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Original Research Article

A Study to Evaluate the Efficacy of Intravenous (IV) Opioids in Attenuating the Stress Response and Serum Cortisol Levels during Endotracheal Intubation: A Comparative Study

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Abstract

Aim: The aim of the present study was to evaluate the efficacy of Intravenous (IV) opioids in attenuating the stress response and serum cortisol levels during endotracheal intubation.

Methods: This study was undertaken in the Department of Anaesthesiology & Critical Care, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar, India .90 patients, with 30 in each group, in different age group, either sex, belonging to ASA I and ASA II scheduled for elective surgical procedures under General Anesthesia were included.

Results: There was equal distribution of male and female in all the three groups. The mean age in Fentanyl Group, Morphine Group and Nalbuphine Group was 33.2, 32.08 and 29.12 respectively. The rise in blood pressure was much less in fentanyl group as compared with morphine and nalbuphine group at all measured time intervals. The rise in Diastolic blood pressure was much less in fentanyl group as compared with morphine and nalbuphine group at all measured time intervals. The result showed no statistical significance in serum cortisol levels between the three groups at SCL_0. Serum cortisol levels are statistically significantly lower at SCL_1 and SCL_2 among all the three groups.

Conclusion: At the dose used in this study, fentanyl was significantly reducing stress response during laryngoscopy and intubation followed by morphine and nalbuphine Hence Intravenous Fentanyl given at the dose of 2 mcg/kg effectively attenuates the stress response after laryngoscopy and intubation as compared to Morphine 0.1mg/kg and nalbuphine0.2mg/kg in that respective order

Keywords: morphine, fentanyl, nalbuphine, laryngoscopy, serum cortisol, endotracheal intubation

Introduction

Laryngoscopy, endotracheal intubation, and other airway manipulations are noxious stimuli that may induce profound changes in cardiovascular physiology, primarily through reflex responses. [1] The rise in pulse rate and blood pressure are usually transitory, variable, unpredictable, and can have detrimental consequences such as myocardial ischemia and cerebral hemorrhage. Laparoscopic surgeries form a crucial part of today's surgical practice but pose a challenge due to significant hemodynamic alterations contributing to elevated heart rate (HR), mean arterial pressure (MAP), and increased systemic and pulmonary vascular resistance along with reduced cardiac output. Such hemodynamic changes predispose the myocardium in vulnerable patients to ischemic changes. Many techniques have been evaluated to attenuate the adverse hemodynamic response such as increasing the depth of anesthesia using drugs such as opioid analgesics, α-2 adrenoreceptors agonists, intravenous lidocaine, beta-blockers, vasodilators, and calcium channel blockers. [2] These agents have been used with varying results and are associated with their own inherent side effects. There is no

single drug with minimal side effects which is cost-effective and available without a license. Hence, anesthesiologists are in constant search for the safest and the most efficient drug which can prevent the exaggerated hemodynamic response to laryngoscopy and intubation.

Fentanyl is a potent μ receptor agonist with rapid onset and relatively short duration of action, minimal respiratory depression, and has the ability to provide cardiovascular stability. [3] Despite these beneficial effects, fentanyl is known to cause bradycardia, nausea, vomiting, pruritus, and muscle rigidity. Moreover, availability of fentanyl in small hospitals is restricted due to tough narcotic laws. [4] Nalbuphine is a mixed agonist/antagonist opioid being agonist at κ receptor and antagonist at μ receptor. It is reported to have a ceiling effect on respiratory depression, cardiovascular stability, longer duration of analgesia, and decreased incidence of nausea and vomiting, which makes it an ideal analgesic during anesthesia. [5]

Several studies have been conducted on drugs like opioids, vasodilators, beta-blockers, lignocaine and α2-agonists to attenuate the pressor response. None of the techniques is exemplary. [6,7] It was reported that dexmedetomidine [8] and magnesium sulphate (MgSO4) [9] were effective in decreasing the pressor response in a nebulised form. Fentanyl is commonly used in an intravenous (IV) form to attenuate pressor response; the nebulised form has not been used for pressor response suppression. However, it has been used in nebulised form for pain relief. [10]

The aim of the present study was to evaluate the efficacy of Intravenous (IV) opioids in attenuating the stress response and serum cortisol levels during endotracheal intubation.

