www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i4.68

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Paper

Comparison of Hemodynamic Effects of IV Etomidate vs IV Propofol in Functional Endoscopic Sinus Surgery

Authors
Dr Rashmi Bengali[1], Dr Shiksha Singh[2*]
Department of Anaesthesia, Govt Medical College Aurangabad
*Corresponding Author
Dr Shiksha Singh
Shiv Niwas Saibaba Road, Jawahar Nagar, Kharv (East), Mumbai 4000051, India
Mob No: 8097981662, Email: *shikshasingh72@gmail.com*

Abstract
Laryngoscopy and endotracheal intubation stimulates cardiovascular responses such as hypertension, tachycardia and dysrhythmias. Sudden hypotension, arrhythmias, and cardiovascular collapse are threatening complications following Injection of induction agent in hemodynamically unstable patients demanding a search for safe inducing agent.
A prospective randomized study was conducted on 60 ASA Grade I and II patients aged 18-60 yrs scheduled for Functional Endoscopic Sinus Surgery (FESS).They were divided into two groups of 30 each. One group received Inj. Etomidate 0.3mg/kg as induction agent Grp E and Inj. Propofol 2mg/kg in Grp F preceeded by Inj. Midazolam 0.02mg/kg and Inj.. Fentanyl 3µgm/kg. as premedication . Patients were maintained on O2 +Nitrous oxide +Isoflurane +intermittent doses of Inj. Vecuronium. Reversal done with Inj. Neostigmine 50 mcg/kg & Inj. Glycopyrrolate 10mcg/kg IV. before extubation . Haemodynamic parameters were observed at different intervals. Statistical data confirmed that Etomidate was a better inducing agent being haemodynamically stable with minimum side effects than Propofol.
Keywords: *Etomidate; Propofol; Haemodynamic stability; FESS.*

Introduction

Induction of anesthesia is considered critical as Laryngoscopy and endotracheal intubation elicit unwanted cardiovascular responses such as hypertension, tachycardia, dysrhythmias[1,2,] and cardiovascular collapse considered as threatening complications .Hence It is desirable to use a safe inducing agent with fewer adverse effects for safety of patients.

Propofol, 2,6-diisopropylphenol is popular induction agent having rapid and smooth induction and recovery with decrease incidence of nausea and vomiting etc,[3,4] while hypotension, dose dependent depression of ventilation, pain on Injection are the major drawbacks.[5,6]

Etomidate, a carboxylated imidazole is characterized by hemodynamic stability, minimal respiratory depression and cerebral protective effects. Its lack of effect on sympathetic nervous

system, baroreceptor reflex regulatory system and its effect of increased coronary perfusion even on patients with moderate cardiac dysfunction makes it an induction agent of choice in cardiac disease patients;[7] though thrombophlebitis and myoclonus are some adverse effects.[8.]

Functional Endoscopic Sinus Surgery (FESS) is a minimal invasive surgical procedure which uses nasal endoscopes to enlarge the nasal drainage pathways of the paranasal sinuses to improve sinus ventilation. These surgeries are carried out under general anaesthesia requiring blood less field and hemodynamic stability.

A study was tailored to evaluate the haemodynamic effects of Propofol and Etomidate in Functional Endoscopic Sinus Surgeries (FESS) and change in blood pressure and heart rate during induction and during intubation being primary objective while pain on Injection, myoclonic movements, post-operative nausea and vomiting were compared as secondary objective.

Aims and Objectives

Primary Aim: To compare the hemodynamic effect of Etomidate and Propofol during induction and intubation

Secondary Aim: To study any adverse effect of Etomidate and Propofol during induction and intubation

Material and Method

Prospective randomized double blind comparative clinical trial was carried out after obtaining approval from ethical committee, in which the hemodynamic effects of IV Etomidate vs IV Propofol in FESS surgeries under general anesthesia were studied. Written informed valid consent was obtained from all patients . Sixty patients of either sex , between 18-60 years of age of ASA Grade I and II posted for FESS surgery under general anesthesia were included. Patients who were not willing or having Hypersensitivity to study drug, seizure disorder, steroid deficiency, COPD, Renal or hepatic failure, obesity and patients having difficult Intubation with MPC grade III and IV were excluded from the study. Thorough preoperative assessment was carried out. Investigations like Haemoglobin, Complete blood counts, Random blood sugar, Liver function test, Urine analysis, Renal function test, radiograph of Chest and Electrocardiogram were performed.

