

Comparison of Different Doses of Fentanyl for Attenuating Stress Response and Side Effects of Etomidate during Induction and Intubation: A Randomized Control Study

S Vijayaragavan¹, M Balamurugan¹, K Vasanth²

¹Associate Professor, Department of Anaesthesiology, Thoothukudi Medical College Hospital, Thoothukudi, Tamil Nadu, India,

²Senior Resident, Department of Anaesthesiology, Thoothukudi Medical College Hospital, Thoothukudi, Tamil Nadu, India

Abstract

Introduction: Etomidate is a rapidly acting induction agent and it has little effect on cardiovascular system and it allows rapid recovery from anaesthesia but associated with side effects. Pre-treatment with narcotic analgesics usually Fentanyl can decrease the incidence of pain on injection and myoclonus during induction of anaesthesia with Etomidate and also attenuates the stress response to endotracheal intubation.

Objective: The objective of this study is to evaluate the efficacy of different doses of Inj.Fentanyl for attenuating the stress response and side effects of Etomidate during induction and intubation.

Methods and Methods: In this prospective randomised study 60 patients undergoing elective surgeries under general anaesthesia included in the study and they were randomly allocated into two groups of 30 each. Group I received 2 µ/kg of Fentanyl and Group II received 5 µ/kg of fentanyl. After 5 minutes of administration of either one of these all patients were induced with etomidate at a dose of 0.3 mg/kg. The parameters monitored are pain on injection, myoclonus, apnoea, heart rate, systemic blood pressure, post operative nausea and vomiting.

Results: We found that the hemodynamic response and side effects were lower in group II with increasing dose of Fentanyl. But at the same time there was increasing incidence of post operative nausea & vomiting and apnoea in group II.

Conclusion: We concluded that at a dose of 5 µg/kg of fentanyl, there is reduction of side effects of etomidate and also there is attenuation of hemodynamic response to intubation in patients undergoing elective surgeries under general anaesthesia with etomidate as induction agent.

Key words: Apnoea, Etomidate, Fentanyl, Pain on injection, Myoclonus, Stress response

INTRODUCTION

Etomidate is a carboxylated, imidazole-containing compound. Its mechanism of action is through gamma-aminobutyric acid (GABA)-A receptor which is by enhancing the affinity of GABA for these receptors.¹ It is a rapidly acting induction agent, and it has little effect on cardiovascular system, and

it allows rapid recovery from anesthesia.^{2,3} However, in spite of these good properties, etomidate has side effects such as pain on injection, myoclonus, post-operative nausea, and vomiting (PONV). Etomidate does not have analgesic properties because of which laryngoscopy and tracheal intubation usually results in increase in heart rate and systemic blood pressure. Pre-treatment with narcotic analgesics usually fentanyl can decrease the incidence of pain on injection and myoclonus during induction of anesthesia with etomidate and also attenuates the stress response to endotracheal intubation.⁴ We designed this prospective, randomized control study to find an optimal pre-induction dose of fentanyl with etomidate as induction agent which attenuates the hemodynamic changes and side-effects during induction and intubation.

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Corresponding Author: Dr. M Balamurugan, Department of Anaesthesiology, Thoothukudi Medical College Hospital, Thoothukudi, Tamil Nadu, India. Phone: +91-9443135904. E-mail: mbalan75@gmail.com

MATERIALS AND METHODS

A total of 60 American Society of Anesthesiologists (ASA) I and II patients of age 18-60 years undergoing elective surgeries under general anesthesia were selected in this prospective, randomized, control study. To detect a 15% difference in heart rate and blood pressure, with beta error of 80% (0.8), the sample size was calculated as 60. Totally, 60 patients of ASA I and II of both sexes and age between 18 and 60 years undergoing elective surgeries under general anesthesia were included in the study. Patients with a history of chronic alcoholism, known allergy to etomidate, known allergy to fentanyl, patients on drugs which may likely to cause cardiovascular changes, obese patients (>25% of ideal body weight), and pregnant patients were excluded from the study. The Institutional Ethical Committee approval for the study was obtained. The informed written consent was obtained from the patients participating in the study was obtained.

