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Research Article

Comparing the Hemodynamic Effects of Intravenous and Volatile Anesthesia in Patients with End Stage Renal Disease Undergoing Laparoscopic Implantation of Peritoneal Dialysis Catheter in a Randomized Double-Blind Clinical Trial

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ABSTRACT

Background: Due to the associated hypertension and cardiovascular disease in patients with ESRD hemodynamic changes during operations are detrimental and may be life-threatening. Therefore, hemodynamic stability is an important criterion in selecting the anesthetic approach.

Methods: 72 ASA class III/IV, ESRD Patients were studied in randomized double blind clinical trial. They were divided into two groups by four-block randomization. A group of patients were induced and maintained by etomidate and second of patients were induced by Na thiopental and maintained by isoflurane. Systolic, diastolic and mean arterial blood pressure and heart rate were measured at interval of pre and post induction, postintubation, pre and post abdominal insufflation during and at the end of surgery and in recovery. The total BP modulators were recorded and postoperative nausea and vomiting was registered in the recovery. Data were analyzed by STATA version 12.

Results: There was no significant difference in physical characteristics between two groups. There was no statistical difference between the groups in SBP and HR (P>0.05), although DBP fluctuation>20% at interval postinduction and prior to abdominal insufflation during surgery and at the end of surgery, was significantly higher in the isoflurane group of patients. (P=0.004, 0.001, 0.003 and 0.009, respectively). Also, the MAP fluctuation at interval of post induction, preinsufflation and at the end of surgery was significantly higher in isoflurane of patients. (P=0.04, 0.001, and 0.02, respectively).

Conclusion: The group anesthetized with isoflurane had a higher hemodynamic fluctuation, compared to the group anesthetized with etomidate. As hemodynamic changes are critical in patients with ESRD, etomidate is a more appropriate anesthetic choice for implantation of peritoneal dialysis catheter by laparoscopic approach.

Introduction

Nowadays, surgical procedures are widely performed around the world, all of which require anesthesia, commonly performed by different methods, including general, spinal, epidural, local, and regional anesthesia [1-2]. Each anesthetic method is selected based on type of surgery, underlying diseases, and postoperative complications for each patient [3-4]. Accordingly, various studies have compared perioperative complications, including postoperative

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pain, nausea/vomiting (PONV), and hemodynamic instability, between different anesthetic techniques [5-6]. Patients with specific conditions like diabetes mellitus and cardiovascular diseases have particularly high anesthesia-related complication rates [7-8]. Yet, the best anesthetic technique for these patients are controversial; some suggest the priority of volatile agents (eg. isoflurane, desflurane and sevoflurane) in cardiac surgery than total intravenous (IV) anesthesia [9], while other stand the point that etomidate provide more stable hemodynamics than propofol in cardiac surgery [10-11].

One of the most important anesthesia-related complications is the intraoperative hemodynamic instability, which can be triggered by several factors, like preoperative dehydration (due to the use of diuretics, laxatives, or nausea/vomiting), vasodilatation, impaired cardiac output, reduced preload, and bleeding [12]. Although several pre- and intra-operative assessments, such as evaluation of the patients' cardiac state and continuous monitoring of vital signs are recommended to reduce intraoperative hemodynamic instability [8, 13], this complication remains critical in patients with special conditions, including end stage renal disease (ESRD).

Patients with ESRD may require implantation of peritoneal dialysis catheter frequently, as an alternative to renal replacement therapy, with laparoscopic approach having more favorable results [14]; nonetheless, these patients are at high risk of anesthesia-related complications, especially hemodynamic instability, because of the associated comorbidities, such as hypertension and cardiovascular diseases [15]. Although several studies have compared the hemodynamic changes of different anesthetic techniques and agents, such as fentanyl, etomidate, propofol, ketamine, and isoflurane [6, 10, 16-19], none have compared etomidate and isoflurane on patients with ESRD undergoing implantation of laparoscopic peritoneal dialysis catheter. Therefore, we aimed to compare these two commonly used anesthetic agents (etomidate and isoflurane) to determine the agent with less hemodynamic variation in these patients.

Methods

Study design

In this double-blind randomized clinical trial (RCT), approved by the Ethics Committee of Tehran University of Medical Sciences (code: IRCT2017070934978N1), 72 patients, scheduled for laparoscopic peritoneal dialysis catheter implantation at Imam-Khomeini Hospital, were enrolled.

