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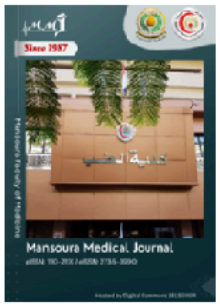

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Myocardial and renal protective effects of Dexmedetomidine vs Magnesium sulphate in patients undergoing elective open abdominal aortic surgery

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ORIGINAL STUDY

Myocardial and Renal Protective Effects of Dexmedetomidine Versus Magnesium Sulfate in Patients Undergoing Elective Open Abdominal Aortic Surgery

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Abstract

Background: **After abdominal aortic aneurysm surgery, the probability of postoperative myocardial infarction is 7 %, while the probability of postoperative cardiac issues without signs of ischemic damage is 36 %.**

Aim: **The goal of the research was to assess the perioperative myocardial protective impact of dexmedetomidine and magnesium sulfate in high-risk studied cases undergoing aortic vascular surgery.**

Patients and methods: **This randomized, double-blinded study was conducted at the Cardiothoracic and Vascular Surgery Center, Mansoura University from May 2023 to October 2023 after approval from the Institutional Review Board of Faculty of Medicine, Mansoura University. Written informed consent was obtained from all studied cases.**

Results: **There were no variations observed among the studied groups as regards cTnI and creatine kinase-MB (CKMB), and there was no variation among the studied groups as regards creatinine clearance (CC) and urine output (UOP).**

Conclusion: **Using dexmedetomidine throughout cardiac surgery protected the heart and the kidneys as evidenced by reduced levels of myocardial-specific and kidney-specific proteins in the urine and higher creatinine clearance.**

Keywords: Abdominal aortic surgery, Dexmedetomidine, Magnesium sulfate, Myocardial, Renal

1. Introduction

As concomitant disorders such as coronary artery disease, hypertension, and diabetes mellitus are frequently present in studied cases undergoing vascular surgery, these individuals are typically considered high-risk cases. Significant homeostatic disturbance and the potential for circulatory decompensation can result from aortic cross-clamping and decamping (Robe et al., 2000).

After abdominal aortic aneurysm surgery, the risk of postoperative myocardial infarction is 7 %; however, 36 % of postoperative cardiac problems, such as pulmonary edema, arrhythmias, or reduced cardiac output, have no signs of ischemic damage (Gilling-Smith et al., 1995). In addition, cardiac ischemia and infrarenal aortic cross-clamping go hand in hand (Svensson et al., 1993).

Previous studies have discovered that elective surgical repair of aortic aneurysms led to increased cardiac troponin I (Andrews et al., 2001). Following major vascular surgery, subclinical myocardial injury is frequent, can be identified by a rise in cardiac troponin levels, which is linked to a higher mortality rate (Haggart et al., 2001).

Dexmedetomidine is a highly selective α-2agonist that causes analgesia without respiratory depression and promotes anxiolysis (Barbagallo et al., 2006). It lowers plasma norepinephrine levels (Bhana et al., 2000), giving individuals with coronary risk factors perioperative cardiac protection, reducing stress reaction to surgery and critical care

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procedures (Talke et al., 1997), maintaining a balance between oxygen supply and demand by lowering heart rate and blood pressure (Biccard et al., 2008).

Magnesium is crucial for maintaining heart rhythm (Toraman et al., 2001), minimizing damage to coronary microvasculature caused by reperfusion, while maintaining coronary microvascular function (Yamamuro et al., 2002). Particularly in studied cases with ischemic heart disease and left ventricular hypertrophy, hypomagnesemia may cause cardiac arrhythmias (Polderman and Girbes, 2004).

Dexmedetomidine and magnesium sulfate's perioperative myocardial protective effects in high-risk studied cases following aortic vascular surgery were thus evaluated in the current research.

2. Patients and methods

This randomized, double-blinded research was conducted at the Cardiothoracic and Vascular Surgery Center, Mansoura University from May 2023 to October 2023 after approval from the Institutional Review Board of Faculty of Medicine, Mansoura University after obtaining a written informed consent from all participants.

2.1. Publication ethical statement

All patients gave their informed consent for inclusion before they participated in this study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by IRB (MS. R.23.03.2131 at 31/03/2023).

2.2. Inclusion criteria

American Society of Anesthesiology physical status III–IV.