In the operating room, appropriate equipment for the airway management and emergency drugs were kept ready. Non-invasive blood pressure monitor, pulse oximeter and electrocardiogram leads were connected to the patient. Pre-operative baseline hemodynamic variables were recorded. An IV line was secured in nonoperative limb and started with dextrose normal saline. A total of 60 Patients were randomly assigned to two groups according to the pre-treatment dose of fentanyl Group I received 2 µ/kg of fentanyl, and Group II received 5 µ/kg of fentanyl. After 5 min of administration of either one of these, all patients were induced with etomidate at a dose of 0.3 mg/kg. The parameters monitored were heart rate, systemic blood pressure at 3 min after administration of fentanyl, 2 min after administration of etomidate, and 1 min after intubation. Complications such as pain on injection, myoclonus, apnea, and PONV were recorded. Statistical analysis done for continuous variable heart rate and blood pressure will be presented as mean ± standard deviation, and individual comparisons were done with student *t*-tests. Frequency counts of gender ratios and side effects among the four groups were analyzed with a chi-square test for linear trends.

RESULTS

A total of 60 patients were enrolled in the study. The demographic profiles of two groups were comparable in terms of age, sex distribution, weight, and ASA physical status. The mean duration of surgery is not statistically significant between both groups (Table 1).

Heart rates at 3 min after administration of fentanyl, 2 min after administration of etomidate, and 1 min after intubation were compared between Group I and II. The increase in heart rate 1 min after intubation was lesser in

Group II when compared to Group I and was found to be statistically significant ($P < 0.001$) (Table 2). In Group I, the increase of heart rate from baseline was 26% while in Group II, the increase of heart rate was only 10%.

Systolic and diastolic blood pressure at 3 min after administration of fentanyl, 2 min after administration of etomidate, and 1 min after intubation were compared between Group I and II. The increase in systolic and diastolic blood pressure 1 min after intubation was lesser in Group II when compared to Group I and was found to be significant ($P < 0.001$) (Tables 3 and 4).

Table 1: Patient characteristics (mean±SD)

Variables	n=30		P value*
	Group I	Group II	
Age (years)	45.96±14.4	46.53±14.01	0.878
Weight (kg)	52.5±5.0	52.9±5.5	0.8471
Gender (M/F)	14/16	15/15	0.940
ASA I/II	13/17	17/13	0.2195

* $P \leq 0.05$ is significant. SD: Standard deviation

Table 2: Heart rate variation during induction and intubation

Heart rate	Mean±SD		P value*
	Group I	Group II	
Baseline values	84.43±4.08	84.12±5.10	0.523
3 min after fentanyl	84.17±5.74	83.12±4.15	0.142
2 min after etomidate	83.41±5.66	82.24±5.01	0.214
After giving suxamethonium	84.55±4.97	83.57±5.07	0.273
1 min after intubation	110.23±4.65	96.06±5.05	<0.001

* $P \leq 0.05$ is significant. SD: Standard deviation

Table 3: Systolic blood pressure variation during induction and intubation

Systolic blood pressure (mmHg)	Mean±SD		P value*
	Group I	Group II	
Baseline values	126.30±5.243	126.20±4.17	0.543
3 min after fentanyl	124.77±5.19	123.76±4.46	0.424
2 min after etomidate	122.76±4.81	120.13±5.24	0.368
After giving suxamethonium	124.53±5.08	122.40±4.85	0.148
1 min after intubation	157.76±8.20	138.06±5.145	<0.001

* $P \leq 0.05$ is significant. SD: Standard deviation

Table 4: Diastolic blood pressure variation during induction and intubation

Diastolic blood pressure (mmHg)	Mean±SD		P value*
	Group I	Group II	
Baseline values	75.80±3.75	75.70±3.76	0.465
3 min after fentanyl	74.50±3.67	73.20±3.35	0.654
2 min after etomidate	75.20±3.92	74.40±3.42	0.452
After giving suxamethonium	78.00±4.12	76.30±3.83	0.376
1 min after intubation	88.40±2.09	82.10±2.18	<0.001

* $P \leq 0.05$ is significant. SD: Standard deviation

Mean arterial blood pressure at 3 min after administration of fentanyl, 2 min after administration of etomidate, and 1 min after intubation were compared between Group I and II. The increase in mean arterial blood pressure 1 min after intubation was lesser in Group II when compared to Group I and was found to be statistically significant ($P < 0.001$) (Table 5). The increase of mean arterial pressure from baseline is 15.6% in Group I while the increase is only 4.2% in Group II.

