IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 1 Ser. 14 (January. 2019), PP 32-37
www.iosrjournals.org

Low Dose Nalbuphine in Attenuation of Hemodynamic Responses to Laryngoscopy and Intubation – A Study

Dr I. Joyshankar Singh[1], Dr. Takhelmayum Hemjit Singh[2], Dr. N. Ratan Singh[3], Dr. Laithangbam Pradipkumar Singh[4], Dr. Ritchie Edmund Pasweth[5], Dr. Rita Rajkumari[6]

[1]*Post Graduate Trainee, Department of Anaesthesiology, RIMS, Imphal*
[2]*Assistant Professor, Department of Anaesthesiology, RIMS, Imphal*
[3]*Associate Professor, Department of Anaesthesiology, RIMS, Imphal*
[4]*Professor, Department of Anaesthesiology, RIMS, Imphal*
[5]*Post Graduate Trainee, Department of Anaesthesiology, RIMS, Imphal*
[6]*Post Graduate Trainee, Department of Anaesthesiology, RIMS, Imphal*
Corresponding Author: Dr. Takhelmayum Hemjit Singh

Abstract: *Various pharmacological interventions and methods have been tried to obtund the hemodynamic responses to laryngoscopy and intubation. A randomised, controlled, double blinded study was conducted in our centre on sixty adult patients scheduled for elective surgical procedures under general anaesthesia, randomised into two groups viz. Group A patients (100µg//kg nalbuphine intravenously) and Group B (150µg/kg nalbuphine intravenously), administered 5 minutes before induction. During laryngoscopy and endotracheal intubation, changes in the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were recorded at baseline, after the study drug, at intubation, 1, 2, 3, 4, 5 and 10 minutes. An increase in the heart rate in group A from 89.10±3.58 to 98.46±2.96 beat per minute (10%), and in group B from 86.83± 2.83 beat per minute to 96.63±3.09 per minute (11%) was observed (p>0.05). A rise in systolic blood pressure during laryngoscopy and intubation compared to the baseline value i.e. 6% from baseline (p=0.01) was observed in both the groups. However, the mean arterial pressure (MAP) dropped from 95.55±2.43 to 87.60±2.46 mmHg (8%) in group A as compared to group B from 95.33±2.40 to 84.53±2.77mm Hg (11%) during intubation (p>0.05) but was significantly decreased when compared to the baseline in both the groups (p=0.02). It was concluded that nalbuphine in the two low doses effectively reduced tachycardia, hypertension associated with laryngoscopy and intubation. It also provided good intra operative haemodynamics and adequate post-operative analgesia.*

Key words*: Laryngoscopy, intubation, hemodynamic responses, nalbuphine, attenuation*

Date of Submission: 12-01-2019 Date of acceptance: 27-01-2019

I. Introduction

Laryngoscopy and intubation are integral parts of general anaesthesia. However, endotracheal intubation often causes a hemodynamic response probably generated by direct laryngoscopy.[1]The hemodynamic responses are characterised by various cardiovascular changes such as tachycardia, rise in blood pressure and a wide variety of cardiac arrhythmias which may not present a problem for most patients.[2] However, hypertension and tachycardia with arrhythmias caused by endotracheal intubation can be deleterious in patients with poor cardiovascular reserve.[3]

Various pharmacological interventions (both intravenous and topical), modified instruments and intubating devices viz. laryngeal mask airway (LMA) & intubating laryngeal mask airway (ILMA), etc. have been tried to obtund the hemodynamic responses to laryngoscopy and intubation.[4] Some of the drugs used for prevention of hemodynamic responses to laryngoscopy and intubation include thiopentone, propofol, esmolol, lignocaine, magnesium, vasodilators, opioids, etc., but each drug has got its own limitations.[5]

On the other hand, nalbuphine is a semi synthetic opioid agonist – antagonist analgesic of phenanthrene series. It acts on kappa receptors as agonist and µ receptors as partial agonist-antagonist with equi-analgesic potency to morphine on a milligram basis.[5] 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,[6,7] even though low dose nalbuphine was associated with lesser grades of analgesia .[8]

The present study was designed to compare the efficacy of two low doses of nalbuphine in attenuation of hemodynamic responses to laryngoscopy and intubation as very minimal data is available in the search for the ideal nalbuphine dose.