After explanation of the research objectives to the patients and obtaining their informed consent, the willing eligible candidates were categorized to either of the two groups by four block randomization method. Patients with ESRD, aged between 20-70, and ASA class III/IV, were included into the study. Patients who had contraindications for administration of Na thiopental and etomidate were not included. The procedure was performed by the same surgeon and abdominal pressure was kept at 10-14 mmHg during surgery. Any patient who required conversion of surgery to laparotomy, or developed any laparoscopic-associated complications was excluded from the study.

Demographic information of the candidates, including age, gender, and weight, as well as underlying diseases, including diabetes and ischemic heart disease (IHD), hypertension (HTN), and valvular heart disease (VHD) were extracted from patients' records and recorded in the study checklist. One group of patients were assigned to received 0.3 mg/kg etomidate (Janssen-cilag, Germany 2mg/ml0) for induction followed by 100 µg/kg for first 10min and 20 µg/kg etomidate for maintenance of the rest of surgery (Etomidate group). The other group were assigned to receive 4 mg/kg thiopental sodium for induction and 1-1.5% isoflurane (Piramal/health care India) for maintenance of anesthesia, (Isoflurane group). In both groups, 0.5 mg/kg atracurium was administered for intubation and 10 mg atracurium each half hour. Premedication was similar in both groups: 0.02 mg/kg midazolam and 2 µg/kg fentanyl. Blood pressure (BP) >160/90 mmHg was controlled by TNG (50-100 µg) or labetalol (20 mg stat) and repeated, if required.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were measured at 6 intervals: before induction and after induction, after intubation, before and after gas insufflation into the abdominal cavity, during and at the end of surgery and at recovery. To prevent postoperative nausea and vomiting, 4 mg ondansetron was given at the end of surgery. Postoperative nausea and vomiting was asked from patients at recovery and recorded as yes/no.

For study, the researcher who recorded the vital signs and other information and patients were unaware of the group assignment.

Statistical analysis

Descriptive results were presented as mean ± standard deviation (SD), for quantitative variables and frequency (percentage) for categorical variables. To compare nausea and vomiting between the groups, chi-square test was used, and for comparing the variables of SBP, DBP, MAP, and HR among different intervals, repeated measures ANOVA and generalized estimating equation (GEE) were used. For the statistical analysis, the statistical software STATA version 12 was used. P values of 0.05 or less were considered statistically significant.

Results

Mean age of participants was 49.50±14.48 (range: 30-70) years. Both groups were similar in terms of mean age, sex distribution, and mean weigh. (P>0.05) (Table 1). The frequency of diabetes mellitus was 16.7% in etomidate group and 27.8% in isoflurane group (P=0.2)

and the frequency of positive history of cardiovascular diseases was 80.6% in etomidate group and 72.2% in isoflurane group (P=0.4). Mean duration of surgery were 55.28±16.08 vs. 53.75±10.65 min, mean abdominal pressure 11.97±1.83 vs. 12.06±1.35 mmHg.

Considering PONV ,13.9% (N=5) of patients in isoflurane group experienced only nausea (P=0.5) and no one vomited, but 11.1% (N=4) of patients in etomidate group had both nausea and vomiting (P=0.05) (Table 2).

The effects of intervention on hemodynamics defined as <20% and >20% fluctuation in each hemodynamic parameter. Effect on DBP and HR at six intervals showed no significant difference. (P=0/135, P=0.389 respectively) (Figure 1 and 2). While SBP had greater frequency of >20% variation in isoflurane group at the following intervals: after induction (P=0.04), before insufflation (P=0.001), during and at the end of surgery. (P=0.003 and 0.009, respectively). (Tables 3,4) and (Figure 3). Comparison of MAP showed that a greater frequency of >20% variation in isoflurane group at the following intervals: after induction, before insufflation and at the end of surgery (P= value 0.04, 0.001, and 0.02, respectively) (Table 3, Figure 4).