There is a significant decrease of pain on injection in Group II while there is a significant increase in PONV in Group II compared to Group I. There is increasing incidence of myoclonus in Group I and apnea in Group II (Table 6).

DISCUSSION

Several studies demonstrated that pain on injection, myoclonus, and increase in arterial blood pressure and heart rate during laryngoscopy and endotracheal intubation can be minimized following pre-treatment with fentanyl. The results of our study demonstrate that increasing the pre-induction dose of fentanyl is more effective at minimizing the side-effects of etomidate. However, at the same time, higher pre-treatment doses of fentanyl also cause a high incidence of apnea and also PONV.

In this study, pre-treatment with fentanyl did not cause chest wall rigidity in any patient. While these findings indicate that the incidence of rigidity is low with even 5 µg/kg fentanyl, it probably is not absent as other studies have described rigidity with even low dose of fentanyl.

Similarly, in this study, no patient required a narcotic antagonist either immediately after surgery or in the

recovery room, also nobody needed mechanical ventilation post-operatively. However, it does not mean that respiratory depression sufficient to require mechanical ventilation or requirement of a narcotic antagonist for reversal of opioid might not be an occasional occurrence.

In a study conducted by Weiss-Bloom and Reich⁵ has been demonstrated that 5-10 µg/kg of fentanyl given before administering etomidate blunt the hemodynamic response to anesthetic induction and tracheal intubation. These findings were well correlated with our study, in which fentanyl 5 µg/kg blunt the hemodynamic response to anesthetic induction and tracheal intubation.

In a study conducted by Ko *et al.*⁶ demonstrated that pre-treatment with fentanyl effectively suppresses the incidence of myoclonus after etomidate administration. This finding was well correlated with our study, in which the incidence of myoclonus was less with higher dose of fentanyl.

In another study conducted by Stockham *et al.*,⁷ fentanyl dosage of up to 500 µg are used, and they concluded that the hemodynamic response to induction-intubation sequence with etomidate as induction agent can be completely eliminated by high dosage of fentanyl of up to 10 µg/kg. In a study conducted by Zhang and Sun⁸ even a low dose of fentanyl (1 µg/kg) are effective in blunting the hemodynamic response to intubation with etomidate as induction agent. In a study conducted by Casati *et al.*,⁹ doses of fentanyl of 3 µg/kg are effective in blunting the hemodynamic responses to intubation with etomidate as induction agent. These findings, when combined with the results of our study, suggest that an optimal pre-induction dose of fentanyl (5 µg/kg) attenuates the increase in heart rate and blood pressure during induction-intubation sequence with etomidate. Hence, with our study, it can be suggested that on further increasing the dose of fentanyl, it may be possible to completely eliminate the hemodynamic response to induction intubation sequence with etomidate.

CONCLUSION

Our study indicates that the effectiveness of fentanyl in reducing the side-effects of etomidate and attenuating the hemodynamic responses associated with the induction intubation sequence is dose-dependent. The data suggest that 5 µg/kg of fentanyl pretreatment reduces the incidence of myoclonus, pain on injection, and increases in heart rate and blood pressure during the induction-intubation sequence in ASA class I and II patients but produce a high incidence of PONV and may cause apnea.

Table 5: Mean arterial blood pressure variation during induction and intubation

Mean arterial blood pressure (mmHg)	Mean±SD		P value*
	Group I	Group II	
Baseline values	92.63±3.59	92.53±3.62	0.432
3 min after fentanyl	90.94±3.36	90.72±3.42	0.367
2 mins after etomidate	91.42±4.12	90.92±3.98	0.418
After giving suxamethonium	93.51±4.65	92.25±3.65	0.181
1 min after intubation	111.52±6.53	100.75±4.44	<0.001

* $P \leq 0.05$ is significant. SD: Standard deviation

Table 6: Side effects of etomidate

Side effects	Pain on injection	Myoclonus	Apnea	PONV
Group I	9	2	0	2
Group II	1	0	3	11
P value*	0.044	0.501	0.271	0.049

* $P \leq 0.05$ is significant. PONV: Postoperative nausea and vomiting

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