2.3. Exclusion criteria

Exclusion criteria included individuals with acute myocardial infarction, congestive heart failure, heart block, obese people, or those in emergency situations.

2.4. Sample size

Using power analysis, the sample size was estimated.

2.5. Randomization

Eligible 84 studied cases were randomly allocated using computer-generated tables, and group assignments were concealed in sequentially numbered sealed opaque envelopes, dividing them into two equal groups: group D (dexmedetomidine group) ($n = 42$), group M (magnesium sulfate group) ($n = 42$). In group D, the studied cases will receive a loading dose of 1 μg/kg dexmedetomidine over 20 min before induction, followed by a maintenance infusion of 0.3 μg/kg/h till the end of procedure.

In group M, the studied cases received magnesium sulfate infusion at the rate of 15 mg/kg/h. Infusion started 20 min before induction, till the end of procedure.

2.6. Anesthetic technique

Before surgery, all studied cases underwent thorough clinical examination, history collection, baseline laboratory investigations (complete blood count, international normalized ratio, liver function, and kidney function tests), baseline serum magnesium (mg/dl), and ECG, and echocardiogram. For the purpose of evaluating valve function, contractility, or existence of aberrant regional wall motion, transthoracic echocardiography was performed on each studied case. All preoperative drugs had been administered consistently. Preoperative care for the studied cases taking anticoagulants was provided by a cardiologist.

A radial artery cannula and a central venous line were implanted for each studied case while under local anesthesia. Before inducing anesthesia, an epidural catheter was placed through the L3–L4 intervertebral region.

After preoxygenation with 100%oxygen, anesthesia was induced gently with intravenous fentanyl (1–2 μg/kg), propofol (1–2 mg/kg), and atracurium (0.5 mg/kg). After tracheal intubation and initiation of mechanical ventilation, anesthesia was maintained using isoflurane (1–1.5 %), fentanyl infusion (1–3 μg/kg/h), atracurium (0.5 mg/kg/h), and oxygen: air (50 : 50). Bolus doses of fentanyl, an increase in isoflurane concentration, or the addition of nitroglycerin infusion were used to treat hypertension during clamping. Fluids, bolus ephedrine doses, lowering isoflurane concentration, and, if necessary, norepinephrine were used to manage hypotension.

Bradycardia was managed with bolus doses of atropine (30 μg/kg). Cases undergoing abdominal aortic surgery above the origin of the renal artery will receive crystalloids (500–1000 ml), mannitol

20 % (100 ml), and furosemide (40 mg) over 30 min before clamping for renal protection.

At the end of procedure and after emergence from anesthesia, the studied cases was transferred to the ICU for close monitoring.

In cases where electrocardiogram showed ischemia abnormalities and troponin I levels were elevated, transthoracic echocardiography was performed after surgery.

2.7. Data collection

Hemodynamic monitoring comprising heart rate, mean arterial blood pressure, oxygen saturation, hemodynamic values was serially collected at following times: at baseline, after induction of anesthesia, every 10 min throughout the procedure, at the end of surgery, and every 2 h in the ICU for 48 h. Arterial blood gases were measured at baseline, before clamping, before and after declamping and at 12th, 24th, and 48th hours postoperatively.

Total intraoperative fentanyl consumption, intraoperative muscle relaxant consumption intraoperatively, total postoperative analgesic consumption within 24 h, central venous pressure at 6 h in the postoperative period, urinary output in the first 24 h postoperatively, and cardiac enzyme troponin I, serum creatinine were measured before the administration of research medication, and at12th, 24th, and 48th hours postoperatively.

Creatinine clearance was measured before the administration of study medication at 12th, 24th, and 48th postoperatively and the urine output was measured 24th and 48th postoperatively. Inflammatory markers such as tumor necrosis factor gamma (TNF-γ), interleukin (IL)-B, and cortisol were measured before the administration of study medication at 12th, 24th, and 48th hours postoperatively.

2.8. Statistical analysis

When appropriate, data were statistically reported using the mean, SD, or frequencies (number of cases). Student's *t* test for independent samples was used to compare numerical variables among research groups. Paired *t* test was used to compare numerical variables within groups. Using χ^2 test, categorical data were compared. When the expected frequency was less than five, Fisher's exact test was used instead. *P* value less than 0.05 was regarded statistically significant. SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, Illinois, USA), version 15, for Microsoft Windows was used to do all statistical calculations.

