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Original Research Article

Effect of Different Dosages of Fentanyl when Etomidate is used as Induction Agent

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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 was to find an optimal pre induction dose of &many with etomidate as induction agent which attenuates the haemodynamic changes and side-effects during induction and intuhatidn.

METHODS AND METHODS: Patients scheduled for elective surgeries under general anaesthesia were eligible for the study. 30 Patients were randomly assigned to two groups according to the pretreatment dose of Fnetanyl.

1) Group I received 2 μg/kg of Fentanyl
2) Group II received 5 μg/kg of Fentanyl

After 5 minutes of administration of either one of these all patients where induced with Etomidate at a dose of 0.3 mg/kg.

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,

1. INTRODUCTION

Etomidate is a carboxylated, imidazole containing compound. Its mechanism of action is through 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 anaesthesia[2]. But in spite of these good properties. etomidate has some side effects which is partly related to inhibition of adrenal synthesis of cortisone. Most prominent side effects are.

a) Pain on injection
b) Myoclonus
c) Post operative nausea and vomiting

The main advantage of etomidate is that it does not cause significant alterations in systolic, diastolic, and mean arterial pressures, heart rate, right atrial pressure, pulmonary - and systemic vascular resistance, stroke volume, cardiac- index, systemic blood flow, and shunt flow in pediatric patients and adults undergoing cardiac surgery[3].

In spite of the above advantages, etomidate does not have analgesic properties because of which laryngoscopy and tracheal intubation usually results in increase in heart rate and systemic blood pressure.

So, in order to avoid this, pretreatment 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[4].

Fentanyl is a phenyl-piperidine derivative synthetic opioid agonist. It has a more rapid onset and shorter duration of action. It can blunt the circulatory responses to direct laryngoscopy for endotracheal intubation[5].

Higher doses of fentanyl has the advantage of stable hemodynamics mainly due to -
a) Lack of direct myocardial depressant effects
b) Absence of histamine release
c) Suppression of stress response to surgery.

The object of this study s to determine whether is an optimal dose of Fentanyl which attenuates the hemodynamic changes and side effects of etomidate during induction and introducing other problems.

AIMS AND OBJECTIVE:

This prospective study was carried out at Anestheisa department, Gnadhi Medical College Bhopal, between August2020, August 2021

SAMPLE SIZE:

In order to detect a 15% difference in heart rate and blood pressure, with beta error of 80% (0.8), the sample size was calculated as 30 in each group.

60 ASA I and II patients of age 18 to 60 years undergoing elective surgeries under general anaesthesia were selected.

Patients whose medical history, laboratory data, or physical examination showed evidence of abnormal hepatic or renal function or severe cardiovascular, pulmonary, neurological, psych iatric, or metabolic disease were excluded from the study.

Selected patients were divided randomly into two groups — either to receive 2 microgm/kg fentanyl (n=30) or to receive 5 μg/kg fentanyl (n=30)..

DESIGN OF STUDY: Prospective Randomised Study
PARTICIPANTS : Patients posted for elective general surgery procedures expected to last one hour or longer.
INCLUSION CRITERIA:

a) Elective surgeries under general anaesthesia
b) Both sexes
c) Age : I 8-60 years
d) ASA l& II

EXCLUSION CRITERIA:

a) Pregnancy
b) Obese patients (>-250o of ideal body weight)
c) Known allergy to etomidate
d) Known allergy to fentanyl
e) Chronic alcoholic
f) Patients on drugs which is likely to cause cardiovascular changes.

2. METHODOLOGY

Patients scheduled for elective surgeries under general anaesthesia were eligible for the study. 60 Patients were randomly assigned to two groups according to the pretreatment dose of fentanyl-

1) Group I received 2 μg/kg of fentanyl
2) Group II received 5 μg/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-1

PARAMETERS TO BE MONITORED:

a) Pain on injection
b) Myoclonus
c) Apnoea
d) Heart rate
e) Systemic blood pressure
f) Post operative nausea and vomiting

STATISTICAL TOOLS TO BE APPLIED:

Continuous data like age, heart rate and blood pressure will be presented as mean +/- SD; individual comparisons were done with student t-tests. Frequency counts of gender ratios and side effects among the four groups were analysed with chi square test for linear trends.

3. RESULTS

There were no significant differences between the groups with respect to age, weight, preoperative heart rate, blood pressure, respiratory rate and duration of stay in recovery room. Males and females were almost evenly distributed between the two groups.

In Group I, no patient become apnoeic while in group II three patients become apnoeic after administration of fentanyl. But none required naloxone for antagonism of opioid.

Also with increasing dose of fentanyl, there was a decreasing incidence of pain on injection, myoclonus. But at the same time there was increasing incidence of post operative nausea and vomiting in group II.

As mentioned in tables 01 to 05, the increase of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure after intubation is significantly lower in group II with increasing dose of fentanyl.

