grafting. Epidural catheters were placed at least 6 hours before transfer to the operating room. An epidural analgesic solution of 0.25% bupivacaine and 10 µg/ml fentanyl was started as continuous infusion at 5 ml/hour and maintained for at least 12 hours after completion of surgery. A 10-cm visual analog scale was used to measure pain at 4th, 6th, 9th and 12th postoperative hours.

Results:

Mean time to extubation was similar between two groups (2.45±0.88 *vs.* 2.59±1.31 for Groups 1 and 2, respectively, p=0.90). In all measurements, mean Visual Analogue Scale VAS scores were significantly lower in Group 1 compared to Group 2 (6.50±1.53 *vs.* 4.09±1.83 at 4th hour, 6.62±1.55 *vs.* 3.71±1.85 at 6th hour, 5.83±1.40 *vs.* 2.93±1.54 at 9th hour and 4.41±1.97 *vs.* 2.50±1.19 at 12th hour, p<0.001 in each comparison).

Conclusion:

Continuous high thoracic epidural analgesia seems to be a good adjunct to general anesthesia, as its pain relief effect becomes obvious at 4th postoperative hour and lasts at least 12th postoperative hour.

Keywords: Coronary artery bypass grafting, High thoracic epidural anesthesia, Pain, Analgesia, Postoperative pain control.

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1. INTRODUCTION

High Thoracic Epidural Analgesia (HTEA), has been used in cardiac surgery for about two decades [1, 2]. The technique provides blockade of the upper thoracic segments by delivering epidural anesthesia through one of the upper 3-4 thoracic intervertebral spaces. Its use has been reported as the sole anesthetic procedure or as an analgesic adjunct to general anesthesia [3]. Earlier studies regarding the use of HTEA as the sole anesthetic protocol in awake patients during off-pump Coronary Artery Bypass Grafting (CABG) reported encouraging results regarding its feasibility [2, 4]. Besides eliminating the need for endotracheal intubation, the rationale of using HTEA during CABG was based on its cardiac sympathetic blockage between thoracic 1 and 2 levels (Th1 and Th2) levels exerting a coronary vasodilatory effect on stenosed coronary vessels. In clinical studies, this effect was translated to attenuation of stress-induced myocardial ischemia and angina relief. Further studies demonstrated that use of HTEA attenuated surgical stress response and thus provided hemodynamic stabilization and anti-arrhythmic effect during CABG. However, its potential complications such as epidural hematoma or abscess and procedural difficulties with epidural catheter placement

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and anesthetic failures have limited the use of HTEA following the initial reports [5].

There have been several studies regarding the use of HTEA combined with general anesthesia during cardiac surgery. These studies reported conflicting results regarding its benefit on postoperative pain management and cardiac outcomes [6 - 14]. The present study aimed to investigate the effect of HTEA combined with general anesthesia on pain management and postoperative outcomes in patients undergoing off-pump CABG.

2. MATERIALS AND METHODS

The study was conducted following the guidelines and approval of Abant Izzet Baysal University Clinical Researches Ethics Committee 30/04/2015 - 2015/21. All patients gave written informed consents allowing their archived data to be used for research purposes at any time without disclosing their identity information. This prospective study was conducted in the Cardiovascular Surgery Department of a tertiary care hospital. The study group was made up of patients undergoing off-pump CABG surgery between December 2015 and March 2018. Eligible patients were those aged > 40 years old and scheduled for elective CABG-only procedure using off-pump technique. Patients with significant spine deformities or abnormal hemostatic parameters (low platelet count or prolonged prothrombin time) and those having any significant cardiac valvular disease (moderate to severe or severe stenosis or regurgitation in aortic, mitral, tricuspid and/or pulmonary valves), moderate to severe left ventricle dysfunction (left ventricle ejection fraction < 45%), low-caliber target coronary artery (<1.0 mm in internal diameter) were excluded. Need for urgent revascularization, severe obesity (a body mass index of more than 40 kg/m^2), advanced chronic obstructive pulmonary disease, history of chronic pain or drug abuse and unwillingness of the patient were also regarded as criteria for exclusion. Based on these criteria patients were divided into two groups; Group 1 received general anesthesia and HTEA whereas Group 2 received general anesthesia alone. All patients were assessed by the anesthesiologist the day before the operation and epidural catheters were placed at least 6 hours before transfer to the operating room. The epidural catheters were placed using hanging drop technique under local anesthesia with the patient in the sitting position. The landmarks that were used to identify the correct intervertebral space were spinous process of the C7 cervical vertebra and inferior angle of the scapula which corresponds to the T7 level. The catheters were inserted 3-4 cm into the epidural space between Th1-Th2 or Th2-Th3 interspace by use of a Tuohy tipped needle and the needle was directed cephalad. The catheters were flushed with saline and then secured accordingly.