Table 1 finds that there was no significant variation among the studied groups as regards history data.

Table 2 shows that there was high statistically significant variation among studied groups as regards morphine (Figs. 1 and 2).

Table 3 shows that there was no statistically significant variation among studied groups as regards CC (Fig. 3).

Table 4 shows that there was no statistical difference among studied groups as regards UOP (Figs. 4 and 5).

Table 5 shows that there was statistically significant variation among studied groups as regards IL-1B at 12, 24, and 48 h (Fig. 6).

Table 1. Comparison among studied cases according to history data.

	Group D ($N = 37$)	Group M ($N = 37$)	Test of significance	*P*
	Age			
Range	41–68	41–68	$t = 0.312$	0.756
Mean ± SD	53.16 ± 8.66	52.54 ± 8.48		
Sex	*n* (%)	*n* (%)		
Female	15 (40.5)	18 (48.6)	$\chi^2 = 0.492$	0.483
Male	22 (59.5)	19 (51.4)		
	BMI			
Range	21.77–29.72	21.43–29.63	$t = 0.483$	0.631
Mean ± SD	25.65 ± 2.44	25.94 ± 2.66		
	ASA			
I	7 (18.9)	8 (21.6)	$\chi^2 = 0.0$	1.0
II	23 (62.2)	25 (67.6)		
III	7 (18.9)	4 (10.8)		
	Creatinine (mg/dl)			
Range	0.52–1.04	0.53–1.07	$t = 0.851$	0.397
Mean ± SD	0.78 ± 0.13	0.76 ± 0.13		

χ^2, χ^2 test; *t*, Student's *t* test.
P, *P* value to compare among studied groups.
*Statistically significant at *P* value less than or equal to 0.05.

Table 2. Comparison of cases according to operation data.

	Group D ($N = 37$)	Group M ($N = 37$)	Test of significance	P
Duration				
Range	120–255	120–255	$t = 0.872$	0.386
Mean ± SD	181.62 ± 39.18	189.73 ± 40.81		
Atracurium				
Range	10–30	10–35	$U = 574.0$	0.215
Median (IQR)	15 (15–25)	20 (15–25)		
Fentanyl				
Range	0–90	0–90	$U = 612.5$	0.426
Median (IQR)	40 (30–70)	40 (0–70)		
Morphine				
Range	0–12	6–15	$U = 317.5$	<0.001[a]
Median (IQR)	6 (3–9)	9 (9–12)		

IQR, interquartile range; *t*, Student's *t* test; *U*, Mann–Whitney test.
P, *P* value to compare among studied groups.
[a] Statistically significant at *P* value less than or equal to 0.05.

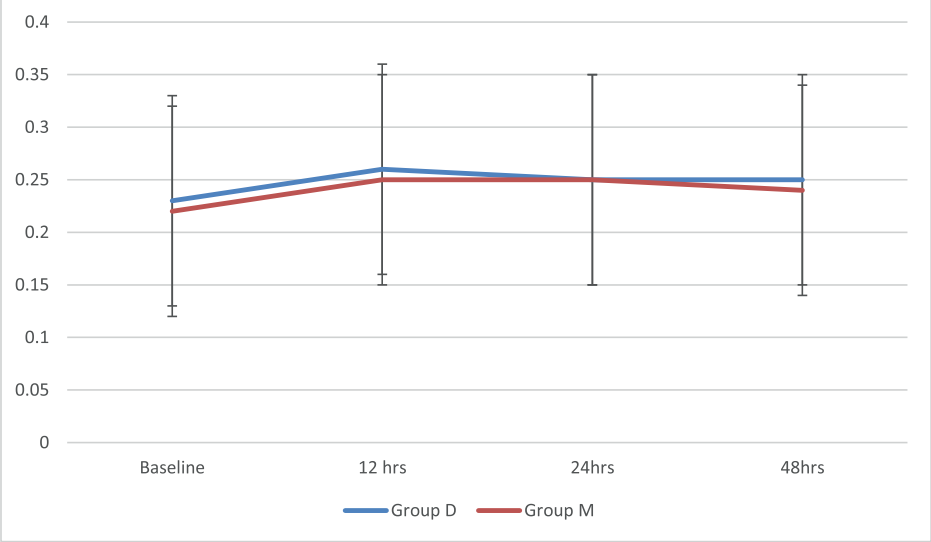

Fig. 1. Comparison of cases according to cTnI.