Patients were randomly assigned into two groups of 30 each.

Group P (n=30) received IV Inj. 1% Propofol 2mg/kg as an induction agent.

Group E (n=30) received IV Inj. Etomidate 0.3mg/kg. as an induction agent.

After confirming NBM status IV line was secured and multipara monitor was attached. Preinduction heart rate, blood pressure, SpO_2 and ECG recording were taken. Preloading with Ringer lactate 10ml/kg and pre oxygenation with 100% O_2 for 3 mins by mask was done. Premedication was done with Inj. Midazolam 0.02mg/kg and Inj. Fentanyl 3µgm/kg. Induction was done with either Inj. Propofol 1% 2mg/kg IV (Group P) or Inj. Etomidate 0.3mg/kg (Group E) IV. Endotracheal intubation was done under the effect of Inj. Vecuronium 0.1 mg/kg and maintenance on O2 +Nitrous oxide + Isoflurane and intermittent doses of Inj. Vecuronium. Haemodynamic responses were compared in both groups by measuring HR, SBP, DBP, MAP, SpO_2, ECG. Basal reading were noted when the patient was shifted to OT (T0), at Induction (T1), at intubation (T2), after intubation (T3), 1 minute after Intubation (T4), 3 minutes after Intubation (T5), 5 minutes after intubation (T6), 10 minutes after Intubation (T7),20 minutes after intubation (T8),30 minutes after intubation (T9) at the end of surgery (T10) and after surgery (T11).

At the end of surgery, patients were reversed with Inj. Neostigmine 50 mcg/kg & Inj. Glycopyrrolate 10mcg/kg IV. and extubation was done on return of reflexes.

Statistical Method Employed

All quantitative data was presented as mean ±SD (standard deviation).

Quantitative data was analysed by Student's t test. Student's unpaired t test for within the group, Student's paired t test for in-between the groups and Qualitative data was analysed by Chi square test. p<0.05 was noted as statistically significant (S) and p>0.05 as statistically not significant (NS)

Result

Comparative evaluation was done for age, sex, weight and height. P value was calculated using t test and was statistically insignificant.(p>0.05).

Table 1: Comparison of Pulse rate within and between the groups

Duration	Pulse Rate				Intergroup P value
	Group P		Group E		
	Mean±SD	P value	Mean±SD	P value	
T0	89.90±8.895		87.03±10.301		0.253
T1	83.70±8.461	0.0001	85.87±9.892	0.04	0.366
T2	106.87±11.482	0.0001	92.70±10.911	0.001	.0001
T3	94.77±8.472	0.001	89.30±10.209	0.02	0.028
1 Min T4	82.23±8.736	0.0001	87.33±10.077	0.728	0.041
3 Min T5	77.40±7.682	0.0001	83.90±9.942	0.0001	0.006
5 Min T6	74.93±6.933	0.0001	83.77±9.676	0.001	0.0001
10 Min T7	75.37±7.541	0.0001	84.63±9.327	0.001	0.0001
20 Min T8	75.73±6.491	0.0001	85.10±9.579	0.01	0.0001
30 Min T9	75.97±7.323	0.0001	85.47±9.540	0.01	0.0001
End Sx T10	78.83±7.212	0.0001	85.97±9.922	0.041	0.002
After Sx T11	89.27±8.056	0.103	89.07±9.377	0.0001	0.930

(P value < 0.05 is significant)

Table 1 shows that the baseline pulse rate was comparable between the two groups. In group P there was increase in mean pulse rate at intubation : T2 (106.87±11.482) followed by decrease till end of surgery T10 (78.83±7.212) which was significant statistically. (p=0.002)

In group E, there was increase in mean pulse rate at intubation: T2 (92.70±10.911) followed by slight decrease till end of surgery T10 (85.97±9.922) which was statistically significant. (p=0.002).

At laryngoscopy, the increase was more in Group P (106.87±11.482) as compared to Group E (92.70±10.911). After laryngoscopy, a decrease in mean HR was found which was more in Group P (78.83±7.212) than in Group E (85.97±9.922).