In the operating room standard monitoring included 12-lead electrocardiogram, invasive blood pressure monitoring through radial artery and central venous pressure through internal jugular vein. Patients with epidural catheter received 3 ml of 2% lidocaine to obtain a sensory (to pinprick) and a temperature block between Th1 and Th8. The level of block was tested using both temperature and pinprick discrimination. Then, an epidural anesthesia solution containing 0.25% bupivacaine and 10 μg/ml Fentanyl was started as continuous infusion at 5 ml/hour. Induction of general anesthesia was performed about 5 minutes after initiation of epidural anesthesia infusion. In both groups, general anesthesia was induced in a standard fashion with administration of 2-5 μg/kg fentanyl, 2.0 mg/kg etomidate and 0.1 mg/kg pancuronium and maintained with inhalation of isoflurane.

In the early postoperative period, patients were transferred to the intensive care unit while endotracheally intubated and ventilated. In the ICU the patients were ventilated using synchronized intermittent mandatory ventilation until they become spontaneously breathing and they were weaned from ventilation support when they could sustain spontaneous respiration without having any deterioration in respiratory parameters in arterial blood gas analysis. A dopamine infusion was started at a rate of 3 to 5 μg/kg/min if urine output was less than 1 ml/hour per kilogram of body weight despite adequate central venous pressure. A 10-cm visual analogous scale was used to measure subjective perception of pain around sternum and anterior chest wall. The earliest measurement of pain was first performed at the 4^{th} postoperative hour and then repeated at 6^{th}, 9^{th} and 12^{th} postoperative hours. Patients were given intravenous paracetamol if they reported VAS > 4 pain. Time for extubation and Troponin I level at 6^{th} and 12^{th} hour after operation were also recorded as secondary outcome parameters.

Major complications were defined as those leading detrimental effects and included epidural hematoma or permanent neurological deficit. Minor complications were defined as those resolved spontaneously such as superficial ecchymosis, dural puncture and vasovagal symptoms during puncture.

2.1. Statistical Analysis

Statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 20.0. Descriptive statistics were reported as mean ± standard deviation for continuous variables and as frequency and percentage for categorical variables. Categorical parameters were compared using chi-square test of Fisher's exact test. Parameters with a normal distribution were compared using independent samples t test whereas parameters not demonstrating normal distribution were compared using Mann-Whitney test. A *p* value of less than 0.05 was considered as statistically signi-ficant.

In order to detect a significant difference between mean VAS score of two groups, we calculated that at least 28 cases per group was needed based on an alpha error of 0.05 and power of (1-beta) 0.80 with an effect size of 0.7 (moderate to high effect size).

3. RESULTS

There were 32 patients in Group 1 (general anesthesia and HTEA) and 24 patients in Group 2 (general anesthesia alone). Mean age was 60.95 ± 9.29 years in Group 1 and 60.46 ± 9.39 years in Group 2 (p= 0.77). Two groups were comparable in terms of gender distribution (p= 0.38), body mass index (p= 0.21), tobacco use (p= 0.08), hypertension (p= 0.44), diabetes (p= 0.53), pulmonary disease (p= 0.84), left ventricle ejection fraction (p= 0.05) (Table **1**).

Table 1. Comparison of baseline characteristics between two groups.

Variables	Group 1	Group 2	*p* Value
	General Anesthesia + HTEA (n=32)	General Anesthesia (n=24)	
Age (years)	60.46±9.39	60.95±9.29	0.77
Male	27 (84.4%)	18 (75.0%)	0.38
Body Mass Index (kg/m^2)	27.46±4.83	29.05±4.61	0.21
Tobacco use	18 (56.3%)	8 (33.3%)	0.08
Hypertension	14 (43.8%)	13 (54.2%)	0.44
Diabetes mellitus	16 (50.0%)	10 (41.7%)	0.53
Pulmonary disease	6 (18.8%)	5 (20.8%)	0.84
Left ventricle ejection fraction	56.21±5.34	58.41±5.92	0.05

Table 2. Secondary clinical outcome parameters.

