Original Research Article

Comparison of intravenous clonidine and intravenous fentanyl to attenuate the hemodynamic stress response to tracheal extubation

Gurudutt[1*], Venugopala K[2], Pavan Kumar P[3]

[1,2,3]Junior Resident, Department of Anaesthesiology and Critical Care Medicine, A.J.I.M.S., Kuntikana, Mangalore 575006
Email: guruduttravi@gmail.com

Abstract

Background: Endotracheal extubation can be associated with hypertension, tachycardia, arrhythmias, myocardial ischemia and raised intracranial pressures due to sympathetic stimulation. **Aim:** To compare the efficacy of clonidine, fentanyl and placebo in decreasing stress response to tracheal extubation in elective general surgery patients. **Materials and Methods:** 180 patients of either sex, ASA grade I -II normotensive, aged 18-65 years undergoing elective general surgeries of 60-180 minutes duration under general anaesthesia were randomized into 3 groups. Anaesthetic technique was standardized. Patients in Group N, F and D received an IV infusion of 100 ml of 0.9% normal saline, fentanyl 1µg/kg and clonidine 0.5µg/kg respectively 10 minutes before extubation for a period of 10 minutes. HR, SBP, DBP, MAP and SPO2 were recorded before, during and after extubation. **Results:** Statistically significant lesser increase in HR, SBP, DBP, MAP were noted after extubation in the clonidine group than the fentanyl group. clonidine group had better extubation quality than the fentanyl group. Ramsay sedation and Aldrete scores were similar in all 3 groups. Hypotension and bradycardia were more with clonidine group than the fentanyl group but none required intervention. **Conclusion:** clonidine 0.5µg/kg infusion administered 10 minutes before tracheal extubation was better compared to fentanyl 1µg/kg infusion in attenuating the hemodynamic stress response with comparable adverse effects. Hence, clonidine infusion can be a safer alternative to fentanyl infusion for attenuating extubation stress response.

Key Words: clonidine, Fentanyl, Extubation, Hemodynamic response.

[*]**Address for Correspondence:**
Dr. Gurudutt, Junior Resident, Department of Anaesthesiology and Critical Care Medicine, A.J.I.M.S., Kuntikana, Mangalore 575006
Email: guruduttravi@gmail.com

Received Date: 19/06/2019 Revised Date: 02/07/2019 Accepted Date: 11/08/2019
DOI: https://doi.org/10.26611/1015111214

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 16 August 2019

INTRODUCTION

Endotracheal extubation is the translaryngeal removal of a tube from trachea via nose or mouth. Complications during and after extubation are more common than during tracheal intubation and induction of anaesthesia. Hypertension and tachycardia are common events during extubation. Arrhythmias, myocardial ischemia, raised intracranial and intraocular pressures can occur.[1] There should be the absence of coughing, straining, laryngospasm, bronchospasm and breath holding for smooth extubation.[2] Drugs that have been recommended for the control of these hemodynamic events including opioids, lignocaine, beta blockers, calcium channel blockers and alpha 2 agonists.[3,4] Clonidine is a centrally acting alpha-2 adrenergic agonist. It acts on presynaptic alpha-2 receptors in the vasomotor center in the brain stem. This binding decreases presynaptic calcium levels, thus inhibiting the release of nor-epinephrine. The net effect is decrease in sympathetic tone, causing decrease in peripheral

How to site this article: Gurudutt, Venugopala K, Pavan Kumar P. Comparison of intravenous clonidine and intravenous fentanyl to attenuate the hemodynamic stress response to tracheal extubation. *MedPulse International Journal of Anesthesiology.* August 2019; 11(2): 157-161. http://medpulse.in/Anesthsiology/index.php

vascular resistance, thus lowering the blood pressure. Fentanyl is an opioid that attenuates hemodynamic response to extubation. It also decreases the airway reflexes to extubation and does not prolong the recovery time.[3] It is found that an infusion of clonidine 1µg/kg is better than fentanyl infusion of 1µg/kg before extubation to decrease the hemodynamic surge during extubation. Clonidine 1 µg/kg infusion has a higher sedation score compared to fentanyl 1 µg/kg infusion.[6] Attenuation of stress response to extubation by clonidine 0.5 µg/kg infusion is as effective as clonidine 1µg/kg infusion,[7] hence in my study I have compared 0.5 µg/kg of clonidine infusion with 1 µg/kg of fentanyl infusion to reduce the sedation score and adverse events associated with 1 µg/kg of clonidine infusion.