TABLE NO 01-HEART RATE

HR	**GRP I**		**GRP II**		**P**
	Means	**SD**	**Means**	**SD**	
Baseline values	**84.43**	**4.082**	**84.123**	**5.1**	**0.523**
3min after fentany	**84.177**	**5.744**	**83.12**	**4.154**	**0.142**
2min after etomidate	**83.41**	**5.661**	**82.24**	**5.014**	**0.214**
After giving suxamethonium	**84.557**	**4.972**	**83.57**	**5.075**	**0.273**
1min after intubation	**110.237**	**4.653**	**96.063**	**5.051**	**<0.001**
% INCREASE FROM BASELINE	**26%**		**10%**		

TABLE NO 02-SYSTOLIC BP

SYSTOLIC BP	**GRP I**		**GRP II**		**P**
	Means	**SD**	**Means**	**SD**	
Baseline values	**126.3**	**5.243**	**126.2**	**4.174**	**0.543**
3min after fentany	**124.77**	**5.198**	**123.767**	**4.462**	**0.424**
2min after etomidate	**122.76**	**4.814**	**120.133**	**5.245**	**0.368**
After giving suxamethonium	**124.533**	**5.083**	**122.4**	**4.857**	**0.148**
1min after intubation	**157.767**	**8.208**	**138.067**	**5.145**	**<0.001**

TABLE NO 03-DIASTOLIC BP

DIASTOLIC BP	**GRP I**		**GRP II**		**P**
	Means	**SD**	**Means**	**SD**	
Baseline values	**75.8**	**3.75**	**75.7**	**3.765**	**0.465**
3min after fentany	**74.5**	**3.67**	**73.2**	**3.35**	**0.654**
2min after etomidate	**75.2**	**3.92**	**74.4**	**3.42**	**0.452**
After giving suxamethonium	**78**	**4.12**	**76.3**	**3.83**	**0.376**
1min after intubation	**88.4**	**2.092**	**82.1**	**2.187**	**<0.001**

TABLE NO 04-MEAN ARTERIAL PRESSURE

MEAN ARTERIAL PRESSURE	GRP I		GRP II		P
	Means	SD	Means	SD	
Baseline values	**92.633**	**3.598**	**92.53**	**3.625**	**0.432**
3min after fentany	**90.944**	**3.362**	**90.722**	**3.428**	**0.367**
2min after etomidate	**91.422**	**4.12**	**90.92**	**3.985**	**0.418**
After giving suxamethonium	**93.511**	**4.651**	**92.25**	**3.654**	**0.181**
1min after intubation	**111.522**	**6.533**	**100.756**	**4.449**	**<0.001**

4. DISCUSSION

In several studies it have been demonstrated that pain on injection, myoclonus and increases in arterial blood pressure and heart rate during laryngoscopy and endotracheal intubation can be minimised following pretreatment with fentanyl.

The results of our study demonstrates that increasing the pre-induction dose of fentanyl are more effective at minimizing the side-effects of etomidate.

But at the same time, higher pre-treatment doses of fentanyl also cause a high incidence of apnoea and also postopertative nausea and vomiting.

In this study, pre-treatment with fentanyl did not cause chest wall rigidity in any patient. While these findings indicate that the incidence or rigidity is low with even Slag/kg fentanyl, it probably is not absent, as other studies have described rigidity with even low dose of fentanyl[6].

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. But it doesn't 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[7].

In a study conducted by Stockham et al in University of Utah, it has been demonstrated that 2.5 μg/kg of fentanyl given before administering etomidate, eliminated all increases in heart rate and blood pressure produced by laryngoscopy and intubation (without causing hypotension) in patients with significant cardiovascular disease (NVI-IA. Class HI and IV).

In a study conducted by Alberti and Casati, doses of fentanyl of 3 μg/kg are effective in blunting the hemodynamic responses to intubation with etornidate as induction agent[8].

In a study conducted by Zhang and Sun et al, even a low dose of fentanyl (1 μg/kg) are effective in blunting the hemodynarnic response to intubation with etomidate as induction agent.

In another study conducted by Stockham and Stanley, fentanyl dosage of upto 500mg 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 upto 10 μg/kg.

These findings, when combined with the results of our study, suggest that an optimal pre induction dose of fentanyl (5μg/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[9].

But our study did not deal that whether hemodynamic responses can be completely eliminated with higher doses of the opioid and, if so, at what physiologic and pharmacologic cost.

Another disadvantage in our study is, it did not evaluate the proposed advantages of etomidate, in patients with limited cardiovascular reserve as it is a cardiostable induction agent.

5. CONCLUSION

Our study indicates that the effectiveness of fentanyl in reducing the side-effects of etomidate and attenuating the haemodynamic responses associated with the induction intubation sequence is dose-dependent. The data analysis suggests that Sug/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 post operative nausea and vomiting and may cause apnoea.

The drawbacks of our study are it did not experiment whether hemodynamic responses can be completely eliminated with higher doses of the opioid and, if so, at what physiological and pharmacological cost.

Another disadvantage in our study is, it did not evaluate the proposed advantages of etomidate, in patients with limited cardiovascular reserve as it is a cardiostable induction agent.

SUMMARY -

Our study was a prospective randomised study including 60 patients undergoing elective surgeries under general anaesthesia. They were randomly allocated into two groups of 30 each.

Group I received 2 μg/kg of fentanyl and Group II received 5 μg/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.

We found that in Group I, no patient become apnoeic while in group II three patients become apnoeic after administration of fentanyl.

Also with increasing dose of fentanyl, there was a decreasing incidence of pain on injection, myoclonus. But at the same time there was increasing incidence of post operative nausea and vomiting in group II.

We also found that the increase of heart rate and blood pressure, during induction-intubation sequence with etomidate is significantly lower in group II with increasing dose oFfentanyl.

Therefore we conclude that at a dose of 5.14 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.

6. REFERENCES

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