Materials and Methods

This study was undertaken in the Department of Anaesthesiology & Critical Care, Jawaharlal Nehru Medical College & Hospital, Bhagalpur, Bihar, India for one year. 90 patients, with 30 in each group, in different age group, either sex, belonging to ASA I and ASA II scheduled for elective surgical procedures under General Anesthesia were included.

Inclusion Criteria: Patients of either sex - Patient with ASA grade I and II. Patients scheduled for Elective surgical procedures under General Anesthesia.

Exclusion Criteria: Patient with anticipated difficult Airway, Hiatus Hernia, GERD,BMI>30,Patients on sedative, Hypnotics, Anti-hypertensive ,Pregnant, Lactating mothers.

Pre-anesthetic evaluation: On the day prior to surgery pre anesthetic evaluation was done. A through clinical examination of the patient was performed including General examination and Systemic examination. Airway assessment was done by Mallampati grading to anticipate difficult intubation. All patients were explained about the Anesthetic technique and written informed consent taken. Patients were kept NPO for 8 hours prior to surgery. Routine investigation done Hb, RBS, Urea, Creatinine, BT, CT, HIV, HbsAg, Chest X-ray, ECG. No specific investigations were required preoperatively pertaining to the study.

Technique of Anesthesia/procedure: 90 patients belonging to ASA grade I and II were randomly divided into 3 groups, each group consist of 30 patients

GROUP I [FENTANYL group] GROUP II [MORPHINE group] GROUP III [NALBUPHINE group)

On the day of surgery, Anesthesia machines and circuits were checked, resuscitation equipments were kept ready. After explaining the procedure and the effects of the drug, informed consent was obtained. In Preoperative ward, Baseline blood samples collected for checking serum cortisol levels in all patients and after ensuring fasting status patient was shifted to the operation theatre and connected to ASA standard monitors and Baseline Heart Rate (HR), Systolic pressure(SBP), Diastolic blood pressure(DBP), Mean Arterial pressure(MAP),SPO2 were recorded. Intravenous access established and Serum Cortisol levels were sent after 5 min of settling in the OT. All patients were premedicated with Inj.Glycopyrrolate 0.2mg, Inj.Ondansetron 4mg administered Intravenously.

All patients were preoxygenated with 100% Oxygen for 3 minutes

GROUP I - patients received Intravenous Fentanyl 2mcg/kg over 1-2 minutes.

GROUP II- patients received Intravenous Morphine.0.1mg/kg over 1-2 minutes

GROUP III - patients received Intravenous Nalbuphine 0.2mg/kg over 1-2 minutes.

After 5 minutes of stabilization period SBP, DBP, MAP, Heart rate, SpO 2 (T1) was recorded and Induction of anaesthesia done with Inj. Propofol 2mg/kg. After ensuring achieval of adequate depth of anaesthesia and ease of ventilation with bag and mask, Inj. Vecuronium 0.1mg/Kg bolus given unless there is no contraindication to facilitate laryngoscopy and intubation. Oxygenation continued by positive pressure mask ventilation using Bain's circuit. At 2 minutes after induction SBP, DBP, MAP,Heart rate, SpO2was recorded. At 3 minutes after induction, using laryngoscope with a Macintosh blade intubation was done with well lubricated, appropriate sized cuffed, disposable oral Endotracheal Tube. After confirmation of the tube

position by capnography tracing and Bilateral auscultation, cuff inflated and tube fixed and connected to anaesthesia machine for controlled ventilation. Anesthesia maintained with 50/50 % of O2 and N2O. Sevoflurane MAC titrated according to hemodynamic variables. SBP, DBP, MAP, Heart rate, SpO2were recorded at 1 minute interval after laryngoscopy and Intubation and blood sample collected after 5 min, 10 min followed by intubation for checking serum cortisol level

STATISTIC METHOD EMPLOYED

All data presented as mean±SD. Demographic data were analysed by student's T test. STATISTICAL SOFTWARE

The statistical software SPSS FOR WINDOWS (V 17) was used for the analysis of the data and Microsoft word and Excel have been used to Generate Tables etc.