AIM

To compare the efficacy of clonidine, fentanyl and placebo in decreasing stress response to tracheal extubation in elective general surgery patients

MATERIALS AND METHODS

A prospective, double-blinded, randomized controlled study was conducted in the Department of Anaesthesiology, A.J.I.M.S. and R.C. in patients posted for elective general surgeries under general anaesthesia from January 2018 to August 2018. Randomization done with sealed enveloped technique.

Inclusion Criteria

ASA (American Society of Anaesthesiologist) grade I and II of either sex, age 18 to 65 years, scheduled under general anaesthesia for elective general surgeries, duration of surgery- 60 to 180 minutes.

Exclusion Criteria

Patients who are or with allergic to clonidine or fentanyl, cardiovascular disorder, respiratory disorder, diabetes, hypertension, obesity (BMI= or >30 kg/m2), difficult airway (Modified Mallampati Grade III and IV), medications that affect HR or blood pressure, pregnant, history of sleep apneoa, hepatic impairment, renal impairment.Using sealed enveloped technique patients were categorized into 3 different groups.Group N: (n=60) 100 ml of normal saline Group F: (n=60) fentanyl (1µg/kg) in 100 ml of normal saline Group D: (n=60) clonidine (0.5µg/kg) in 100 ml of normal saline.

All the patients were kept nil oral 8 hours before surgery. Patients were given Inj. Glycopyrrolate 10µg/kg iv, Inj.Midazolam 40µg/kg iv, Inj. Ondansetron 100µg/kg iv, Inj. Ranitidine 1mg/kg iv as premedication. Three lead electrocardiogram, non-invasive blood pressure, pulse oximeter and capnograph were attached for monitoring. 100% oxygen for 3 minutes was given as pre-oxygenation. Induction of the patient is done with Inj. Fentanyl 2µg/kg iv, Inj. Thiopentone sodium 5 mg/kg iv, Inj. Atracurium 0.5 mg/kg iv and intubation were done with a suitable endotracheal tube. Oxygen and nitrous oxide were used in the ratio of 40:60 for the maintenance of anaesthesia along with isoflurane 0.8 to 1.5%. Inj. Atracurium 0.125mg/kg iv was repeated at intervals with capnograph monitoring for the maintenance of muscle relaxation. Volume replacement and maintenance were done with ringer lactate and DNS. Isoflurane was cut off 10 minutes before anticipated extubation time in all the 3 groups. Test drugs were prepared by the persons not involved in the study and were handed over to the anaesthetists, who were unaware of the drugs. Group N patients received 100 ml of normal saline, Group F patients received 1µg/kg of fentanyl in 100 ml of normal saline and Group D received 0.5µg/kg of clonidine in 100 ml of normal saline over a period of 10 minutes before the anticipated extubation time. Patients were reversed with Inj. Neostigmine 50 µg/kg iv and Inj.Glycopyrrolate 10µg/kg iv after adequate spontaneous breathing efforts. Baseline hemodynamic parameters like HR and systolic, diastolic and mean arterial blood pressures were recorded. Baseline saturation is also recorded. All the above parameters were recorded after induction and intubation, 10 minutes before extubation, 5 minutes before extubation, during extubation and at 2, 4,6,8,10,25,40,55,70,85,100,115,130 minutes after extubation. Quality of extubation was evaluated based on cough immediately after extubation, using a five-point rating scale (extubation quality score):

1. No coughing
2. Smooth extubation, minimal coughing (1 or 2 times)
3. Moderate coughing (3 or 4 times)
4. Severe coughing (5-10 times) and straining
5. Poor extubation, very uncomfortable (laryngospasm and coughing >10 times).

Postoperative sedation was assessed on a six-point scale (Ramsay scale).

1. Anxious or agitated and restless or both
2. Cooperative, oriented and tranquilized.
3. Drowsy but responds to commands.
4. Asleep, brisk response to light glabellar tap or loud auditory stimulus.
5. Asleep, sluggish response to light glabellar tap or loud auditory stimulus.
6. Asleep and unarousable.

Aldrete scoring was also recorded at 25 minutes following extubation before sending the patients from the recovery room to the wards.

One way ANOVA test is used for Continuous variables like

1. Age
2. Surgery duration
3. Body Mass Index
4. Heart rate
5. Systolic Blood Pressure
6. Diastolic Blood Pressure
7. Mean Arterial Pressure.