Table 2: Comparison of SBP within and between the groups

Duration	Systolic BP				Intergroup P value
	Group P		Group E		
	Mean±SD	P value	Mean±SD	P value	
T0	120.60±8.704		116.40±13.011		0.147
T1	111.97±13.763	0.0001	114.20±12.530	0.01	0.514
T2	115.70±7.264	0.003	129.53±11.776	0.001	0.0001
T3	105.33±11.281	0.0001	125.47±11.410	0.001	0.0001
1 Min T4	98.30±9.910	0.0001	123.10±10.199	0.001	0.0001
3 Min T5	97.23±7.749	0.0001	117.93±8.932	0.129	0.0001
5 Min T6	100.47±6.004	0.0001	116.33±8.766	0.954	0.0001
10 Min T7	102.00±6.777	0.0001	115.93±8.654	0.663	0.0001
20 Min T8	106.23±7.767	0.0001	114.90±9.897	0.115	0.0001
30 Min T9	110.33±8.527	0.0001	115.87±9.627	0.558	0.022
End Sx T10	115.40±9.039	0.0001	116.13±10.595	0.733	0.774
After Sx T11	118.83±8.200	0.04	117.73±12.031	0.018	0.681

(P value < 0.05 is significant)

Table 2 shows that the baseline mean systolic BP (SBP) was comparable in both the groups. In Group P the baseline mean SBP at (T0) was 115.70±7.264, with fall in mean SBP after intubation at T3 (105.33±11.281) till 30 mins after

intubation T9 (110.33±8.527) which was statistically significant. (p= 0.02)

In Group E, the baseline mean SBP at T0 was 116.40±13.011. There was statistically significant increase in mean SBP at T2 (129.53±11.776), T3 (125.47±11.410) and 1 minute after intubation T4 (123.10±10.199).

Thus, there was significant fall in SBP in Group P as compared to Group E and the decrease was statistically significant. (p= 0.02)

Table 3: Comparison of DBP within and between the groups

Duration	Diastolic BP				Intergroup P value
	Group P		Group E		
	Mean±SD	P value	Mean±SD	P value	
T0	75.23±8.411		72.20±8.393		0.167
T1	69.07±9.857	0.007	72.27±7.100	0.910	0.154
T2	72.00±9.281	0.157	84.47±8.924	0.001	0.0001
T3	61.53±10.884	0.0001	80.53±8.068	0.001	0.0001
1 Min T4	57.73±9.425	0.0001	78.13±7.682	0.001	0.0001
3 Min T5	58.00±7.273	0.0001	76.17±7.630	0.01	0.0001
5 Min T6	58.57±8.097	0.0001	74.60±7.578	0.01	0.0001
10 Min T7	60.53±7.691	0.0001	72.53±7.181	0.596	0.0001
20 Min T8	66.13±8.947	0.0001	72.33±7.845	0.804	0.006
30 Min T9	66.03±9.984	0.0001	72.93±7.177	0.183	0.003
End Sx T10	70.27±8.513	0.013	72.37±7.650	0.749	0.319
After Sx T11	74.50±8.963	0.666	73.80±7.322	0.017	0.742

(P value < 0.05 is significant)

Table 3 shows that the baseline mean diastolic BP (DBP) was comparable in both the groups. In Group P the baseline mean DBP (T0) was 75.23±8.411. having significant fall from T3 i. e. after intubation till 30 mins after intubation :T10 (66.03±9.984) and this fall was statistically significant. (p= 0.003)

In Group E, the baseline mean DBP (T0) was 72.20±8.393. An increase is seen at laryngoscopy T2 (84.47±8.924), after laryngoscopy T3 (80.53±8.068), 1 min T4 (78.13±7.682), 3 min T5 (76.17±7.630) and 5 min after intubation T6 (74.60±7.578). However, after 5 min (T6) till end of surgery (T10) there was no significant change

Thus, there was significant fall in DBP in Group P as compared to Group E and the decrease was statistically significant. (p= 0.003)

Table 4: Comparison of MAP within and between the groups

Duration	MAP				Intergroup P value
	Group P		Group E		
	Mean±SD	P value	Mean±SD	P value	
T0	87.67±6.666		86.93±8.053		0.702
T1	80.20±11.034	0.001	86.24±6.549	0.109	0.012
T2	82.43±9.825	0.019	99.49±7.580	0.001	0.0001
T3	74.07±10.770	0.0001	95.51±7.012	0.001	0.0001
1 Min T4	68.53±8.764	0.0001	93.12±6.936	0.001	0.0001
3 Min T5	68.90±7.312	0.0001	90.09±6.403	0.001	0.0001
5 Min T6	69.60±6.657	0.0001	88.51±6.428	0.016	0.0001
10 Min T7	71.53±6.822	0.0001	87.00±6.234	0.916	0.0001
20 Min T8	77.07±8.956	0.0001	86.52±7.007	0.453	0.0001
30 Min T9	78.47±9.475	0.0001	87.24±6.510	0.565	0.0001
End Sx T10	81.33±8.624	0.001	86.96±7.177	0.957	0.008
After Sx T11	85.50±7.099	0.102	88.44±6.896	0.002	0.109

