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ORIGINAL ARTICLE.

Epidural versus General Anesthesia Supplemented with Dexmedetomidine Regarding Attenuation of Reperfusion Injury During Aorto-Femoral Bypass.

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ABSTRACT

Background: Aorto-femoral bypass surgery is associated with remote organ injury due to ischemia-reperfusion injury. The aim of this study was to compare general anesthesia supplemented with dexmedetomidine infusion with epidural anesthesia regarding the ability to attenuate ischemia-reperfusion injury during aorto-femoral bypass surgery by measuring malondialdehyde serum level before and after revascularization.

Methods: 52 patients scheduled for aorto-femoral bypass surgery were included in the study. Patients were randomized into two groups: group EP, anesthetized by epidural anesthesia and group GA, anesthetized by general anesthesia supplemented with dexmedetomidine infusion. Malondialdehyde serum level was measured using an ELISA kit and the optical density method. Hemodynamic variability was recorded at different time points during the study. Intra-operative data (duration of surgery, duration of cross clamping, estimated blood loss, volume of given crystalloids, colloids, packed RBCs, fresh frozen plasma) were all recorded. Post-operative complications (hypertension, tachycardia, hypotension, bradycardia, and shivering) were also recorded.

Results: Malondialdehyde serum levels were significantly lower in the GA group at 2hrs. and 5 hrs. after revascularization but not after 24hrs. Heart rate was significantly lower in the GA group through most of the operation time. Post-operative hypertension and tachycardia were significantly higher in the GA group were as post-operative shivering was significantly higher in the EP group.

Conclusions: Dexmedetomidine supplementation to general anesthesia can attenuate ischemic-reperfusion injury after 2 and 5hrs. of revascularization more than epidural anesthesia can do alone. Hypertension and tachycardia are more common after discontinuation of dexmedetomidine in the post-operative period. Shivering is significantly reduced after dexmedetomidine infusion.

Key words: Dexmedetomidine; Ischemia-reperfusion injury; Malondialdehyde; Revascularization; Aorto-femoral bypass; Critical limb ischemia.

INTRODUCTION

Aorto-femoral bypass surgery is associated with vital organ injury that can occur during the ischemic time or after reperfusion which is called the ischemic-reperfusion injury (IRI). Various techniques have been investigated to control such mechanisms of injury including pre- and post-conditioning strategies, the use of volatile anesthetics, and α2 adrenergic agonists [1]. Choosing the anesthetic technique for lower limb revascularization has been a debate for many years, Epidural anesthesia with continued epidural analgesia in the post-operative period has been related to decreased post-operative morbidity and ICU stay [2]. However, general anesthesia was found to have less cardiac complications during vascular surgery when compared to regional anesthesia [3]. In a study by Yüceyar et.al, authors concluded that epidural anesthesia may help to attenuate lipid peroxidation initiated by ischemic-reperfusion injury more than general anesthesia can do alone [4]. Unfortunately, epidural anesthesia has its own limitations. Ischemia leads to a dysfunction in the

electron transport chain of the mitochondria, resulting in anerobic metabolism with decreased ATP and antioxidants production. During reperfusion, a gush of oxygen to the previously ischemic tissues leads to production of reactive oxygen species (ROS) due to a deficiency in antioxidants production during the ischemic phase. ROS causes oxidative stress that leads to endothelial dysfunction, DNA damage, and local inflammatory responses. ROS are injurious to structural lipids forming cell membranes and permeability barriers between cells in the form of the lipid bilayer in a process called lipid peroxidation that can produce remote organ injury [5]. Malondialdehyde (MDA), which is a secondary end-product of lipid peroxidation, is a well-known marker of oxidative stress in a lot of research activities [6]. Dexmedetomidine was proven to have antioxidant actions and organ protective properties during conditions involving IRI, such as myocardial protection [7], lungs [8], kidneys [9] and spinal cord protection [10]. It also decreases free radical release by inhibiting lipid peroxidation [11]. Considering the previous data, our research question was, "does adding dexmedetomidine infusion to general anesthesia lead to a reduction of reperfusion injury in a manner that is more, less, or the same as epidural anesthesia?" Our aim was to compare epidural anesthesia to general anesthesia with supplemental dexmedetomidine infusion regarding the reduction of the severity of IRI after revascularization in aorto-femoral bypass surgery by measuring the lipid peroxidation biomarker MDA, before and after revascularization and to compare the effect of both techniques on hemodynamics and post-operative complications.