Table 1- Comparison of demographic characteristics between the groups

		Etomidate	Isoflurane	Total	P value
Sex, No(%)	Female	16(44.4%)	17(47.2%)	33	0.8
	Male	20(55.6%)	19(52.8%)	39	
Age (years), mean ± SD		49.11±15.22	49.89±13.90	49.50±14.48	0.8
Weight (kg), mean ± SD		68.22±11.08	64.50±10.67	66.36±10.96	0.1

Table 2- Comparing the frequency of nausea and vomiting in recovery room between the groups

		Etomidate	Isoflurane	Total	P value
Nausea	No	32(88.9%)	31(86.1%)	63(87.5%)	0.5
	Yes	4(11.1%)	5(13.9%)	9(12.5%)	
Vomiting	No	32(88.9%)	36(100)	68(94.4%)	0.05
	Yes	4(11.1%)	0	4(5.6%)	

Table 3- Comparing the blood pressure variation between the two study groups in the 6 time intervals

		Intervals	Categories	Isoflurane	Etomidate	P value	P value
Systolic blood pressure		After induction	<20%	29 (80.6%)	20 (55.6%)	0.04	
			>20%	7 (19.4%)	16 (44.4%)		0.083
		After intubation	<20%	20 (55.6%)	20 (55.6%)	0.99	
			>20%	16 (44.4%)	16 (44.4%)		
		Before gas injection to abdomen	<20%	32 (88.9%)	18 (50%)	0.001	
			>20%	4 (11.1%)	18 (50%)		
		After gas injection to abdomen	<20%	30 (83.3%)	27 (75%)	0.5	
			>20%	6 (16.7%)	9 (25%)		
		During surgery	<20%	33 (91.7%)	21 (58.3%)	0.003	
			>20%	3 (8.3%)	15 (41.7%)		
		At the end of surgery	<20%	33 (91.7%)	23 (63.9%)	0.009	
			>20%	3 (8.3%)	13 (36.1%)		
		In recovery room	<20%	32 (88.9%)	31 (86.1%)	0.7	
			>20%	4 (11.1%)	5 (13.9%)		
Diastolic blood pressure		After induction	<20%	28 (77.8%)	16 (44.4%)	0.07	
			>20%	8 (22.2%)	20 (55.6%)		0/135
		After intubation	<20%	28 (77.8%)	24 (66.7%)	0.4	
			>20%	8 (22.2%)	12 (33.3%)		
		Before gas injection to abdomen	<20%	36 (100%)	36 (100%)	0.00	
			>20%	0	0		
		After gas injection to abdomen	<20%	27 (75%)	27 (75%)	0.99	
			>20%	9 (25%)	9 (25%)		
		During surgery	<20%	30 (83.3%)	25 (69.4%)	0.2	
			>20%	6 (16.7%)	11 (30.6%)		
		At the end of surgery	<20%	30 (83.3%)	22 (61.1%)	0.06	
			>20%	6 (16.7%)	14 (38.9%)		
		In recovery room	<20%	33 (91.7%)	27 (75%)	0.1	
			>20%	3 (8.3%)	9 (25%)		
MAP Mean	arterial	After induction	<20%	28 (77.8%)	19 (52.8%)	0.04	
			>20%	8 (22.2%)	17 (47.2%)		0.232

After intubation	<20%	19 (52.8%)	19 (52.8%)	0.99
	>20%	17 (47.2%)	17 (47.2%)	
Before gas injection to abdomen	<20%	33 (91.7%)	20 (55.6%)	0.001
	>20%	3 (8.3%)	16 (44.4%)	
After gas injection to abdomen	<20%	30 (83.3%)	26 (72.2%)	0.2
	>20%	6 (16.7%)	10 (27.8%)	
During surgery	<20%	30 (83.3%)	25 (69.4%)	0.07
	>20%	6 (16.7%)	11 (30.6%)	
At the end of surgery	<20%	32 (88.9%)	24 (66.7%)	0.02
	>20%	4 (11.1%)	10 (27.8%)	

Table 4- Comparing the heart rate variation between the two study groups in the 6 time intervals.