Table 6 shows that there was statistically significant variation among studied groups as regards cortisol at 12 h (Fig. 7).

3. Discussion

In this study, we found that there had been no variation among studied groups as regards history data.

Ji et al. (2013a) found that the distributions of age (>65 years), sex (male), BMI, race (nonwhite), smoking, last creatinine level, dialysis, and the proportion of studied cases with chronic lung disease, cerebrovascular disease, peripheral vascular disease, diabetes, hypertension, and chronic kidney disease (CKD) were similar among groups.

Leino et al. (2011) noted variations among groups regarding concurrent and preoperative cardiac medicines, baseline laboratory data, length of anesthesia throughout CABG, and time to extubation or duration of study drug infusion. In this study, we illustrated that there had been high variation among studied groups as regards the use of morphine.

Makhni et al. (2017) found that when compared with the magnesium group, the group receiving intrathecal dexmedetomidine experienced significant delay in time until the first rescue analgesia, and both groups experienced decreased mean total dose and frequency of analgesics, although the dexmedetomidine group experienced a noticeably greater decrease. Similar results are noted by Mahendru et al. (2013), Gupta et al. (2011), and Al-Mustafa et al. (2009).

We discovered that there had been no variation among analyzed groups in the present research with reference to cTnI and CKMB.

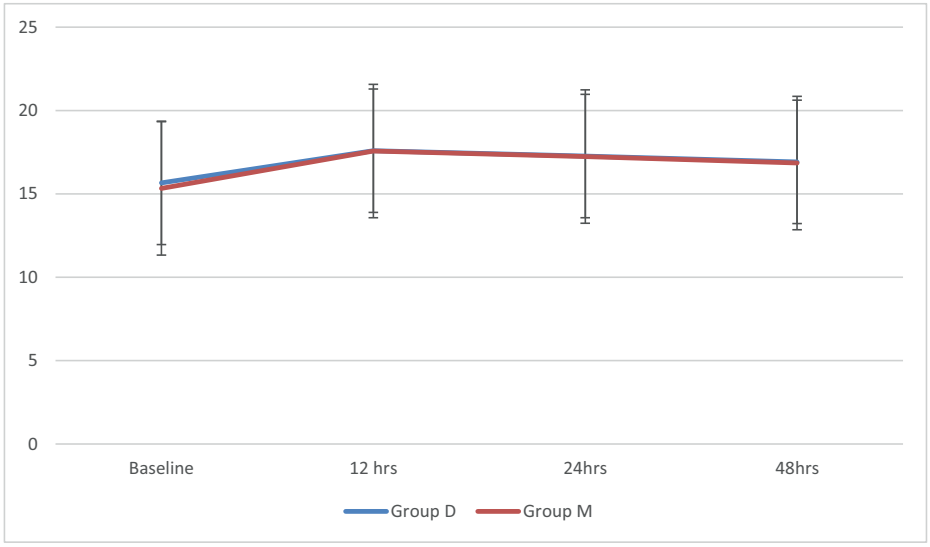

Fig. 2. Comparison of cases according to CKMB.

Table 3. Comparison of cases according to CC.

	Group D ($N = 37$)	Group M ($N = 37$)	Test of significance	P
Baseline				
Range	74.82–150.2	80.29–154.13	$t = 0.642$	0.523
Mean ± SD	112.41 ± 20.29	115.32 ± 18.65		
12 h				
Range	74.32–144.5	79.22–147.86	$t = 0.900$	0.371
Mean ± SD	109.63 ± 19.81	113.56 ± 17.69		
24 h				
Range	74.07–144.5	78.68–144.78	$t = 1.023$	0.310
Mean ± SD	108.24 ± 19.81	112.68 ± 17.44		
48 h				
Range	74.82–151.7	79.49–157.21	$t = 0.651$	0.517
Mean ± SD	112.69 ± 20.38	115.64 ± 18.57		

t, Student's *t* test.
P, *P* value to compare among studied groups.
*Statistically significant at *P* value less than or equal to 0.05.