METHODS

Ethics and registration: This is a comparative prospective single-blinded randomized clinical trial that was conducted in Zagazig University hospitals after obtaining institutional review board approval. This study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. A formal written informed consent to participate in the study was signed by all patients. This study was carried out during the period from September 2018 to October 2020 in Zagazig University hospitals.

Patients:52 out of 60 ASA II and III patients aging from 50-80 years old, both sexes, diagnosed as having diagnosed with critical limb ischemia (CLI) and scheduled for aorto-femoral bypass surgery were included in the study. ASA IV patients, patients with uncontrolled hypertension (systolic blood pressure >160 mm Hg or diastolic blood pressure >100 mm Hg), hepatic or renal impairment, patients taking vitamin C or vitamin E or any other medication that have an antioxidant action, and patients with a history of allergy to any of the used medications were excluded from the study.

Sample size calculation: Sample size was 26 patients in each group based on a study by Yuceyar et.al. with a 2-sided confidence interval of 98%, power of 80%, the ratio of sample size was 1% calculated using https://www.surveysystem.com/sscalc.htm. We decided to recruit 30 patients in each group to account for study dropouts and data loss.

Randomization and blinding:8 patients were excluded from the study for not meeting inclusion criteria. The remaining 52 patients were equally randomized using computer-generated random numbers to receive either epidural or general anesthesia. Before biochemical analysis for MDA serum level, the clinical pathology doctor was blinded by replacing the label containing the group name and patient number by a colored label having only numbers. The EP group was given red and green labels, and the GA group was given yellow and blue labels.

Anesthetic management: On arrival to OR a peripheral venous cannula was inserted for all patients and 5 ml of venous blood was drown into a plain tube. All patients were given 0.06 mg/kg of midazolam IV. ECG monitoring, pulse oximetry, and non-invasive blood pressure monitors were attached to all patients.

EP group: After sterilization of the back with povidone iodine, local anesthesia was given using 5 ml of 2% lidocaine infiltration. With an 18-gauge Tuohy needle, a 20-gauge epidural catheter was inserted at L2-3 or L3-4 level and advanced for 2–3cm into the epidural space. Correct placement of the catheter was tested by 3 ml lidocaine 1.5% and negative aspiration of blood or CSF, then patients received 1-2 ml/segment (according to height) of bupivacaine (0.5%), 5mg/ml, plus 20µg of fentanyl aiming to achieve an anesthetic dermatomal level of T4-T6, then maintenance infusion was done using infusion of bupivacaine (0.25%), 2.5 mg/mL, and 2µg/mL fentanyl at a rate of 8 mL/hr. until the end of surgery. Post-operative analgesia was maintained with bupivacaine (0.125%) 1.25 mg/mL, and 2µg/ml fentanyl at a rate of 8 mL/hr.

Ga group:Induction was done by fentanyl 1.5µg/kg, propofol 2 mg/kg titrated slowly to sleep, and cisatracurium 0.1mg/kg 2 minutes before intubation. Dexmedetomidine loading dose of 0.5µg started immediately after intubation for 10 minutes, then maintenance of infusion was done by 0.4µg/kg/hr. Maintenance of anesthesia was achieved by isoflurane 1.5%, and

cisatracurium infusion (2μg/kg/min) stopped 30 minutes before the end of surgery. After skin closure, muscle relaxation was reversed by 0.05mg/kg neostigmine plus 0.02mg/kg atropine, the oral cavity suctioned, and patients were extubated awake. Post-operative analgesia was provided by morphine 0.1mg/kg every 8 hrs. plus 1 gram of IV paracetamol every 8 hrs.