Intervals	Categories	Isoflurane	Etomidate	P value	P value
After induction	<20%	29 (80.6%)	30 (83.3%)	0.7	
	>20%	7 (19.4%)	6 (16.7%)		0.389
After intubation	<20%	29 (80.6%)	29 (80.6%)	0.99	
	>20%	7 (19.4%)	7 (19.4%)		
Before gas injection to abdomen	<20%	29 (80.6%)	32 (88.9%)	0.3	
	>20%	7 (19.4%)	4 (11.1%)		
After gas injection to abdomen	<20%	26 (72.2%)	21 (58.3%)	0.2	
	>20%	10 (27.8%)	15 (41.7%)		
During surgery	<20%	26 (72.2%)	29 (80.6%)	0.4	
	>20%	10 (27.8%)	7 (19.4%)		
At the end of surgery	<20%	28 (77.8%)	30 (83.3%)	0.5	
	>20%	8 (22.2%)	6 (16.7%)		
In recovery room	<20%	30 (83.3%)	30 (83.3%)	0.99	
	>20%	6 (16.7%)	6 (16.7%)		
	>20%	30 (83.3%)	30 (83.3%)		

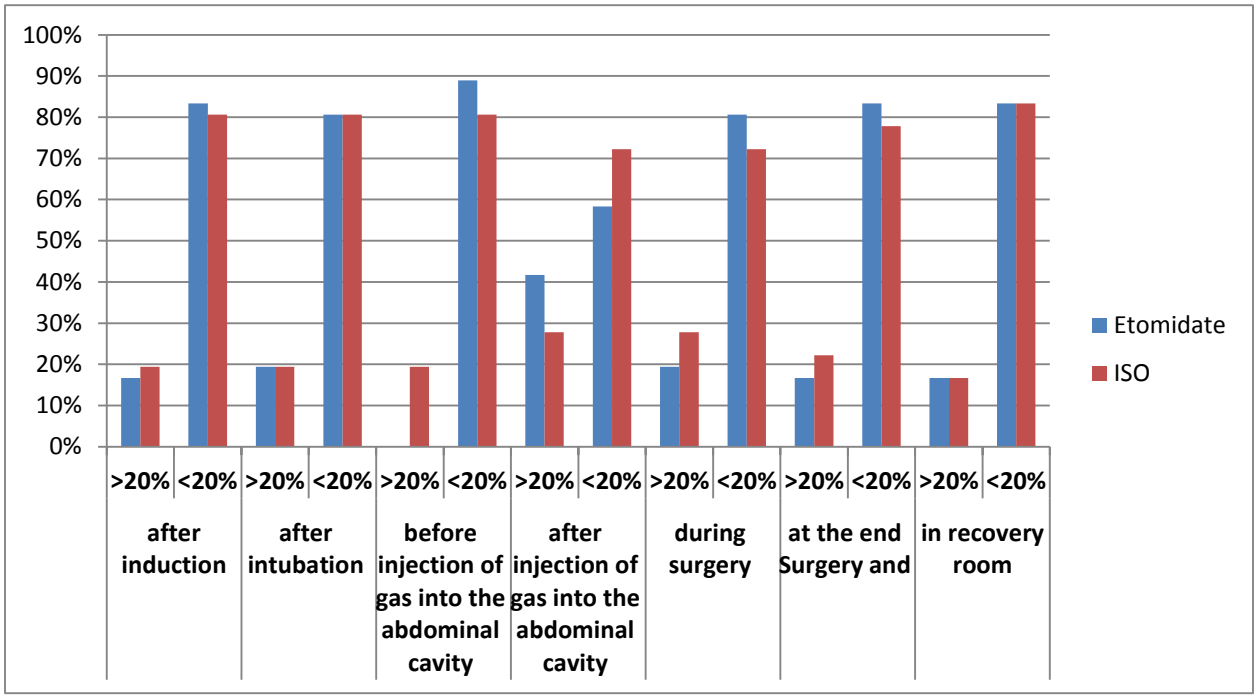

Figure 1- Incidence of more than 20% variation in systolic blood pressure from baseline in both groups at different time intervals.