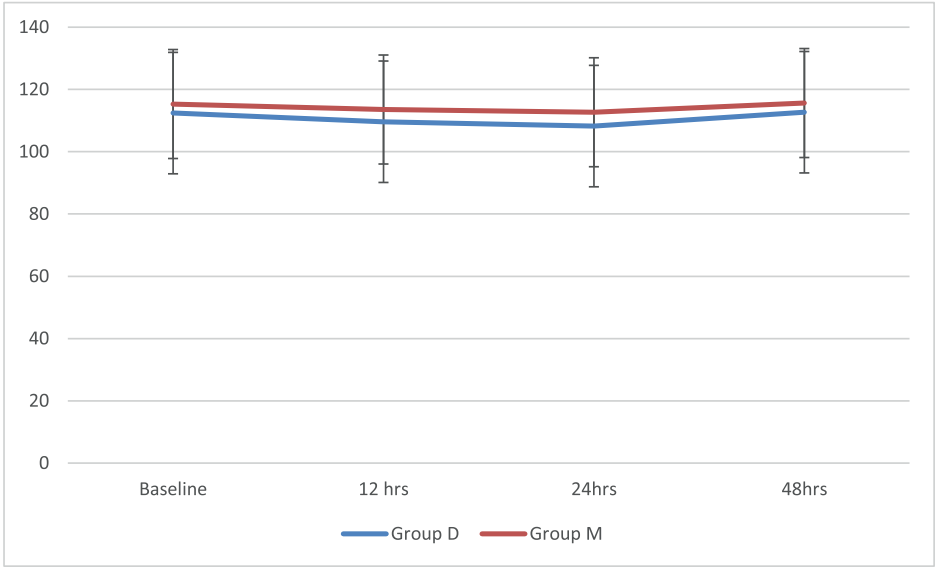

Fig. 3. Comparison of cases according to CC.

Table 4. Comparison of cases according to UOP.

	Group D ($N = 37$)	Group M ($N = 37$)	Test of significance	P
24 h				
Range	70–110	70–110	$t = 0.930$	0.356
Mean ± SD	90.54 ± 12.52	87.97 ± 11.21		
48 h				
Range	70–105	70–105	$t = 0.846$	0.400
Mean ± SD	87.97 ± 10.37	90.14 ± 11.58		

t, Student's *t* test.
P, *P* value to compare studied groups.
*Statistically significant at *P* value less than or equal to 0.05.

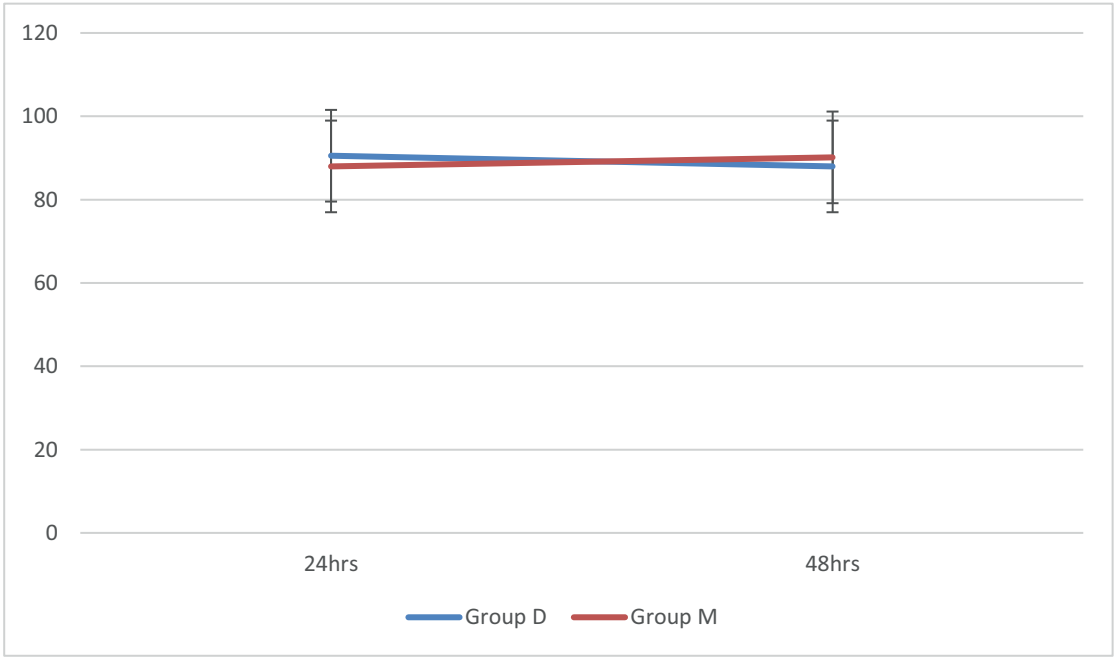

Fig. 4. Comparison among cases according to UOP.