Management of intraoperative complications: Hypertension (MAP 20% more than basal value) was managed by incremental boluses of 50μg fentanyl or nitroglycerine infusion starting at a rate of 0.5μg/kg/min, then titrated to MAP that is within 20% of basal patients MAP measurements, hypotension (MAP 20% less than the basal value) was managed by 250ml of Ringer's solution increased if patient was fluid responsive, a 10 mg bolus of ephedrine or/and an infusion of norepinephrine at a rate of 0.05μg/kg/min as a starting dose increased if needed. Bradycardia (heart rate below 50 bpm) was managed by a bolus of atropine (30μg/kg). Tachycardia (heart rate above 90 bpm) was managed by 250ml of ringer's solution, increased if needed if the patient was expected to be hypovolemic, 50μg bolus doses of fentanyl.

Post-operative care: After the end of surgery Patients were transferred immediately to the ICU for post-operative care. Hypertension was treated with morphine 0.1mg/kg if pain was suspected or with nitroglycerine infusion if the patient wasn't in pain. Hypotension was treated with Ringer's solution 200-250ml boluses, which were increased if the patient was responsive, or norepinephrine 0.05μg/kg/min initial dose, then managed according to response. Tachycardia was treated with 0.1mg/kg of morphine if the patient was in pain, Ringer's solution 200-250ml if the patient was suspected to be hypovolemic. Bradycardia was treated with 30μg/kg of atropine. Post-operative shivering was managed by using blankets and worm fluid infusions; otherwise, pethidine 25mg increments was given if the previous measures were unsuccessful. Post-operative nausea or vomiting were treated with 1mg of granisetron.

Laboratory work: Measurement of basal MDA serum level then at 2, 5, and 24hrs. After revascularization using MDA ELISA kit. MDA serum level was checked using (Human Malondialdehyde ELISA Kit) provided by (Bioassay Technology Laboratory, www.bt-laboratory.com, 1008 Junjiang Inter, Bldg. 228 Ningguo Rd, Yangpu Dist, Shanghai, China).

Specimen collection: 5 ml of venous blood were taken from each patient before anesthesia and placed in a plane tube for measurement of MDA basal level. Samples were then labeled by the group name and patient number in the group. Samples were then left to clot, then centrifuged at 2000–3000 revolutions per minute (RPM) for 20 minutes to separate the serum. Serum was collected in aliquot tubes and stored at -80º C until all samples were collected. The process was repeated for all samples that were collected after 2hrs, 5hrs and 24hrs of revascularization. Before testing, all samples were brought to room temperature, centrifuged again, and the supernatant collected carefully.

Assay principle:Plates have been coated with human MDA antibody. MDA present in the sample is added and binds to antibodies coated on the wells. The biotinylated human MDA antibody is added and binds to MDA in the sample. The Streptavidin-HRP is added and binds to the biotinylated MDA antibody. After incubation, Streptavidin-HRP is washed away during the washing step. Substrate solution is then added, and color develops in proportion to the amount of human MDA. The reaction is terminated by the addition of an acidic stop solution, and absorbance is measured at 450 nm within 10 minutes.

Calculation of results: A standard curve was constructed by plotting the average optical density for each standard on the vertical (Y) axis against the concentration on the horizontal (X) axis, and a best fit curve was drawn through the points on the graph as shown in figure (1).

Study outcomes: Primary study outcome was the effect of both anesthetic techniques on serum MDA through comparison between the two groups and comparison in the same group at different times during the study.