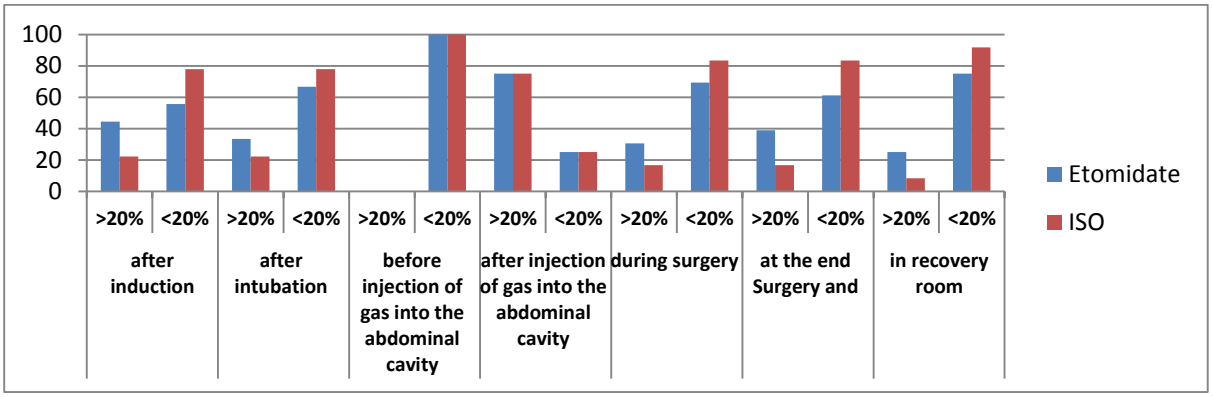

Figure 2- Incidence of more than 20% variation in diastolic blood pressure from baseline in both groups at different time intervals.

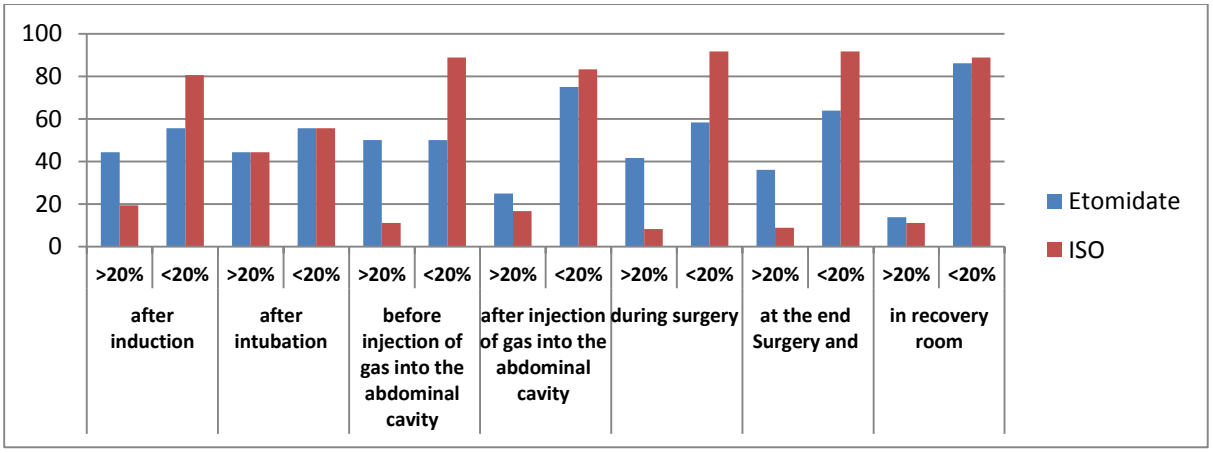

Figure 3- Incidence of more than 20% variation in mean arterial pressure from baseline in both groups at different time intervals.

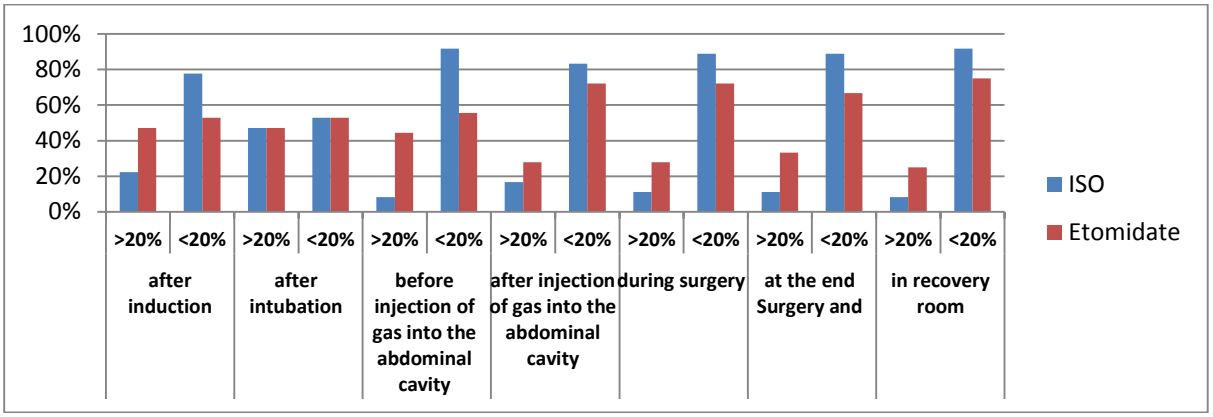

Figure 4- Incidence of more than 20% variation in heart rate from baseline in both groups at different time intervals.