(P value < 0.05 is significant)

Table 4 shows that the baseline mean arterial pressure (MAP) in both groups is comparable. In Group P, the baseline MAP at T0 was 87.67±6.666. with significant decrease from baseline value till end of surgery T10 (81.33±8.624) and the decrease was statistically significant. (p=0.008).

In Group E, the baseline mean MAP (T0) was 86.93±8.053.with slight increase in mean MAP at laryngoscopy T2 (99.49±7.580), after laryngoscopy T3 (95.51±7.012),1 min T4 (93.12±6.936), 3 min T5 (90.09±6.403) and 5 min after intubation T6 (88.51±6.428). No change in mean MAP after 5 min of intubation till end of surgery T10 (86.96±7.177) was seen.

Thus, there was statistically significant fall in MAP in Group P as compared to Group E . (p= 0.008)

The SpO2 in both the groups was maintained at 100% throughout the surgery and also in the post op period.

Table 5: Comparison of Side effects between the groups

Side Effects	Group P N (%)	Group E N (%)	Total	P Value
Pain	10 (33.33)	00(00)	10(16.67)	> **0.05 (NS)**
Myoclonus	00 (00)	02(6.67)	02(3.33)	
None	20(66.67)	28(93.33)	48(80.00)	
Total	**30 (100)**	**30(100)**	**60(100)**	

(P value < 0.05 is significant)

Table 5 shows there was pain during induction in 10 (33.33%) patients in Group P. In group E, myoclonus was seen in 2 (6.67%) patients. These values were not statistically significant. (p >0.05).

Discussion

Laryngoscopy and tracheal intubation provoke transient but marked sympathoadrenal response leading to hypertension and tachycardia though transitory and variable and may not be significant in otherwise normal individuals but is potentially harmful in cardiovascular compromised patients[9].

In our study we observed increase in mean pulse rate at laryngoscopy from 89.90 to 106.87 followed by statistically significant decrease in rate till end of surgery in Grp P (p=0.002).Where as in Grp E there was rise in mean pulse rate at laryngoscopy from 87.03 to 92.70 followed by fall to 85.97.The variation was more with Propofol indicating better stability with Etomidate. Our results were similar to studies done by, Shagun Bhatia Shah[10] et al and Supriya Aggarwal et al[11] They used Inj. Propofol 2mg/kg and Inj. Etomidate 0.3mg/kg in a comparative study and noted that an increase in heart rate was more from baseline in Propofol group than Etomidate group at induction (p<0.05).

The baseline mean systolic BP (SBP) in Group P (T0) was 115.70 with significant fall after intubation T3 (105.33) till 30 mins after intubation T9 (110.33) (p= 0.02)

In Group E, the baseline mean SBP at T0 was 116.40. There was statistically significant increase in mean SBP at T2 (129.53), T3 (125.47) and 1 minute after intubation T4 (123.10) followed by negligible decrease in mean at T10 (116.13).

Whereas the baseline mean diastolic BP (DBP) in Group P (T0) was 75.23. There was significant fall till 30 mins after intubation T10 (66.03) (p= 0.003). In Group E, the baseline mean DBP (T0) was 72.20. An increase in mean DBP at T2 (84.47), at T3 (80.53), T4 (78.13), T5 (76.17) and T6(74.60) was seen. Thereafter no significant change was observed. Thus, there was significant fall in DBP in Group P as compared to Group E and the decrease was statistically significant. (p= 0.003)

In Group P, the baseline MAP (T0) was 87.67. with statistically significant decrease till end of surgery T10 (81.33) (p=0.008).In Group E, the

baseline mean MAP (T0) was 86.93 with slight increase at T2 (99.49), T3 (95.51), T4 (93.12), T5 (90.09) and T6 (88.51).followed by no change till end of surgery T10 (86.96).