Secondary study outcomes were hemodynamic variability during operation, including HR and MAP variability; intra-operative data, including duration of surgery from skin incision to skin closure; cross-clamping time from time of application to time of removal; estimated blood loss by measurement of blood in the surgical suction container; and visual estimation of the blood in the surgical sponges and laparotomy pads. A fully soaked surgical sponge was estimated to hold 10 ml of blood and a fully soaked laparotomy pad was estimated to hold 100–150 ml of blood (amount of given intravenous fluids and blood products); post-operative complications included hypertension (MAP more than 20% of baseline values), tachycardia (heart rate more than 95 bpm), hypotension (MAP less than 20% of baseline values), bradycardia (heart rate less than 50 bpm), hypoxia, shivering, nausea and vomiting.

Data collection: Patients' demographic data, including age, sex, ASA status, weight, height, BMI, smoking habit, and comorbidities, were

recorded before the study. MDA serum levels were measured for all patients before the study then 2hrs, 5hrs and 24hrs after revascularization. Intra-operative data of patients were recorded including the duration of surgery, duration of cross clamp application, blood loss, volume of PRBCs, FFP, crystalloids and colloids.

Hemodynamic variability, including HR and MAP, were recorded before starting the study (T0), 5 minutes after induction of GA or after reaching T4-T6 level of block (T1), : 15 minutes after induction or 15 minutes after reaching T4-T6 level of block (T2), just before clamping (T3), 5 minutes after clamping (T4), 15 minutes after clamping (T5), just before de-clamping (T6), 5 minutes after de-clamping (T7), 15 minutes after de-clamping (T8), at the end of surgery (T9), 15 minutes after arrival to ICU (T10).

Post-operative complications, including patients who had hypertension, tachycardia, hypotension, bradycardia, hypoxia, shivering, nausea, and vomiting, were recorded.

STATISTICAL ANALYSIS

Data collected throughout (history, basic clinical examination, laboratory investigations and outcome measures) was coded, entered, and analyzed using Microsoft Excel software. Data were then imported into the Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data, qualitative data represented as numbers and percentages, quantitative data represented by mean ± SD, the following tests were used to test differences for significance; difference and association of qualitative variables by Chi square test (X2). Differences between quantitative independent groups by t test. The P value was set at <0.05 for significant results and <0.001 for a highly significant result.

RESULTS

Table (1) shows the distribution of demographic data and comorbidities of the studied groups. No significant differences were found between the studied groups regarding demographic data or comorbidities. D.M was the main comorbidity among the study subjects.

Table (2) shows the results of MDA serum levels of the studied groups. Baseline MDA levels of both groups were comparable. At T1, MDA levels increased significantly in relation to baseline in both groups (both P* and P** < 0.001), MDA was significantly lower in the GA (4.12±0.49) group in comparison to the EP group (4.55±0.66); (P = 0.01). At T2, in the EP group, MDA decreased in relation to T1, but was still significantly higher than baseline (P* < 0.001); in the GA group, MDA decreased in relation to T1, and was insignificant in comparison to baseline (P** = 0.6) but was significantly lower than EP group values (P = 0.01). At T3, MDA was comparable in both groups in relation to each other and in relation to baseline values.Table (3) shows intra-operative data of patients. No significant differences were found regarding any of the intra-operative data recorded except for the volume of crystalloid infusion in the EP group (3284.61±492.09) which was significantly higher than the GA group (2719.23±519.24); (P < 0.001).

Table (4) and Figure (2) show hemodynamic variability of both groups. Baseline values of HR and MAP were comparable in both groups. At T1 and T2, HR values were significantly higher in GA group in relation to EP group; P was < 0.001 and 0.02 respectively. At T3-T8, HR values in GA group were significantly below EP group; the P value was < 0.001 at T3-T7 and equal to 0.02 at T8. HR values were comparable in both groups at T9 and T10. MAP values were comparable in both groups all over the recording times.

Table (5) shows the comparison of post-operative complications of the studied groups. More patients had post-operative hypertension in the GA group, and comparison was significant (P = 0.01). Patients who had post-operative tachycardia in the GA group were significantly more in comparison to EP group (P =0.04). Post-operative shivering was significantly less in GA group in comparison to EP group (P = 0.03). The comparison of the two groups in relation to post-operative hypotension, bradycardia, hypoxia, nausea, and vomiting were all insignificant.