Results

Table 1: Gender distribution

Gender	**Fentanyl Group**	**Morphine Group**	**Nalbuphine Group**	
Male	15	15	15	30
Female	15	15	15	30
Total	**30**	**30**	**30**	**90**

There was equal distribution of male and female in all the three groups.

Table 2: Age distribution

Age	N	Mean	SD
Fentanyl Group	30	33.2	6.64
Morphine Group	30	32.08	8.62
Nalbuphine Group	30	29.12	5.35

The mean age in Fentanyl Group, Morphine Group and Nalbuphine Group was 33.2, 32.08 and 29.12 respectively.

Table 3: Systolic Blood pressure

SBP		**N**	**Mean**	**SD**	**P Value**
SBP 0	Fentanyl	30	121.70	7.35	0.244
	Morphine	30	117.60	7.58	
	Nalbuphine	30	120.50	8.53	
	Total	90	119.93	7.90	
SBP 1	Fentanyl	30	128.10	6.76	0.002
	Morphine	30	129.10	7.75	
	Nalbuphine	30	136.10	7.38	
	Total	90	131.10	8.03	
SBP 2	Fentanyl	30	118.70	6.56	0.001
	Morphine	30	122.50	7.10	
	Nalbuphine	30	131.30	7.69	
	Total	90	124.17	8.80	
SBP 3	Fentanyl	30	108.60	6.16	0.001
	Morphine	30	114.00	6.90	
	Nalbuphine	30	126.50	7.54	
	Total	90	116.37	10.15	
SBP 4	Fentanyl	30	97.10	6.17	0.001
	Morphine	30	105.00	6.51	
	Nalbuphine	30	121.30	8.81	
	Total	90	107.80	12.42	

The rise in systolic blood pressure was much less in fentanyl group as compared with morphine and nalbuphine group at all measured time intervals.

Table 4: Diastolic blood pressure

DBP		N	Mean	SD	P Value
DBP 0	Fentanyl	30	72.70	5.16	0.244
	Morphine	30	75.50	5.87	
	Nalbuphine	30	77.70	8.19	
	Total	90	75.30	6.75	
DBP 1	Fentanyl	30	77.30	5.67	0.002
	Morphine	30	84.40	5.93	
	Nalbuphine	30	91.20	7.61	
	Total	90	84.30	8.55	
DBP 2	Fentanyl	30	70.60	5.03	0.001
	Morphine	30	78.40	5.72	
	Nalbuphine	30	86.80	6.66	
	Total	90	78.60	8.80	
DBP 3	Fentanyl	30	63.70	5.00	0.001
	Morphine	30	71.60	4.93	
	Nalbuphine	30	83.30	6.94	
	Total	90	72.87	9.86	
DBP 4	Fentanyl	30	97.10	6.17	0.001
	Morphine	30	78.60	6.93	
	Nalbuphine	30	66.03	11.03	
	Total	90	68.88	9.21	

The rise in Diastolic blood pressure was much less in fentanyl group as compared with morphine and nalbuphine group at all measured time intervals.

Table 5: Serum cortisol levels between the three groups

SCL		N	Mean	SD	P Value
SCL 0	Fentanyl	30	22.90	5.08	0.098
	Morphine	30	26.35	5.57	
	Nalbuphine	30	25.46	4.81	
	Total	90	24.90	5.29	
SCL 1	Fentanyl	30	11.150	1.57	0.002
	Morphine	30	16.000	2.55	
	Nalbuphine	30	20.555	3.02	
	Total	90	15.902	4.56	
SCL 2	Fentanyl	30	7.980	1.07	0.001
	Morphine	30	11.365	1.34	
	Nalbuphine	30	20.335	1.93	
	Total	90	13.227	5.46	

The result showed no statistical significance in serum cortisol levels between the three groups SCL 0. Serum cortisol level is statistically significantly lower at SCL 1 and SCL 2 among all the three groups.

Discussion

Laryngoscopy and Intubation constitute a period of extreme haemodynamic stress and associated with intense sympathetic activity manifested as Hypertension and Tachycardia. [11] Hemodynamic variations that occur during the process are usually unpredictable and transitory. Normal healthy person can tolerate this response, but in susceptible individuals, this transient sympathetic response can evoke life-threatening complications. [12] Various non-pharmacological and pharmacological methods have been used to attenuate the haemodynamic response to laryngoscopy and endotracheal intubation.