Pearson's Chi-squared test is used for Categorical variables like

1. ASA Physical Status
2. Gender
3. Extubation Quality Score
4. Ramsay Sedation Score
5. Bradycardia
6. Hypotension
7. Vomiting.

Statistical analysis is made with IBM SPSS 16.0 software and a P value of <0.05 is considered significant.

Sample Size Calculation

Calculated using the following formula based on the earlier study by Liyakath *et al*[6] comparing effects of clonidine (1 µg/kg) with fentanyl (1µg/kg) and considering systolic blood pressure as a variable. In their study, maximum systolic blood pressure in the fentanyl group and clonidine group were found to be 136±13 mmHg and 130±9 mmHg. Applying µ1=136 and µ2=130, n is calculated as 55. Considering 10% compensation for "drop out" or "loss of follow up" sample size is taken as 60 for each groups.

RESULTS

Parameters	Description of the patient	score
Activity level	Moves all extremities voluntarily/on comman	1
	Moves to extremities	2
	Can noe moves extremities	3
Respiration	Breaths deeply and coughs freely	2
	Is dyspneic , with shallow, limitied breathing	1
	Is aspneic	0
Circulation(Blood Pressure)	Is 20 mmHg>Preanesthetic level	2
	Is 20 to 50 mmHg> Preanesthetic level	1
	Is 50 mmHg> Preanesthetic level	0
Consciousness	Is fully awake	2
	Is arousable on calling	1
	Is not responding	0
Oxygen saturation as determined by pulse oximetry	Has level>90% when brathing room air	2
	Requires supplemental oxygen to maintain level > 90 %	1
	Has Level < 90% with oxygen supplementation	0

Maximum total score is 10; a score of ≥9 is required for discharge

One hundred and eighty patients were allocated into 3 groups of 60 each -group N received 100 ml of normal saline, group F received 1µg/kg of fentanyl in 100 ml of normal saline, group C received 0.5µg/kg of clonidine in 100 ml of normal saline. Mean age of the study patients was 39.13 ±10.86 years, 101 female patients, 79 male patients, and there is no difference in demographic data, ASA and duration of surgery of the study group. Clonidine group had a statistically significant lesser increase in HR than the fentanyl group during extubation and up to 100 minutes after extubation. Clonidine group had statistically significant control of SBP than the fentanyl group during extubation and upto 70 minutes after extubation. Clonidinne group showed a lesser rise in DBP and mean arterial pressure compared to fentanyl group from 5 minutes before extubation to 130 minutes after extubation which was statistically significant. Clonidine group had a better quality of extubation compared to the fentanyl group. Ramsay sedation score in the initial 25 minutes of the post-operative period was statistically insignificant between the Clonidine and fentanyl groups. When compared to fentanyl group bradycardia was found to be more with the Clonidine group but none required intervention. Clonidine group had less vomiting compared to the fentanyl group and found to be statistically insignificant Clonidine group had hypotension in more patients compared to fentanyl group which had no hypotension and also found to be statistically insignificant. Adverse effects like respiratory depression, laryngospasm, bronchospasm or desaturation were not observed in both the groups. Recoveryprofile is similar in clonidine and fentanyl group.

Table 1: Extubation quality score

Group	Extubation Quality Score				P value
	1.00	2.00	3.00	4.00	
Normal Saline	0	10	41	9	
Fentanyl	1	35	24	0	<0.0001
Clonidine	10	41	9	0	
Total	**11**	**86**	**74**	**9**	

Table 2: Ramsay sedation score

Group	Ramsay Sedation Score			Total
	1.00	2.00	3.00	
Normal Saline	5	54	1	
Fentanyl	3	54	3	0.199
Clonidine	0	57	3	
Total	8	165	7	

Table 3: Complications

Complications	Normal Saline	Fentanyl	Clonidine	P value
Bradycardia	0	2	6	0.026
Hypotension	0	0	2	0.132
Vomiting	8	6	2	0.146