Variables		Group 1	Group 2	*p* Value
		General Anesthesia + HTEA (n=32)	General Anesthesia (n=24)	
Time to extubating		2.59±1.31	2.45±0.88	0.90
Troponin I (ng/ml)*				
	6th postoperative hour	0.36±0.86	0.59±1.03	0.36
	12th postoperative hour	0.38±0.85	0.78±1.38	0.19
Postoperative dopamine infusion		5 (15.6%)	4 (16.7%)	0.91
Postoperative atrial fibrillation		8 (25.0%)	7 (29.2%)	0.76
*Normal below <0.04 ng/ml				

Table 3. Comparison of postoperative variables between groups.

Variables	Group 1	Group 2	*p* Value
	General Anesthesia + HTEA (n=32)	General Anesthesia (n=24)	
VAS for pain			
4th postoperative hour	4.09±1.83	6.50±1.53	<0.001
6th postoperative hour	3.71±1.85	6.62±1.55	<0.001
9th postoperative hour	2.93±1.54	5.83±1.40	<0.001
12thpostoperative hour	2.50±1.19	4.41±1.97	<0.001
Number of patients with VAS > 4			
4th postoperative hour	14 (43.8%)	21 (87.5%)	<0.001
6th postoperative hour	12 (37.5%)	22 (91.7%)	<0.001
9th postoperative hour	6 (18.8%)	19 (79.2%)	<0.001
12thpostoperative hour	2 (6.3%)	11 (45.8%)	<0.001

None of the patients had major or minor complications and all of them were extubated within maximum 8 hours after surgery. Mean time to extubate was similar between two group (2.45 ± 0.88 *vs.* 2.59 ± 1.31 for groups 1 and 2, respectively, p= 0.90) and only 1 patient in group 1 had prolonged extubation time (> 4 hours). All patients had a slight increase in Troponin I values but mean Troponin I values did not differ between two groups both at 6th (p= 0.36) and 12th postoperative hour (p= 0.19). Four patients (16.7%) in Group 1 and 5 patients (15.6%) in Group required low dose dopamine infusion during the early postoperative course (p= 0.76) (Table **2**).

Mean VAS scores were significantly higher in Group 1 compared to Group 2 in all measurements (p< 0.001). In Group 1, VAS> 4 was higher in all measurement times compared to Group 2 (Table **3**).

4. DISCUSSION

Our study demonstrated that HTEA was quite helpful in pain control during postoperative period and the benefit of HTEA has become noticeable at 4 hours after surgery. Use of HTEA did not result in any procedural (*i.e.* catheter related) complications and epidural administration of analgesic solutions had no effect on hemodynamic stability during induction of anesthesia, suggesting its safety and feasibility in

patients undergoing off-pump coronary artery bypass surgery.

Use of high thoracic epidural route for analgesia or anesthesia during and after cardiac surgery has been controversial. Earlier studies reported encouraging results regarding the use of HTEA as the sole anesthetic procedure. Karagoz *et al*. [2] used the technique in a total of 137 patients undergoing off-pump CABG and they reported that 96.3% of patients were able to remain awake without supplemental general anesthesia with a pneumothorax rate of 28.4%, suggesting that pneumothorax was a common troublesome complication associated with the use of HTEA in awake patients. In this series, almost half of the patients did not require an intensive care unit stay, mean length of hospital stay was 1 day (range 0-3 days) and angiographically confirmed graft patency was 100%.

In another earlier study, Chakravarthy *et al.* [3] used HTEA in 15 patients undergoing multivessel off-pump CABG. The authors reported that mean intensive care unit stay was 18.2 ± 4.2 hours and mean hospital stay was 3.2 ± 1.2 days. These two studies highlighted that HTEA during off-pump CABG as the sole anesthetic was almost completely problem-free except for the common development of pneumothorax during surgery. Although this complication rarely caused conversion to general anesthesia, it might be challenging or time-consuming during surgery.