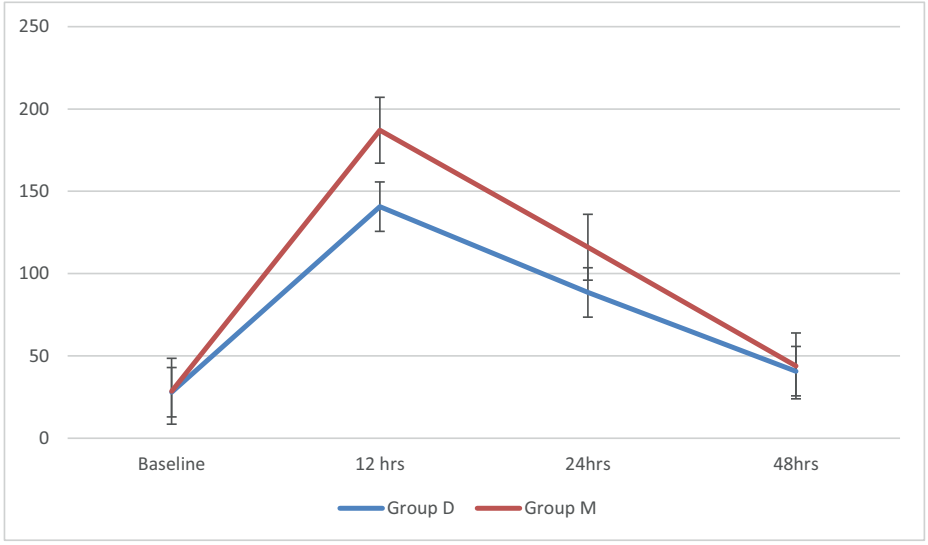

Fig. 5. Comparison of cases according to TNF. TNF, tumor necrosis factor.

Table 5. Comparison of cases according to interleukin-1B.

	Group D ($N = 37$)	Group M ($N = 37$)	Test of significance	P
Baseline				
Range	30–55	30–54.6	$t = 0.639$	0.674
Mean ± SD	42.96 ± 7.8	44.07 ± 7.19		
12 h				
Range	75.5–301.4	126–338.8	$t = 5.127$	<0.001[a]
Mean ± SD	181.08 ± 56.81	248.45 ± 56.24		
24 h				
Range	55.1–207.7	91.4–247.7	$t = 3.583$	0.001[a]
Mean ± SD	121.38 ± 38.4	152.96 ± 37.4		
48 h				
Range	34.3–84.9	34.6–107.5	$t = 3.038$	0.003[a]
Mean ± SD	53.33 ± 12.97	64.91 ± 19.21		

t, Student's *t* test.
P, *P* value to compare the studied groups.
[a] Statistically significant at *P* value less than or equal to 0.05.