Table 1: Distribution of demographic data and comorbidities

			Ep (n=26)	GA (n=26)	P
Age (years)			62.57±5.81	60.07±3.71	0.07
Weight (kg)			75.65±10.49	79.84±12.16	0.18
Height (cm)			172.69±7.27	173.23±6.69	0.78
BMI			26.11±5.59	26.54±4.32	0.75
Sex	**Female**	N	4	7	
		%	15.40%	26.90%	
	Male	N	22	19	0.18
		%	84.60%	73.10%	
ASA	**ASA II**	N	16	14	
		%	61.50%	53.80%	
	ASA III	N	10	12	0.26
		%	38.50%	46.20%	
Smoking	**No**	N	8	12	
		%	30.70%	46.20%	0.11
	Yes	N	18	14	
		%	69.20%	53.80%	
Comorbidities	**DM**	N	6	4	0.31
		%	23.10%	15.40%	
	DM HTN	N	2	5	0.18
		%	7.70%	19.20%	
	DM IHD	N	4	3	0.56
		%	15.40%	11.50%	
	DM IHD HTN	N	5	7	0.44
		%	19.20%	26.90%	
	HTN	N	4	2	0.16
		%	15.40%	7.70%	
	HTN IHD	N	2	3	0.56
		%	7.70%	11.50%	
	IHD	N	3	2	0.48
		%	11.50%	7.70%	

BMI: body mass index. **ASA**: American society of Anesthesiologists' classification**. DM:** diabetes mellitus**. HTN:** hypertension**. IHD:** ischemic heart disease**.**

Table 2: MDA serum level measurements in different time points during the study.

Time	EP	GA	P	P*	P**
	MDA (nmol/ml)	MDA (nmol/ml)			
T0	3.54±3.2	3.52±2.6	0.83		
T1	4.55±0.66	4.12±0.49	0.01*	<0.001*	<0.001*
T2	3.87±0.27	3.64±0.42	0.02*	<0.001*	0.613
T3	3.42±0.42	3.39±0.22	0.73	0.27	0.06

T0: patient arrival to OR. **T1:** 2 hours after revascularization**. T2:** 5 hours after revascularization. **T3:** 24 hours after revascularization. P stands for comparison of the two groups at a specified time. P* stands for comparison within the EP group between MDA serum level at a specific time and the baseline. P** stands for comparison within the GA group between the MDA serum level at a specific time and the baseline.

Table 3: Intraoperative data of patients.

Intraoperative data of patients	EP (n=26)	GA (n=26)	p
Duration of surgery (min)	238.3±11.03	236.82±10.85	0.65
Cross clamp duration (min)	67±8.5	67.3±6.75	0.95
Blood loss (ml)	1050±210.23	1088±258.19	0.55

Intraoperative data of patients	EP (n=26)	GA (n=26)	p
Crystalloids (ml)	3284.61±492.09	2719.23±519.24	<0.001*
Colloids (ml)	603.48±188.63	676.92±208.43	0.19
PRBCs (ml)	395±97.82	426.92±122.66	0.3
FFP (ml)	294.61±75.97	245±86.08	0.84

PRBCs: packed red blood cells. **FFP:** fresh frozen plasma.

Table 4: Heart rate and mean arterial blood pressure variability.