There was equal distribution of male and female in all the three groups. The mean age in Fentanyl Group, Morphine Group and Nalbuphine Group was 33.2, 32.08 and 29.12 respectively. The rise in blood pressure was much less in fentanyl group as compared with morphine and nalbuphine group at all measured time intervals. Fentanyl attenuates the cardiovascular response by its action on opioid receptors and by decreasing sympathetic outflow. [13] Optimal time of administration of fentanyl is five minutes before laryngoscopy and intubation, as described by Ko et al.

[14] Mixed opioid agonist/antagonists have also been studied and their efficacy on prevention of hemodynamic response to airway manipulation is still debatable. The desirability of agents with partial antagonist activity lies in the possibility of a decrease in abuse potential and a limitation to the extent of side effects, particularly respiratory depression. The analgesic potency of nalbuphine equals that of morphine on a milligram basis. The greatest advantage with nalbuphine is its ceiling effect on respiratory depression when compared to pure opioid agonists. Nath et al [15] compared two doses of nalbuphine (group 1: 0.1 mg/kg and group 2: 0.2 mg/kg) and found better hemodynamic control with higher dose of nalbuphine. Chawda et al [16] showed that nalbuphine prevented hemodynamic response associated with intubation when administered at a dose 0.2 mg/kg five minutes before laryngoscopy. Sharma and Parikh [17] observed higher SBP in the nalbuphine group than the fentanyl group at one, three, five, 10- and 15-minutes post intubation, whereas in our study at one-minute post intubation and after that SBP was below baseline and comparable between the groups with a p-value of >0.05. Buchh et al [18] compared nalbuphine and fentanyl and observed a non-significant fall in SBP in both the groups following administration of test drugs. They found a rise in SBP immediately after intubation which was the highest in the fentanyl group and did not return to baseline throughout the study period, whereas in the nalbuphine group it remained higher than baseline only until five minutes after intubation.

The rise in Diastolic blood pressure was much less in fentanyl group as compared with morphine and nalbuphine group at all measured time intervals. The result showed no statistical significance in serum cortisol levels between the three groups SCL_0. Serum cortisol levels are statistically significantly lower at SCL_1 and SCL_2 among all the three groups. Khanday et al [19] in his study comparing fentanyl and nalbuphine for attenuation of hemodynamic response, found a fall in SBP, DBP, and MAP from baseline in the nalbuphine group before intubation. After endotracheal intubation, significant elevation was observed in both the groups, with higher values being noted in the nalbuphine group. The initial fall in all hemodynamic parameters in the nalbuphine group could have been because of its strong kappa agonistic action. Rise in hemodynamic parameters following intubation was due to sympathoadrenal stimulation. A study by Madhu et al [20] comparing nalbuphine and fentanyl in patients undergoing laparoscopic appendicectomy found no significant difference in HR, SBP, DBP, or MAP between the groups after creation of pneumoperitoneum

Conclusion

At the dose used in this study, fentanyl was significantly reducing stress response during laryngoscopy and intubation followed by morphine and nalbuphine Hence Intravenous Fentanyl given at the dose of 2 mcg/kg effectively attenuates the stress response after laryngoscopy and intubation as compared to Morphine 0.1mg/kg and nalbuphine0.2mg/kg in that respective order.

