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Original Research Article

Comparison between Fentanyl and Nalbuphine in Blunting Hemodynamic Stress Response to Laryngoscopy and Endotracheal Intubation in Etomidate Induction of General Anesthesia

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Abstract

Background: Propofol has a favourable pharmacokinetic and pharmacodynamic profile making it the most commonly used intravenous induction agent for general anesthesia but adverse cardiovascular effects like hypotension and bradycardia are well-documented. Therefore, hemodynamic stability associated with etomidate makes it an ideal induction agent in patients with compromised cardiac reserves. Laryngoscopy and intubation elicits a noxious stimulus, leading to intense sympathetic activity. Various drugs have been tried to attenuate this response. Opioids are known to aid in maintaining proper depth of anaesthesia and attenuating the pressor response. Keeping this background in mind this study was designed to compare the efficacy of 2mcg/kg fentanyl with 0.2mg/kg nalbuphine in attenuating haemodynamic pressor response caused by laryngoscopy and intubation with etomidate induction.

Aim and Objectives: Primary objective of this study is to compare change in mean heart rate and mean arterial pressure from baseline after laryngoscopy and intubation between both groups, secondary objectives is to compare safety profile of both the drugs.

Material and Methods: This prospective randomized double blind study was conducted in a tertiary hospital associated with a medical college, 60 patients undergoing elective surgeries in general anaesthesia were randomly allocated to one of the two groups. Patients belonging to Group I were administered 2mcg/kg fentanyl in 10ml of normal saline whereas patients belonging to Group II were administered with 0.2mg/kg of nalbuphine in 10ml of normal saline, 150 seconds before injecting iv Etomidate 0.3mg/kg administered over 20 seconds, all vital parameters of the patients were recorded every minute for the first five minutes then every 5 minutes till completion of the surgery. Students t test, chi square test were used as per the requirement and a P value of <0.05 was considered statistically significant.

Result: Mean heart rate in group I at 1 minute was 87.3 bpm, at 2 minutes 79.4 bpm at 5 minutes 66.7 bpm, whereas in group II mean heart rate at 1 minute was 91.4 bpm, at 2 minutes 83.6 bpm, at 5 minutes 71.1 bpm. Mean arterial blood pressure in group I at 1 minute was 99.5

mmHg, at 2 minutes 93.8 mmHg, at 5 minutes 77.3 mmHg whereas mean arterial pressure in group II at 1 minute was 105.4 mmHg, at 2 minutes 98.9 mmHg, at 5 minutes 82.5 mmHg. Out of 60 patients 11 patients from group I developed minor side effects whereas in group II 5 patients developed such side effects.

Conclusion: Both groups were comparable with respect to demographic characteristics. Compared to nalbuphine, fentanyl causes a significant reduction in hemodynamic pressor response due to laryngoscopy and intubation after induction of general anaesthesia using etomidate as induction agent. Whereas safety profile of both the drugs was observed to be comparable in our study.

Keywords: Etomidate, Nalbuphine, Fentanyl, Haemodynamic Stress Response, Laryngoscopy, Intubation

Introduction

Propofol is a potent intravenous hypnotic drug that was developed by Imperial Chemical Industries Limited (London, UK) [1]. It has a favourable pharmacokinetic (PK) and pharmacodynamic profile, which has resulted in it becoming the most commonly used intravenous anaesthetic for the past three decades. [2]

The adverse effects of propofol like pain on injection, cardiovascular (bradycardia, hypotension) and metabolic (hyperlipidaemia secondary to infusion of lipid formulation) side effects are well documented. [3]

Etomidate is an imidazole derived sedative hypnotic agent directly acting on gamma amino butyric acid receptor complex, blocking neuroexcitation and producing anesthesia. It has a stable hemodynamic profile and minimal effects on respiratory system as compared to other induction agents. [4]

When laryngoscopy and intubation is carried out, there is mechanical irritation of stretch receptors situated in the respiratory tract leading to reflex haemodynamic responses through a sympathetic reflex. Fibers formed by the vagus and glossopharyngeal nerves supply the heart, blood vessels and adrenal medulla, causing a stimulatory adrenosympathetic response resulting in increased blood pressure, heart rate and plasma catecholamines. [5]

Various drugs and techniques have been used in current anaesthesia practice to attenuate these adverse effects, including deep level of general anaesthesia before endotracheal intubation with inhalation agents like halothane, use of supraglottic intubating devices like laryngeal mask airway, use of drugs such as calcium channel blockers, ACE inhibitors, Alpha 2 agonists, Beta -adrenergic blocking agents, magnesium sulphate, and opioids. [6,7,8,9]

Opioids leading from the front, nitro-glycerine, sodium nitroprusside, β blockers, CCBs have been tested in treating hemodynamic variations with inconsistent outcomes. [10]

Effectiveness of Fentanyl as an ideal choice to prevent increased HR and BP during L&I have been time tested. However its undesirable effects like respiratory depression and chest tightness are not hidden. [11]