	HR			MAP		
Time	**EP**	**GA**	**p**	**EP**	**GA**	**p**
T0	79.2±8	77.2±6.4	0.83	96.6±10.3	97.1±9.2	0.99
T1	70.15±7.2	82±8.1	<0.001*	90.2±8.5	102.5±8.3	0.69
T2	70.76±6.4	77.15±8.3	0.02*	93.1±11.2	95.1±10.7	0.95
T3	76.19±5.1	67.8±7.4	<0.001*	88.2±8.5	87.3±10.2	0.96
T4	80.88±8.2	69.5±8.2	<0.001*	101.8±6.8	94.4±9.6	0.89
T5	83.2±7.5	72.7±6.8	<0.001*	102.9±7.8	96.7±7.5	0.84
T6	82.5±6.8	72.73±7.4	<0.001*	102.2±8.4	95.2±10.2	0.82
T7	78.15±7.4	69.26±8.5	<0.001*	79.2±8.6	82.2±9.4	0.9
T8	70.07±6.7	65.42±9.1	0.02*	81.2±10.2	82.1±7.9	0.97
T9	70.42±5.7	66.46±10.2	0.06	98.4±9.5	96.2±8.7	0.92
T10	71.38±7.8	68.07±9.5	0.09	97.2±8.4	95.4±7.6	0.93

T0: heart rate before starting the study**, T1:** 5 minutes after induction of GA or after reaching T4-T6 level of block**, T2:** 15 minutes after induction or 15 minutes after reaching T4-T6 level of block**, T3:** just before clamping**, T4:** 5 minutes after clamping, **T5:** 15 minutes after clamping, **T6:** just before de-clamping, **T7:** 5 minutes after de-clamping, **T8:** 15 minutes after de-clamping, **T9:** at the end of surgery and **T10:** 15 minutes after arrival to ICU.

Table 5: post-operative complications.

Post-operative complications	EP (26)	GA (26)	P
Hypertension	**4 (15.4%)**	**9 (34.6%)**	**0.01***
Hypotension	**7 (26.9%)**	**4 (15.4%)**	**0.25**
Tachycardia	**6 (23.1%)**	**11 (42.3%)**	**0.04***
Bradycardia	**3 (11.5%)**	**1 (3.8%)**	**0.24**
Hypoxia	**6 (23.1%)**	**4 (15.4%)**	**0.41**
Nausea & Vomiting	**3 (11.5%)**	**2 (7.6%)**	**0.56**
Shivering	**11 (42.3%)**	**4 (15.4%)**	**0.03***

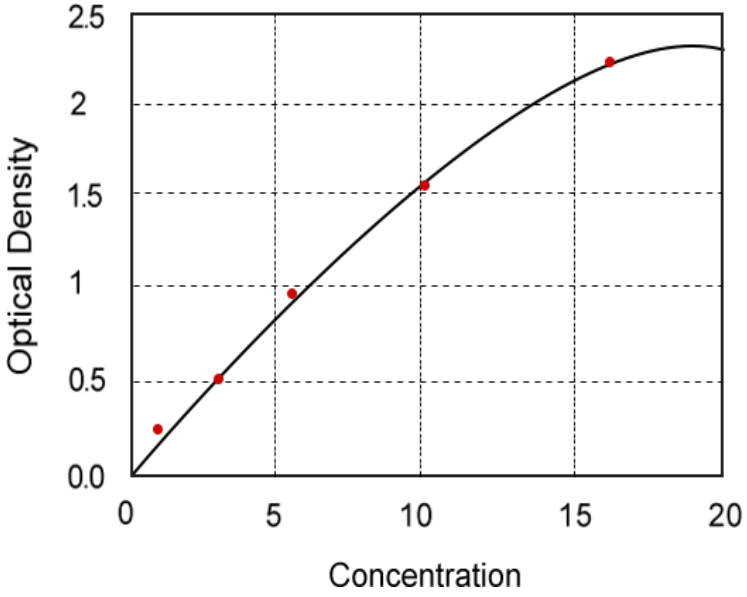

Figure 1: The standard curve for calculation of MDA.