In 1992 Michael Muzi et al[12] explored the possibility that the commonly observed hypotension that occurs during induction of anaesthesia with Propofol in humans seems to be related to its direct effects on venous smooth muscle tone and presumably venous return. The changes in blood pressure in our study were corresponding to the studies done by Michael Muzi et al[12]. In a research article published by Osmar Creagh et al[13] in 2010, it was stated that the mechanism that provides the basis for its cardiovascular stability is the capacity to bind and stimulate peripheral alpha-2β adrenergic receptors with a subsequent vasoconstriction. Alterations in the function or number of these receptors may account for abnormal responses during Etomidate induction.

Jing Wu et al[14], also observed that Etomidate is much safer than Propofol for first-trimester surgical abortions and using a lower dose of Etomidate, supplemented with Fentanyl and Midazolam, in reducing adverse effects like myoclonus and postoperative nausea and vomiting.

Amit Kumar et al in 2018[15] also conducted a similar study for elective non-cardiac surgery to compare Propofol and Etomidate as anaesthetic agents and found that Etomidate is a better intravenous induction agent of anaesthesia than Propofol in hemodynamically unstable patient also as it has faster onset of action with less pain and post-operative nausea, vomiting with good hemodynamic stability.

The SpO_2 in both the groups was maintained at 100% throughout the surgery and also in the post op period.ECG monitoring was done in both the groups throughout the procedure. However no ECG changes were seen in either group throughout surgery and also in the postoperative period.

Side Effects

There was pain on Injection in 10 patients (33.33%) in Propofol group. Although this was not significant statistically, it was clinically significant in Propofol group. Ulsamer B et al in 1988[16] also found high incidence of pain upon Injection to be a disadvantage of Propofol in their study. In 2013 Jose Carlos rittes et al[17] concluded that both lipid and nanoemulsion formulations of Propofol elicited pain on intravenous Injection; however, the nanoemulsion solution elicited a less intense pain. Y.Nyman et al in 2006[18] conducted a study in which they observed that Propofol is associated with a high incidence of Injection pain in children, even if given together with lidocaine.

In the Etomidate group, 2 patients (6.67%) had myoclonus. This was not statistically significant but it was clinically significant in Etomidate group. Miner et al in 2007[19] also observed high incidence of myoclonus (20% vs 1.8%) in Etomidate and Propofol group respectively. Ulsamer B et al in 1988[16] in their study found that with Etomidate, the occurrence of myoclonia and poor mask ventilation proved to be unsuitable for induction of anesthesia unless supplemented by an opioid and/or benzodiazepine. Stockham RJ et al in 1988[20] in their study of haemodynamic changes and side effects of Etomidate induction found that increasing pre-induction doses of Fentanyl are more effective at minimising side-effects like myoclonus. Their results suggested that 500 micrograms of Fentanyl in a haemodynamically stable patient is an ideal pretreatment dose prior to anaesthetic induction with Etomidate.

Schwarzkopf KR et al in 2003[21] also concluded that Midazolam 0.015 mg/kg I.V,when administered 90 seconds before induction of anaesthesia with Etomidate, is effective in reducing Etomidate-induced myoclonic muscle movements.

In our study, all patients were observed for 24 hrs in the postoperative period. Only 1 patient in Etomidate group had nausea which was managed conservatively. Post operative vomiting was not observed in either group.

The results of the present study should encourage the routine use of Etomidate as an Induction agent in patients undergoing general anaesthesia, by providing Improved haemodynamics and fewer side effects.

Conclusion

It can be concluded from above conducted study that IV Etomidate is a better induction agent than IV Propofol being more stable hemodynamically with minimal effects on heart rate, systemic blood pressure, diastolic blood pressure and mean arterial pressure. IV Etomidate causes no pain on Injection when compared with IV Propofol. Minimal side effects like myoclonus are observed with Etomidate which can be avoided by benzodiazepines and/or opioid when given as premedication.

However, the study has to be done on a larger population and in high risk patients for further evaluation.