DISCUSSION

Endotracheal extubation is one of the frequently performed procedures in the field of anaesthesia. There is sympathetic stimulation which may cause detrimental effects in known hypertensive and coronary artery disease patients. Clonidine 0.5µg/kg and fentanyl 1 µg/kg are the lowest possible doses studied for this purpose with significant effect. In the present study these two drugs were chosen to compare and find the better drug with the least adverse effects. In our study, clonidine usage was associated with lesser increase in heart rate compared with fentanyl. The decrease in heart rate between the clonidine and fentanyl groups were statistically significant from the time of extubation till the study length, that is 130 minutes after extubation. In a randomized, double- blind, controlled study, Nishina *et al*[3] compared the effects of fentanyl 1 and 2 µg/kg IV with those of a control group (placebo) on hemodynamic changes during tracheal extubation and emergence from anesthesia in 60 patients who underwent elective gynecologic surgery. Although those authors recommended the 2-µg/kg dose—because while the number of patients who experienced coughs or strains was similar among the 3 groups, the severity of these symptoms was attenuated in the fentanyl group that received the higher dose—they reported that the 1- and 2-µg/kg doses were associated with a significantly reduced HR ($P < 0.05$) but found no significant difference in the prevalence of cough compared with placebo. Cough scores were significantly lower in the clonidine group than in the placebo group ($P < 0.05$), but there were no between-group differences in the prevalence of breath holding and desaturation. HR, SBP, and DBP were significantly increased from baseline at extubation in both groups ($P < 0.05$), but the increase was significantly less substantial with clonidine. In our study clonidine group had statistically significant control of SBP than the fentanyl group during extubation and upto 70 minutes after extubation. In our study clonidine group showed a lesser rise in DBP and mean arterial pressure compared to fentanyl group from 5 minutes before extubation to 130 minutes after extubation which was statistically significant. In our study, the fentanyl group had 58.3%, 40% patients had minimal and moderate cough respectively. In the clonidine group 68.3%, 15% patients had minimal and moderate cough respectively. More sample size in our study would have caused the difference. R. Aksu *et al*., found laryngospasm in 1 (5%) patient in the fentanyl group. In our study, no patient had respiratory depression, laryngospasm, bronchospasm or desaturation in either groups. Aspiration of blood which is a risk of rhinoplasty surgeries might have caused the laryngospasm. In our study, hypotension was observed in 2(3.3%) patients in the clonidine group of which none required vasopressors. R. Aksu *et al*., observed bradycardia in 4 patients (2 in each group) that is 10% patients in each group and these patients received atropine therapy when HR<45/min. Nasocardiac reflex would have aggravated the bradycardia. In our study, bradycardia was observed in 2(3.3%) patients in the fentanyl group and 6(10%) patients in the clonidine group which was statistically significant but clinically none of the patients required atropine. Bajwa *et al*. observed a fall in oxygen saturation up to 94-95% in the

clonidine group, after the completion of clonidine infusion (1 µg/kg in 20 minutes).[10] In our study the least SpO2 recorded was 98%. Yildiz *et al* observed significant sedation (with a short period of apnea in 3 cases) and a fall in SpO2 values immediately after drug infusion 1 µg/kg in 5 minutes.[11] In our study lesser dose(0.5 µg/kg)in more time (10 minutes) decreased the incidence of apnea.In our study, comparing the Ramsay sedation score during initial 25 minutes post-operatively among clonidine(0.5µg/kg) group with the other groups, fentanyl (1µg/kg) and normal saline produced a P value of 0.199, which was statistically insignificant. In our study lesser dose (0.5 µg/kg) decreased the sedative effect (Ramsay score 2-3).

CONCLUSION

Clonidine 0.5µg/kg infusion administered 10 minutes before tracheal extubation was better compared to fentanyl 1µg/kg infusion in attenuating the hemodynamic stress response with comparable adverse effects. Hence, Clonidine infusion can be a safer alternative to fentanyl infusion for attenuating extubation stress response. Further studies can be done with a larger sample size and different doses of Clonidine using neuromuscular block monitoring.

REFERENCES

1. Minogue SC, Ralph J, Lampa MJ. Laryngotracheal topicalization with lidocaine before intubation decreases the incidence of coughing on emergence from general anesthesia. *Anesth Analg* 2004;99:1253-7.
2. Cranfield KA, Bromley LM. Minimum alveolar concentration of desflurane for tracheal extubation in deeply anaesthetized, unpremedicated children. *Br J Anaesth* 1997;78:370-1.
3. Nishina K, Mikawa K, Maekawa N, Obara H. Fentanyl attenuates cardiovascular responses *to* tracheal extubation. *Acta Anaesthesiol Scand* 1995;39(1):85-9.
4. Batra YK, Singh H, Singh SP. Blood pressure and Pulse rate changes during tracheal extubation, influence of topical or intravenous lidocaine. *Indian J of Anaesth* 1986;34:31-4.

Source of Support: None Declared
Conflict of Interest: None Declared