However, data regarding the use of HTEA as the sole anesthetic procedure during cardiac surgery is scarce since it has not gained much popularity. However, there have been several studies about use of HTEA as an adjunct to general anesthesia during off-pump CABG. A retrospective study reported by Salvi *et al.* [15] on 106 patients was probably the first reporting on use of HTEA combined with general anesthesia in patients undergoing off-pump CABG. The authors reported that 1 patient had postoperative paraplegia, but magnetic resonance imaging revealed that this complication was not secondary to medullary compression due to epidural or spinal hematoma. Since pathophysiology of this rare complication could not be clarified in this individual case, it is difficult to make an assumption regarding development of permanent neurological deficit after use of HTEA in cardiac surgery. Results of that study were quite close to those of ours; mean visual analog scale score of < 2 throughout the day after surgery, mean time to extubate of 4.6 ± 2.9 hours, average intensive care unit stay 1.5 ± 0.8 days.

Kessler *et al*. [16] compared 3 anesthetic techniques (general, combined general anesthesia and HTEA or HTEA alone) in patients undergoing off-pump CABG. The authors found no difference among groups regarding safety, feasibility and patients' satisfaction however they reported that combination of two techniques achieved an effective reduction in heart rate which facilitated multiple bypass to the target coronary arteries. The authors also highlighted the effectiveness of pain relief in patients receiving high thoracic epidural analgesia compared to those who received general anesthesia alone. In our study, there were no significant differences in heart rate, systolic and diastolic blood pressure values and none of the patients had significant hemodynamic changes during the operation. In keeping with the results of this study, we also observed lower VAS scores with high thoracic epidural anesthesia however this effect lasted at least 12 hours after surgery.

In our study, troponin levels were low in both groups and without a significant difference between the groups. In one recent study, mean serum levels of Troponin I and inflammatory markers were reported to be significantly lower in patients receiving HTEA as an adjunct to general anesthesia compared to those receiving general anesthesia alone during off-pump CABG [8]. However, like ours, this study also revealed quite low mean Troponin I levels in the postoperative period and the authors reported that the difference in Troponin levels was significant only at 5th postoperative day (0.64 *vs.* 0.12 in control and study groups, respectively, $p< 0.05$). The study also reported lower Interleukin-6 and TNF alpha within 5 days after the operation. We think that, since studies about HTEA during off-pump CABG excluded patients with low myocardial functions, myocardial preservation effect of high thoracic epidural anesthesia during off-pump CABG remained a theory. This effect is still awaiting confirmation in the clinical setting especially for the patients with diminished myocardial reserve.

Since HTEA slows down the heart rate, reduces stress response and inhibits sympathetic activity, some studies focused on whether patients receiving HTEA have lower risk of atrial fibrillation postoperatively. In one large prospective study where a total of 226 patients were randomized to two groups as to receive thoracic epidural analgesia added to general anesthesia or general anesthesia alone, incidence of atrial fibrillation was significantly lower in the study group (20% *vs*. 35%, OR:0.41, 0.22-0.78 in 95% confidence interval, $p = 0.006$) [7]. Supporting this was another prospective trial which reported a significant reduction in atrial fibrillation incidence and this reduction was attributed to lower levels of plasma epinephrine levels in HTEA group [6]. In our study, we found no significant difference in atrial fibrillation frequency between two groups.

The present study was limited by its small sample size, which precluded the generalizability of our results. Since patient selection was primarily based on eligibility for epidural catheter insertion by the anesthesiologist, average patient age was relatively young when compared to a real-world population undergoing off-pump CABG. The study focused on in-hospital course of the patients, which limited us to draw more definitive conclusions.

CONCLUSION

In conclusion, HTEA is feasible, and it helps pain control during the early course after off-pump CABG. Continuous HTEA seems to be a good adjunct to general anesthesia, as its pain relief effect becomes particularly obvious after 4th postoperative hour when the effect of general anesthesia is eliminated.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The research was conducted following the guidelines and approval of Abant Izzet Baysal University Clinical Researches

Ethics Committee 30/04/2015 - 2015/21.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Informed consent was obtained from all the participants of the work.

AVAILABILITY OF DATA AND MATERIALS

All data and materials are available in hospital's registry.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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