References

1. Saricaoglu F,Uzan S, Arun O, Arun F, Aypar U.A clinical comparison of Etomidate-lipuro,Propofol and admixture at induction. Saudi J Anaesth.2011;5:62-6.
2. Sarkar M, Laussen PC, Zurakowski D, Shukla A, Kussman B, Odegard KC. Hemodynamic responses to Etomidate on induction of anesthesia in pediatric patients.Anesth Analg.2005;101:645-50.
3. Shinn HK, Lee MH, Moon SY, et al. Post-operative nausea and vomiting after gynecologic laparoscopic surgery: comparison between Propofol and sevoflurane. Korean J Anesthesiol. 2011;60:36-40.
4. Grundmann U, Silomon M, Bach F, et al. Recovery profile and side effects of remifentanil-based anaesthesia with desflurane or Propofol for laparoscopic cholecystectomy. Acta Anaesthesiol Scand. 2001;45:320-6
5. Maruyama K, Nishikawa Y, Nakagawa H, et al. Can intravenous atropine prevent bradycardia and hypotension during induction of total intravenous anesthesia with Propofol and remifentanil? J Anesth. 2010;24:293-6.
6. Ozgul U, Begec Z, Erdogan MA, et al. Effect of alkalinisation of lignocaine for Propofol Inj.ection pain: a prospective, randomised, double-blind study. Anaesth Intensive Care. 2013;4:501-4.
7. Morel J, Salard M, Castelain C, et al. Haemodynamic consequences of Etomidate administration in elective cardiac surgery: a randomized double-blinded study. Br J Anaesth. 2011;107:503-9.
8. Nyman Y, Von Hofsten K, Palm C, et al. Etomidate-Lipuro is associated with considerably less Inj.ection pain in children compared with Propofol with added lidocaine. Br J Anaesth. 2006;97:536-9.
9. King BD: Harris L, Greifenstein F, Elder J, Dripps RD. Reflex circulatory responses to direct laryngoscopy and intubation under general anaesthesia. Anaesthesiology. 1951;12:556-66
10. Shah Shagun, Chowdhury I,Bhargava A, Sabbharwal B. Comparison of hemodynamic effects of intravenous Etomidate versus Propofol during induction and intubation using entropy guided hypnosis levels.Journal of Anaesthesiology Clinical Pharmacology. 2015;31(2):180
11. Supriya Aggarwal, Vipin Kumar Goyal, Shashi Kala Chaturvedi, Vijay Mathur, Birbal Baj, Alok Kumar. A comparative study between Propofol and Etomidate in patients under general anaesthesia. Brazilian journal of Anesthesiology. 2016;237-241
12. Muzi M, Berens RA, Kampine JP, et al. Venodilation contributes to Propofol-

mediated hypotension in humans. Anesth Analg. 1992;74:877-83.
13. Creagh O,Torres H,Rodriguez N,Gatica SR.Alpha-2B adrenergic receptor mediated hemodynamic profile of Etomidate. P R Health Sci J.2010;29:91-5.
14. Wu J, Yao S, Wu Z, et al. A comparison of anesthetic regimens using Etomidate and Propofol in patients undergoing first-trimester abortions: double-blind, randomized clinical trial of safety and efficacy. Contraception. 2013;87:55-62.
15. Kumar A, Shekhawat K, Sharma R, Mangwana P.A comparison of Propofol and Etomidate as anaesthetic agents for elective non-cardiac surgery. International Journal of Research in Medical Sciences.2018;6(10):3454.
16. Ulsamer B, Doenicke A, Laschat M. Propofol in comparison with Etomidate for the induction of anesthesia. Anaesthesist 1986;35: 535–42.
17. Rittles J, Cagno G, Perez M, Mathias L.Comparative evaluation of Propofol nanoemulsion with solutol and soy lecithin for general anesthesia.Brazilian journal of Anesthesiology.(English edition).2016;66(3):225-230.
18. Nyman Y, Von Hofsten K, Palm C, et al. Etomidate-Lipuro is associated with considerably less Inj.ection pain in children compared with Propofol with added lidocaine. Br J Anaesth. 2006;97:536-9.
19. Miner JR, Danahy M, Moch A, et al. Randomized clinical trial of Etomidate versus Propofol for procedural sedation in the emergency department. Ann Emerg Med. 2007;49:15-22.
20. Stockham RJ, Stanley TH, Pace NL, Gillmor S, Groen F, Hilkens P. Fentanyl pretreatment modifies anaesthetic induction with Etomidate. Anaesth Intensive Care 1988;16:171–6.
21. Schwarzkopf KR, Hueter L, Simon M, Fritz HG. Midazolam pretreatment reduces Etomidate-induced myoclonic movements. Anaesth Intensive Care 2003;31:18–20.