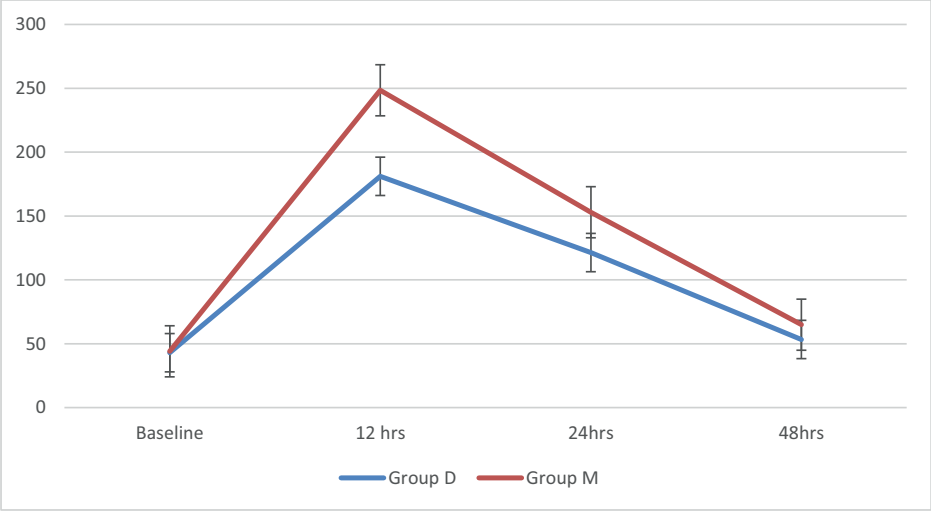

Fig. 6. Comparison of cases according to IL-1B. IL-1B, interleukin-1B.

Ammar et al. (2016) observed that except for the 48 h postoperatively (T5), when concentrations were comparable and close to baseline values in both groups, those in the dexmedetomidine group showed lower levels of myocardial-specific proteins (cTn-I, CKMB) than those in the control group.

According to a retrospective research conducted on 724 studied cases undergoing coronary artery

Table 6. Comparison of cases according to cortisol.

	Group D ($N = 37$)	Group M ($N = 37$)	Test of significance	P
Baseline				
Range	203.7–348.8	202.8–353	$t = 0.718$	0.475
Mean ± SD	284.49 ± 39.76	276.68 ± 52.94		
12 h				
Range	266.8–508.7	298–545.3	$t = 2.498$	0.015[a]
Mean ± SD	390.29 ± 56.63	431.31 ± 82.28		
24 h				
Range	236.2–449.8	258.3–465.5	$t = 1.580$	0.118
Mean ± SD	342.24 ± 50.27	364.28 ± 68.35		
48 h				
Range	205.1–364.5	214.4–368.1	$t = 0.429$	0.669
Mean ± SD	296.31 ± 41.27	291.58 ± 52.77		

t, Student's *t* test.
P, *P* value to compare studied groups.
[a] Statistically significant at *P* value less than or equal to 0.05.

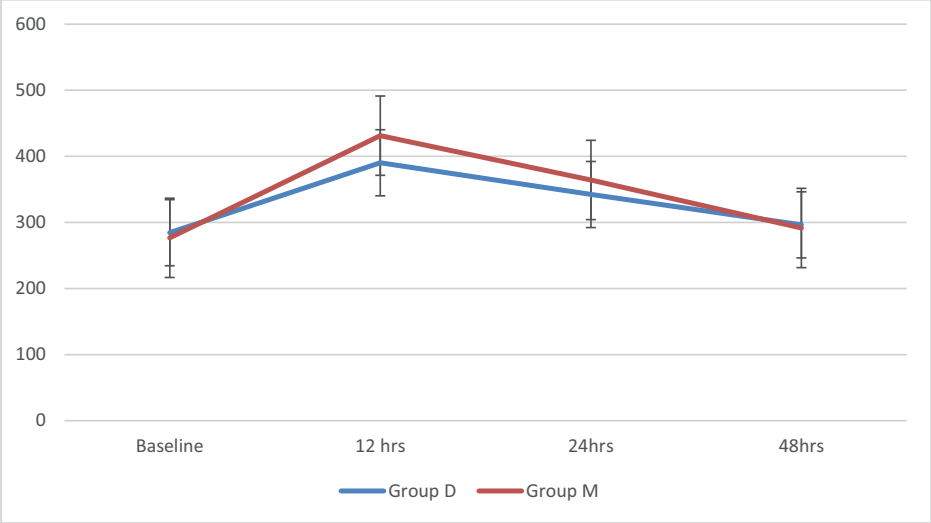

Fig. 7. Comparison of cases according to cortisol.

bypass grafting surgery, postoperative dexmedetomidine infusion that began after CPB and continued for less than 24 h was linked to better cardiac results as shown by better in-hospital, 30-day, and 1-year survival rates (Ji et al., 2014).

Dexmedetomidine demonstrated a positive impact on postoperative in-hospital and 1-year mortality as well as the incidence of postoperative complications (perioperative myocardial infarction, heart block, or cardiac arrest), according to the results of another retrospective trial that looked at the effects of perioperative dexmedetomidine infusion on 1134 studied cases undergoing CABG surgery and CABG surgery plus valvular or other procedures (Ji et al., 2013b).