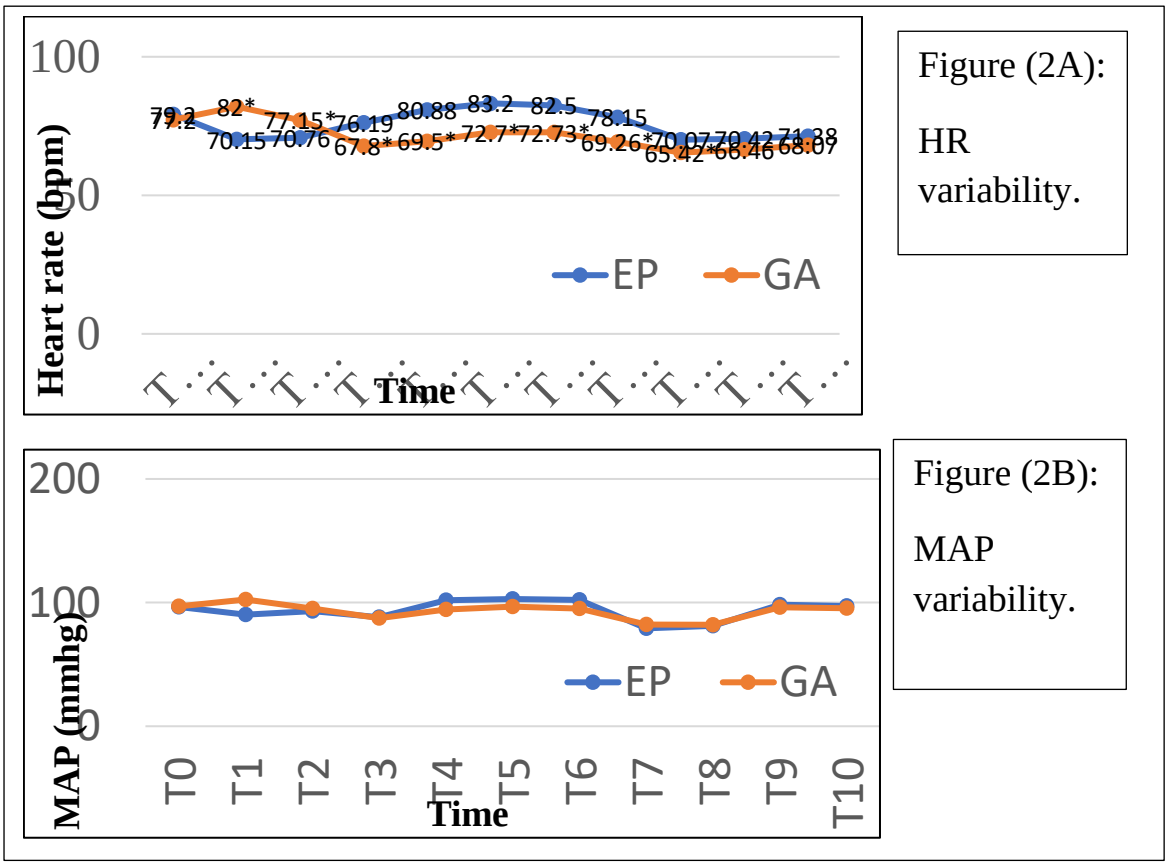

Figure 2: Hemodynamic variability recorded at different time points during the study.

DISCUSSION

Our main concern was to compare the effect of general anesthesia supplemented with dexmedetomidine with the effect of epidural anesthesia on IRI during aorto-femoral bypass surgery through measurement of MDA serum levels, also to compare the effect of both techniques on hemodynamic fluctuation and post-operative complications.The comparison of epidural anesthesia as a sole anesthetic technique with general anesthesia supplemented with dexmedetomidine infusion has been a totally new idea that wasn't explored before, especially in the field of aortic reconstructive surgery, and the measurement of MDA as a marker for oxidative stress and IRI provides a strong point of comparison being a specific marker for IRI. However, this study was limited by the restricted number of cases and the need for special kits to measure MDA. Our patients had comparable