II. Methods

After obtaining approval from the Research Ethics Board of the institute, a randomised, controlled, double blinded study was conducted in our centre on patients (ASA I or II, aged 18 – 60 years of either sex) undergoing elective surgery under general anaesthesia. Patients physically dependent on narcotics, with history of drug allergy to nalbuphine, cerebrovascular, neurologic, respiratory and ischemic heart disease, renal and hepatic dysfunction, uncontrolled hypertension, poorly controlled diabetes mellitus and on beta blockers, anti-depressants, anti-anxiety, anti-convulsants or anti-psychotics were excluded from the study.

The sample size was calculated as 26 in each group based on the difference in the mean systolic blood pressure between the two doses of study drug at 1 minute post intubation.[8] Assuming a 5% drop out rate, the final sample size is rounded to include 30 in each group. Using a web based computer generated stratified randomisation chart, the patients were divided into two groups of 30 each and each of the sample were allocated into one of the groups depending on the randomisation chart. The primary investigator and the patient were not aware of the study drug which was prepared in a coded syringe by a colleague, to make the study double blinded. A multi-parameter monitor was used to measure hemodynamic variables like – heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP). Sedation Score was measured by modified Ramsay sedation score[9] and duration of analgesia (time to first rescue analgesic request) - measured by visual analogue score[10] (VAS)> 4.

All the patients were examined a day before surgery and kept nil orally overnight. On the day of surgery, at preoperative room, intravenous access was secured with 18 G catheter and intravenous fluids at 5 ml/kg, baseline parameters like pulse rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, oxygen saturation and ECG were recorded. After premedication with 0.2 mg glycopyrolate intramuscularly half an hour before the surgery, the patients were administered the study drug (i.e. inj. nalbuphine) intravenously according to their respective groups five minutes before scheduled surgery i.e.:-

Group A patients received 100µg//kg nalbuphine intravenously.

Group B patients received 150µg/kg nalbuphine intravenously.

A uniform anaesthetic technique was used in all the two groups. After 3 mins of pre-oxygenation with 100% oxygen, anaesthesia was induced with intravenous 1% injection propofol at 1.5 mg/kg and intravenous succinylcholine 2mg/kg was given to facilitate endotrachael intubation. Anaesthesia was maintained with N_2O and O_2 with traces of isoflurane and intermittent positive pressure ventilation (IPPV) along with intermittent doses of intravenous non depolarising muscle relaxant (NDMR). During laryngoscopy and endotracheal intubation, the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure changes were recorded at baseline, after the study drug, after intubation, 1, 2, 3, 4, 5 and 10minutes.Side effects (if any)were recorded in detail and the findings of the study entered in proforma prepared for the study.

The collected data were analysed by using windows based statistical package for social sciences (SPSS) version 21.0(Armonk, NY: IBM Corp.). Appropriate statistical analysis of the data was done using student't' test for continuous variables and Chi square (χ^2) test for the categorical variables; $p<0.05$ was considered statistically significant.

III. Results

The demographic and ASA distribution between the two groups are shown in Table 1 and were comparable in both the groups. The mean ± SD of the heart rate between the two groups i.e group A and group B and the percentage of rise from the baseline values are shown in table 2 and 3. It was observed there that there was no significant rise in the mean heart rate ($p>0.05$). However, the intragroup changes in each of the group A and group B, were significant at induction ($p<0.001$) and one minute thereafter ($p=0.01$).