Nalbuphine is an opioid belonging to the agonist-antagonist group and is recommended for the management of moderate to severe pain. It acts on kappa receptors as agonist and μ receptors as partial agonist-antagonist with equianalgesic potency to morphine on a milligram basis. [12]

Its cardiovascular stability, longer duration of analgesia, no respiratory depression, less nausea and vomiting and potential safety in over dosage makes it an ideal analgesic for use in balanced anaesthesia. [13,14]

Nalbuphine exhibits ceiling effect such that increase in dose greater than 30 mg does not produce further respiratory depression in the absence of other medications affecting respiration. Nalbuphine may partially reverse or block opioid - induced respiratory depression from mu agonist analgesic. [15,16]

Keeping this background in mind this study was designed to compare the efficacy of fentanyl with nalbuphine in attenuating haemodynamic stress response induced by laryngoscopy and intubation using etomidate as induction agent in patients undergoing surgeries under general anaesthesia.

Material and Methods

After obtaining Institutional Ethical Committee approval and informed consent from patients, a prospective randomized clinical study was conducted.

Sixty consenting patients of American society of anesthesiology (ASA) class I and II between the age group of 20-60 years planned for surgeries requiring general anesthesia were selected and included in the study. These patients were randomly divided into 2 groups consisting of 30 patients each.

Inclusion criteria: Consenting patients, ASA class I and class II patients, patients aged between 20-60 years, patients undergoing surgeries requiring general anesthesia.

Exclusion criteria: Patient's refusal, ASA class III and above, participants with history of allergy to any of the study drugs, anticipated or unanticipated difficult airway, cardiac disease, pregnant or lactating females, significant hepatic or renal insufficiency were not included in the study.

- Group I (n=30) received 2 mcg/kg fentanyl in 10ml normal saline.
- Group II (n=30) received 0.2mg/kg nalbuphine in 10 ml normal saline

Technique: On arrival in the operation theatre, patient's body weight was recorded. All routine monitoring devices were attached (NIBP, pulse oximeter, ECG). A 20G i/v canula was inserted at dorsum of left hand and connected to a 500ml Ringer Lactate drip and NIBP cuff on right hand and baseline readings of mean arterial blood pressure (MAP), heart rate (HR), peripheral oxygen saturation (SPO2) were recorded.

Patients were pre-oxygenated with 100% oxygen by facemask for 3 minutes. 150 seconds after the pretreatment with 2mcg/kg fentanyl in 10 ml normal saline in group I patients and 0.2mg/kg nalbuphine in 10ml normal saline in Group II patients, anesthesia was induced with etomidate 0.3 mg/kg IV over 20 seconds after confirming onset of etomidate action which was confirmed by loss of consciousness. injection vecuronium bromide 0.1mg/kg was injected intravenously to both the groups and were subsequently intubated with appropriately sized cuffed endo tracheal tube after 3 minutes. After intubation all vital parameters were recorded every minute for 5 minutes then every 5 minutes till end of surgery. Maintenance dose of vecuronium bromide was given after appearance of curare notch in EtCO2 monitor. The anesthesia was maintained with oxygen: nitrous oxide mixture in the ratio of 1:1, isoflurane in the concentration of 1 % and vecuronium bromide @ 0.01-0.015 mg/kg body weight every 20-40 minutes. Patient was reversed with glycopyrrolate @ 0.01 mg/kg and neostigmine @ 0.04-0.07 mg/kg body weight and was extubated and shifted to post anesthesia care unit after following verbal commands and neck holding for 5 seconds was present.

Result

Out of 60 patients, 30 patients in group I were pretreated with fentanyl and 30 patients in group II were pre-treated with nalbuphine prior to etomidate induction under general anaesthesia. Both the groups were comparable demographically.

Table 1: Comparison of demographic characteristics between both the groups

Demographics	Group I (Fentanyl)	Group II (Propofol)	P value
Age	39.80 ± 10.68	42.10 ± 9.63	0.384 NS
Weight	62.20 ± 8.07	63.50 ± 6.51	0.495 NS
ASA Status	25:5	26:4	0.718 NS
Male: Female	19:11	20:10	0.786 NS
Mean Arterial Pressure	95.77 ± 6.354	95.47 ± 6.286	0.854 NS
Heart Rate	80.43 ± 6.307	79.93 ± 4.416	0.895 NS

Chi square test is applied. The result is not significant at $p < .05$.

Table 2: Comparison of heart rate (HR) between both the groups at different time intervals.

Time Interval	Group I	Group II	P Value
Baseline	80.4 ± 6.31	79.9 ± 4.42	0.895
After one minute	87.3±6.63	91.5±6.97	0.021
After two minutes	79.4±6.07	83.6±6.81	0.011
After five minutes	66.7±5.91	71.1±6.73	0.009

Chi square test is applied. The result is not significant at $p < .05$.