baseline serum MDA that were 3.54±3.2 and 3.52±2.6 nmol/ml for the EP group and GA group, respectively, these results were consistent with the results of Bhutia et.al. [12] and the results of Turker and Erisir [13]. After 2hrs of revascularization, MDA increased significantly in both groups in relation to baseline, indicating the occurrence of lipid peroxidation, but were still lower than MDA levels recorded for the general anesthesia group in the study of Yüceyar et.al. [4]. GA group had a significantly lower MDA levels in comparison to the EP group, suggesting a lower severity of oxidative injury in the GA group after 2 hrs. of revascularization. After 5 hrs. of revascularization, MDA in the GA group was significantly below the EP group, which was consistent with the results of Kundra et.al. [14]. After 24 hrs. of revascularization, MDA was comparable between the two groups.

MDA serum level has been used to assess the severity of reperfusion injury in a study by Papalambros et.al. who measured MDA during abdominal aortic reconstructive surgery for aneurysm and found that an increased MDA level is associated with the duration of cross clamping and a worse outcome [15]. In another study by Mahmoud et.al. MDA was measured to assess the severity of reperfusion injury after de-clamping in surgery for an abdominal aneurysm and results were comparable to our results [16].

This study also showed that the EP group had significantly more crystalloid infusion than the GA group. These results were consistent with the results of Todd Sitzman et.al [17], Soliman and Zohry [18], and Owczuk et.al [19]. In a study by Renghi et.al [20], patients in the combined general epidural group received the same volume of crystalloid infusion as the general anesthesia only group. However, their study was on minimally invasive aortic surgery with less blood loss and duration of surgery [20]. Regarding intra-operative fluctuation of HR, the baseline HR values were equal in both groups. Otherwise, heart rate in the GA group was significantly higher than in the EP group after induction and tell 15 minutes after induction, and this could be explained by the stress response to laryngoscopy and intubation especially, we started dexmedetomidine infusion after intubation. After that, the heart rate values of the GA group were significantly lower than the heart rate values of `the EP group through the remaining time of the operation. Our results were consistent with the results of Soliman and Zohry [18].

In this study, the two groups were comparable considering MAP measurements during surgery. These results are consistent with the results of Panaretou et.al. as they didn't find significant differences between general and combined general epidural techniques regarding MAP fluctuation during infra-renal aortic surgery [21]. In the study of Soliman and Zohary, the combined general epidural group with dexmedetomidine infusion provided more hemodynamic stability than the combined general epidural without dexmedetomidine infusion [18].Concerning post-operative complications, patients who had post-operative hypertension and tachycardia in the GA were significantly more than the EP group patients who had post-operative hypertension and tachycardia. In a study by Salah et.al., critically ill patients who had dexmedetomidine infusion had a higher incidence of hypertension and tachycardia after discontinuation, hypertensive patients had the highest incidence of experiencing this effect [22], their findings can explain our results concerning post-operative hypertension and tachycardia.These findings are also consistent with the findings of Vnn et.al [23].

Post-operative shivering was significantly less in the GA group than in the EP group. In a study by Kasem et.al., dexmedetomidine was superior to magnesium sulphate and pethidine in controlling intra- and post-operative shivering [24]. In a meta-analysis conducted by Liu et.al. dexmedetomidine was addressed as superior to other agents in the prevention of post-operative shivering if started two hours before the end of surgery [25].

CONCLUSIONS

According to the results of the present study, supplemental dexmedetomidine infusion with general anesthesia for aorto-femoral bypass surgery can attenuate IRI more than epidural anesthesia after 2hrs. and 5hrs of reperfusion, as evidenced by lower MDA levels, and is comparable after 24 hrs. of reperfusion. However, in the post-operative period, discontinuation of dexmedetomidine may produce more hypertension and tachycardia but still have a prophylactic effect against post-operative shivering.

Recommendations We recommend that dexmedetomidine be part of the anesthetic technique for vascular surgery involving IRI, either as a supplement to general anesthesia or as a sedative during epidural anesthesia.

Conflict of interest None

Financial disclosures None

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