Discussion

ESRD is associated with cardiovascular diseases including HTN and blood pressure fluctuations in patients with HTN are associated with increased mortality [18]. In our study, 76.4% of patients had a positive history of heart disease (HTN, VHD and IHD), and all patients were in ASA class III and IV. Therefore, it's essential to find a method that produces the least fluctuations in blood pressure. The results of the present double-blind RCT on comparison of hemodynamic variations between the groups receiving IV etomidate and volatile isoflurane, showed no statistical difference between the groups regarding DBP and HR, while a higher percentage of patients in isoflurane group had SBP

variations >20% at four of the six measured times (after induction, before gas insufflation of abdomen, during and at the end of surgery) and MAP variation >20% in three of the six measured times (after induction, before gas injection to abdomen, and at the end of surgery). Also, studying the mean changes in DBP, SBP, MAP, and HR indicated higher MAP in etomidate than isoflurane group. Previous studies comparing the anesthetic-related complications of etomidate vs. isoflurane have addressed different populations and different surgical procedures [17, 20-25] and as far as the authors are concerned, none have focused on ESRD patients with ASA class III/IV undergoing peritoneal catheter implantation. In a study by Giese and colleagues in 1985, hemodynamic changes on anesthetic induction with thiopental sodium and etomidate were evaluated in candidates of abdominal laparotomy with ASA class I and II, and the results showed a significant difference in hemodynamic status of healthy patients in thiopental sodium group [26]. Perhaps the reason for the difference between their results and ours is that they have only studied healthy patients (ASA class I and II), while we have studied patients with ASA class III and IV. Also, in the present study, both maintenance and induction doses of etomidate have been used, but in their study etomidate have been used only for induction [26].

In the study by Behzad Nazemroaya and colleague (2017), the complications of etomidate and thiopental sodium in children undergoing ECT has been studied and the results showed that nausea and vomiting were more frequent in children who received etomidate than patients who received thiopental sodium [27] which is consistent with the results of the present study. The study by Giese and colleagues reported that the incidence of nausea and vomiting was similar in the two groups of thiopental sodium and etomidate and was not associated with receiving fentanyl premedication [26].

However, in the present study, the frequency of nausea was not significantly different in recovery room between the groups receiving etomidate or isoflurane, while incidence of vomiting was significantly higher in recovery room in the etomidate group than that of the isoflurane group. This difference may be due to the fact that the patients were undergoing laparoscopic surgery, while in the study by Giese study and colleagues, all patients underwent laparotomy, and the fact that the patients in the present study had received infusion of etomidate, while in the study by Giese and colleagues, only the induction dose was administered, and all patients received ondansetron [26].

According to the results of our study, it seems that the use of etomidate as TIVA, especially in high risk patients with hemodynamic changes, is associated with higher risk of PONV for patients who received etomidate, as in our study, despite receiving 4 mg ondansetron in both groups to for preventing nausea and vomiting, the etomidate group had a greater frequency of vomiting in recovery than the isoflurane group. Apparently, it is better to use anti-nausea and vomiting combination therapy when using etomidate in these patients.

One of the limitations of this study was the lack of access to BIS monitoring, without which the chance of light anesthesia increase resulting in more hemodynamic changes, especially at the time of intubation. However, there was no significant difference between the two groups in the studied interval in hemodynamic parameters in our study. Although in all patients, the depth of anesthesia was increased or decreased, and intervention was required to control the hemodynamic parameters.

Conclusion

This study showed that using isoflurane for anaesthesia in patients can lead to higher hemodynamic fluctuation, compared to the patients whom anesthetized with etomidate. As hemodynamic changes are critical in patients with ESRD, etomidate is a more appropriate anesthetic choice for implantation of peritoneal dialysis catheter by laparoscopic approach.

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