A meta-analysis of randomized, controlled trials included 840 cases who underwent noncardiac surgery. All-cause mortality [odds ratio (OR): 0.27; 95 % confidence interval (CI): 0.01−7.13, $P = 0.44$), myocardial ischemia (OR: 0.65, 95 % CI: 0.26−1.63, $P = 0.36$), and nonfatal myocardial infarction (OR: 0.26, 95 % CI: 0.04−1.60, $P = 0.14$) were all linked to better cardiac results after dexmedetomidine (Biccard et al., 2008).

It is widely recognized that cardiac procedures cause stimulation of the sympathetic nervous system and systemic inflammatory response, both of which have potential to cause damage to most body organs, such as the kidneys and the heart. Anti-inflammatory actions of dexmedetomidine and its ability to stabilize the sympathetic nervous system can influence the common pathway that causes these injuries (Hauber et al., 2015).

In this study, we found that regarding CC and UOP, there had been no variation among tested groups.

Also, Ammar et al. (2016) observed that at day 1 following surgery, creatinine clearance significantly rose in both groups, but it had been much higher in the dexmedetomidine group. At days 4 and 7, nevertheless, it nearly reached baseline levels in both groups.

The infusion of dexmedetomidine throughout the surgery and for 4 h after surgery generated a mean increase of 74 % in urine output ($P < 0.001$) in the studied cases who were scheduled for CABG surgery and had normal renal function. Throughout the study period (0−24−48 h), perioperative creatinine clearance increased in both groups, with significant time impact ($P < 0.001$), but there were no significant group variations ($P = 0.93$). In the dexmedetomidine group, the mean urine output increased from 1408 ± 623 ml before surgery to 5599 ± 1386 ml throughout the 24 h after catheter installation, and from 1314 ± 487 to 4497 ± 840 ml in the placebo group ($P < 0.001$ among groups) (Leino et al., 2011).

Dexmedetomidine is thought to have diuretic action through sympatholysis-mediated suppression of sodium reabsorption in renal tubular cells by alpha-2 adrenergic impact, which must be noted is a positive impact, even though it does not necessarily show good effect regarding renal function (Rouch et al., 1997).

The effect of post-bypass dexmedetomidine on probable acute renal injury in individuals having cardiac surgery was examined in a retrospective trial. The incidence of total renal damage was significantly reduced by post-bypass dexmedetomidine (26.1 vs. 33.75 %; adjusted OR: 0.7033; 95 % CI: 0.540−0.916; $P = 0.0089$). In addition, it resulted in fewer complications and 30-day fatalities (Ji et al., 2013a).

They conducted histopathologic analysis by Kocoglu et al. (2009) to evaluate dexmedetomidine's

impact on rat renal I/R damage. The authors concluded that dexmedetomidine is useful in enhancing the tolerance of kidneys against I/R injury because it reduced histopathologic abnormalities linked to renal I/R injury.

This research showed high variations among the studied groups as regards TNF at 12 and 24 h and IL-1B at 12, 24, and 48 h.

Ammar et al. (2016) observed a considerable increase in TNF-α and IL-1β levels in both groups at all stages following the start of surgery; however, these levels were lower in the dexmedetomidine group at all these points.

In this study, we demonstrated that there were statistical variations among the studied groups as regards cortisol at 12 h.

Leino et al. (2011) found that plasma norepinephrine and cortisol concentrations had been smaller in dexmedetomidine-treated studied cases ($P < 0.001$).

Furthermore, Ammar et al. (2016) found that following the start of surgery, plasma norepinephrine and cortisol levels increased at various time points in both groups. However, these levels were lower in the dexmedetomidine group. At T5, norepinephrine levels in both groups were comparable but remained higher than baseline levels, while cortisol levels in both groups had almost returned to normal levels.

3.1. Conclusion

Using dexmedetomidine throughout cardiac surgery protected the heart and kidneys, evidenced by reduced levels of myocardial-specific and kidney-specific proteins in the urine and higher creatinine clearance. It might improve results for those who already have cardiac or renal impairment.

Conflicts of interest

There are no conflicts of interest.

Acknowledgements

The author declare herby that the study did not receive any form of financial support but as the study was done in vascular surgery center Faculty of medicine and all equipment from this center.

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