Table 1. Showing the demographic profile of group A & group B

Parameters	**Group A**	**Group B**	t-test	p-value
Age (years) (Mean±SD)	38.50 ± 2.34	41.17 ± 2.57	0.7	0.4
Weight(Kg.) (Mean±SD)	55.20 ± 1.76	55.3 7± 1.47	0.07	0.9
M:F	4:26	5:25		
ASA I:II	11:19	10:20		

Table 2. Showing the comparison of mean heart rate between group A & group B (Intergroup) at different time points (Mean±SD and the % changes)

Parameters	**Group A**		**Group B**		't' test	P value
	Mean±SD bpm	%change from baseline	Mean±SD bpm	% change from baseline		
HRb	89.10±3.58		86.83±2.83		0.491	0.627
HRs	87.46±3.28	-2.25	85.76±2.92	-1.16	0.399	0.693
HRi	98.46±2.96	+10.11	96.63±3.09	+11.63	0.393	0.697
HR1	93.30±3.04	+4.50	93.70±3.04	+8.14	-0.087	0.931
HR2	89.16±2.84	0	92.10±3.63	+6.98	-0.604	0.551
HR3	84.16±2.60	-5.61	87.33±3.11	+1.16	-0.770	0.447
HR4	83.33±2.68	-6.74	85.33±2.84	-1.16	-0.481	0.634
HR5	81.80±2.52	+8.99	84.53±2.80	-2.33	-0.677	0.504
HR10	82.93±2.53	-7.87	83.43±2.40	-3.49	-0.143	0.887

($p<0.05$, considered significant; HR- heart rate; b-baseline; s-study drug; i-laryngoscopy & intubation;1-1 min, 2-2 min, 3-3 min, 4-4 min, 5-5min &10 -10 min – time intervals after intubation)

Table 3: Showing the intragroup comparison of heart rate with the base line value at different time point in the Group A and Group B

Parameters	**Group A**		**Group B**	
	p-value	't' test	p-value	't' test
HRb– HRs	0.96	0.34	0.77	0.45
HRb–Hri	2.94	0.01	4.27	0.00
HRb - HR1	1.53	0.14	2.63	0.01
HRb - HR2	0.03	0.98	1.61	0.12
HRb - HR3	1.85	0.08	0.19	0.85
HRb - HR4	2.00	0.06	0.59	0.56
HRb - HR5	2.35	0.03	0.98	0.33
HRb - HR10	1.82	0.08	1.45	0.16

($p<0.05$, considered significant;HR- heart rate; b-baseline; s-study drug; i-laryngoscopy &intubation;1-1 min, 2-2 min, 3-3 min, 4-4 min, 5-5min &10 -10 min – time intervals after intubation)

The intergroup comparison of the mean ±SD of systolic blood pressure between group A and group B and the percentage of rise from the baseline value are shown in table 4. It was observed there that there was no significant rise in the mean systolic blood pressure ($p>0.05$) between the groups. Table 5 shows the intragroup comparison from the baseline at various time intervals, and the changes were statistically significant ($p<0.05$) at various time intervals post laryngoscopy and intubation. Similar trend was found in mean arterial pressure (Fig. 1) except insignificant finding in the 10^{th}minute post laryngoscopy and intubation.

Table 4. Showing the intergroup comparison of systolic blood pressure between group A and group B at different time points(Mean±SD and the % changes)

Parameters	**Group A**		**Group B**		't' test	P value
	mean±SD mmHg	% change from baseline	mean±SD mmHg	% change from baseline		
SBPb	129.20 ± 2.73		131.90 ±3.25		-1.24	0.22
SBPs	121.47 ± 2.65	-6.20	119.27 ±2.33	-9.16	-0.31	0.75
SBPi	137.13 ± 2.86	+6.20	139.70 ±3.55	+6.11	-1.17	0.24
SBP1	119.93 ± 2.60	-7.75	123.87 ±3.18	-6.11	-1.39	0.17
SBP2	111.63 ± 2.81	-13.95	113.30 ±2.12	-13.74	-1.07	0.29
SBP3	111.87 ± 3.26	-13.95	109.77 ±1.90	-16.79	-0.17	0.86
SBP4	112.60 ± 3.24	-13.17	108.47 ±2.07	-17.56	0.16	0.87
SBP5	113.37 ± 3.08	-12.40	112.20 ±2.20	-14.50	-0.48	0.62
SBP10	122.33 ± 3.15	+5.43	121.47 ±3.58	-7.63	-0.45	0.65