Mean heart rate in group I at one minute was 87.3 bpm, at 2 minutes 79.4 bpm at 5 minutes 66.7 bpm, whereas in group II mean heart rate at one minute was 91.5 bpm, at 2 minutes 83.6 bpm, at 5 minutes 71.1 bpm.

Table 3: Comparison of Mean Arterial Blood Pressure (MAP) between both groups at different time intervals.

Time Interval	Group I	Group II	P Value
Baseline	95.8 ± 6.35	95.5 ± 6.29	0.854
After one minute	99.5± 6.83	105.4± 7.33	0.002
After two minutes	93.8± 6.75	98.9± 7.84	0.009
After five minutes	77.3± 6.61	82.5± 7.37	0.003

Chi square test is applied. The result is not significant at $p < .05$.

Mean arterial blood pressure in group one at one minute was 99.5 mmHg, at 2 minutes 93.8 mmHg, at 5 minutes 77.3 mmHg whereas mean arterial pressure in group II at 1 minute was 105.4 mmHg, at 2 minutes 98.9 mmHg, at 5 minutes 82.5 mmHg.

Table 4: Comparison of Safety Profile of both the drugs.

Side Effect	Group I	Group II	P Value
Bradycardia	3(9.99)	1(3.33)	0.612
Hypotension	2(6.66)	1(3.33)	0.554
Nausea & Vomiting	4(13.32)	2(6.66)	0.671
Sedation	2(6.66)	1(3.33)	0.554

Chi square test is applied. The result is not significant at $p < .05$.

Out of 30 patients from group I, 11 patients developed minor side effects like bradycardia 3(9.99), hypotension 2(6.66%), nausea vomiting 4(13.32%), sedation 2(6.66%) whereas in group II 5 patients developed minor side effects like

bradycardia 1(3.33%), hypotension 1(3.33%), nausea vomiting 2(6.66%), sedation 1(3.33%).None of the patients developed respiratory depression.

Discussion

This study was aimed at comparing efficacy of fentanyl with nalbuphine in attenuating stress response induced by laryngoscopy and intubation in patient undergoing surgeries under general anaesthesia where etomidate has been used as intravenous induction agent.

Propofol's favourable pharmacodynamic and pharmacokinetic profile has made it the most commonly used intravenous anaesthetic agent for the past three decades but it's adverse cardiovascular effects (hypotension & bradycardia) are well-documented. On the other hand, Etomidate is an imidazole ring containing sedative hypnotic agent which directly acts on gamma amino butyric acid receptor complex & blocks neuroexcitation and produces anesthesia. It has a stable hemodynamic profile and minimal effects on respiratory system as compared to other induction agents. [2,3,4]

Laryngoscopy and intubation has an irritant effect on stretch receptors of respiratory tract causing reflex haemodynamic responses through a sympathetic reflex. Fibers formed by the vagus and glossopharyngeal nerves supplies heart, blood vessels and adrenal medulla, causing a stimulatory adrenosympathetic response leading to increased blood pressure, heart rate and plasma catecholamines.

Fentanyl is known for its favourable pharmacodynamic profile providing excellent cardiovascular stability, with a rapid onset and a rapid recovery it has surpassed all other measures at attenuating the hemodynamic stress response following laryngoscopy and intubation. It readily crosses the blood brain barrier. In small doses (2µg/kg), it has a short duration of action as plasma concentrations falls below effective levels during redistribution phase. [16] Despite of fentanyl's frequent association with side effects like respiratory depression and pruritus it is still first choice of drug in preventing laryngoscopy and endotracheal intubation associated haemodynamic stress response.

Whereas Nalbuphine, has a unique advantage of ceiling-effect against respiratory depression in comparison to fentanyl. [17] Nalbuphine is not a narcotic drug and it can be used as an alternative to fentanyl in conditions where fentanyl can't be used or is not available due to strict laws associated with narcotic drugs. Nalbuphine is a drug belonging to agonist-antagonist opioid group and unlike other members of this group it does not increase blood pressure, pulmonary artery pressure or heart rate. [18]

None of the previous studies compared fentanyl and nalbuphine in terms of blunting laryngoscopy induced stress response where etomidate was used as the induction agent. Keeping this background in mind we decided to compare the efficacy of fentanyl in comparison with nalbuphine in prevention of stress response caused by laryngoscopy and intubation in elective patients undergoing general anaesthesia where etomidate is used as the induction agent. [19]

Doses of the drugs administered in this study, time of induction and the duration of intubation, smooth and quick laryngoscopy and adequate depth of anaesthesia are the key factors of this study and all these parameters have been decided carefully based on previous studies. All demographic characteristics such as gender, weight, ASA status and age were similar in both groups.

Conclusion

Based upon analysis of the data from our study we conclude that pretreatment with 0.2mcg/kg fentanyl prior to laryngoscopy and endotracheal intubation in patients induced by 0.3mg/kg Etomidate under general anaesthesia was found to be more effective in attenuating the haemodynamic

stress response as compared to 0.2mg/kg nalbuphine without any significant increase in side effects.

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