References

1. Hagberg CA, editor. Hagberg and Benumof's Airway Management, E-Book. Elsevier Health Sciences; 2022 Aug 2.
2. Tariq MA, Iqbal Z. Efficacy of nalbuphine in preventing haemodynamic response to laryngoscopy and intubation. Journal of Postgraduate Medical Institute. 2014 Apr 17; 2 8(2).
3. Gurulingappa, Aleem MA, Awati MN, Adarsh S. Attenuation of Cardiovascular Responses to Direct Laryngoscopy and Intubation-A Comparative Study Between iv Bolus Fentanyl, Lignocaine and Placebo(NS). J Clin Diagn Res. 2012 Dec;6(10):1749-52.
4. Kothari D, Sharma CK. Effect of nalbuphine and pentazocine on attenuation of hemodynamic changes during laryngoscopy and endotracheal intubation: A clinical study. Anesth Essays Res. 2013 Sep-Dec;7(3):326-30
5. A comparative clinical study on the effects of dexmedetomidine and nalbuphine on hemodynamics of patients undergoing laparoscopic cholecystectomy. Mishra A, Lakra L, Suwalka U, Hembrom B, Haque E. Glob J Res Anal. 2018;7:33–36.
6. Teong CY, Huang CC, Sun FJ. The Haemodynamic Response to Endotracheal Intubation at Different Time of Fentanyl Given During Induction: A Randomised Controlled Trial. Sci Rep. 2020 Jun 1;10(1):8829.
7. Ganesan P, Balachander H, Elakkumanan LB. Evaluation of nebulized lignocaine versus intravenous lignocaine for attenuation of pressor response to laryngoscopy and intubation. Current Medical Issues. 2020 Jul 1; 18(3):184-8.
8. Kumar NRR, Jonnavithula N, Padhy S, Sanapala V, Naik VV. Evaluation of nebulised dexmedetomidine in blunting haemodynamic response to intubation: A prospective randomised study. Indian J Anaesth. 2020 Oct; 64(10):874-879.
9. Elmeligy MS, Elmeliegy MF. Effect of magnesium sulfate nebulization on stress response induced tracheal intubation; Prospective, randomized study. Open Journal of Anesthesiology. 2021 Apr 27;11(04):128.
10. Singh AP, Jena SS, Meena RK, Tewari M, Rastogi V. Nebulised fentanyl for post-operative pain relief, a prospective double-blind

controlled randomised clinical trial. Indian J Anaesth. 2013 Nov;57(6):583-6.
11. Reid and Brace: Irritation of respiratory tract and its reflex effect on heart-surgery Gynaecology obstetrics. 1940;70:157.
12. Fox EJ, Sklar GS, Hill CH, VillanueVar, King BD. Complications related to the pressor response to endotracheal intubation. Anesthesiology. 1977;47:524-5.
13. Gunalan S, Venkatraman R, Sivarajan G, Sunder P. Comparative Evaluation of Bolus Administration of Dexmedetomidine and Fentanyl for Stress Attenuation During Laryngoscopy and Endotracheal Intubation. J Clin Diagn Res. 2015 Sep;9(9):UC06-9.
14. Ko SH, Kim DC, Han YJ, Song HS. Small-dose fentanyl: optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesth Analg. 1998 Mar;86(3): 658-61.
15. Nath R, Dutta S, Khandelwal A. Attenuation of hemodynamic response during laryngoscopy and intubation with low dose intravenous nalbuphine. J Hemotol Transfus. 2015;3:1036.
16. Chawda PM, Pareek MK, Mehta KD. Effect of nalbuphine on haemodynamic response to orotracheal intubation. J Anaesthesiol Clin Pharmacol. 2010 Oct;26(4):458-60.
17. Sharma N, Parikh H. A comparative study of hemodynamic responses to intubation: Fentanyl versus nalbuphine. Gujarat Med J. 20 14 Aug;69(2):48-53.
18. Buchh A, Gupta K, Sharma D, Anwar U, Pandey MN, Kalra P. Comparative evaluation of fentanyl versus nalbuphine for attenuation of hemodynamic changes during airway stimulation. Int J Res Med Sci. 2018 Jan 24;6 (2):632.
19. Khanday SB, Mir AH, Sofi KP, Lone AQ, Shah AN. Evaluation and Comparison of Fentanyl versus Nalbuphine for Attenuation of Hemodynamic Response to Laryngoscopy and Endotracheal Intubation in General Anesthesia. Anesth Essays Res. 2019 Jan-Mar;13(1):111-118.
20. Madhu S, Balarama RP, Savdi VP, Ramadas KT. A randomized controlled parallel study of nalbuphine and fentanyl on hemodynamic response to laryngoscopic and laparoscopic stress in patients undergoing laparoscopic appendectomy under general anaesthesia. Indian J Clin Anaesth. 2018;5:505-11.