($p<0.05$, considered significant; SBP-systolic blood pressure; (b-baseline; s-study drug; i-laryngoscopy &intubation; 1-1 min, 2-2 min, 3-3 min, 4-4 min, 5-5min &10 -10 min – time intervals after intubation)

Table5: Showing the intragroup comparison of SBP with the baseline value at different time points between Group A and Group B

Parameters	**Group A**		**Group B**	
	p-value	't' test	p-value	't' test
SBPb - SBPs	4.28	0.00	5.65	0.00
SBPb - SBPi	2.85	0.01	2.65	0.01
SBPb - SBP1	3.06	0.01	2.22	0.03
SBPb - SBP2	4.95	0.00	6.16	0.00
SBPb - SBP3	4.58	0.00	6.32	0.00
SBPb - SBP4	4.57	0.00	6.21	0.00
SBPb - SBP5	4.31	0.00	5.39	0.00
SBPb - SBP10	1.77	0.09	2.60	0.02

(p<0.05, considered significant; b-baseline; s-study drug; i-laryngoscopy & intubation; 1-1 min, 2-2 min, 3-3 min, 4-4 min, 5-5min and 10 -10 min – time intervals after intubation)

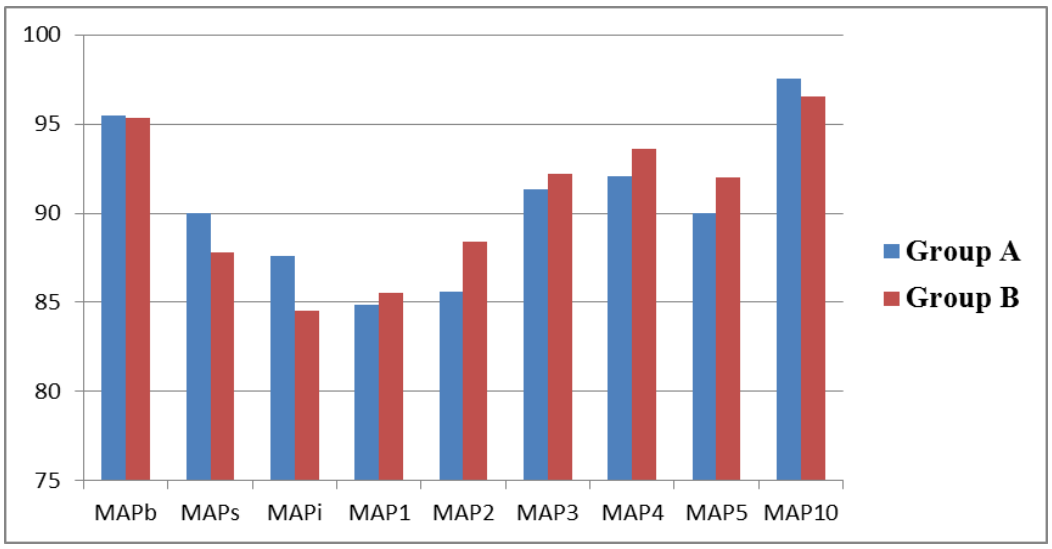

Fig. 1.Change in mean arterial blood pressure at various time intervals between the two groups

The sedation score and the time to first rescue analgesic (TFAR) are shown in Fig. 2. The Ramsay Sedation Score measured in the post anaesthetic care unit in the two groups were comparable with a sedation score of 1.27 ± 0.08 and1.37 ±. 09 in group A and B respectively (p=0.4). The time to first rescue analgesic were115.50 ± 2.88 min. and 115.97 ± 2.40 min. in group A and group B respectively (p=0.9).

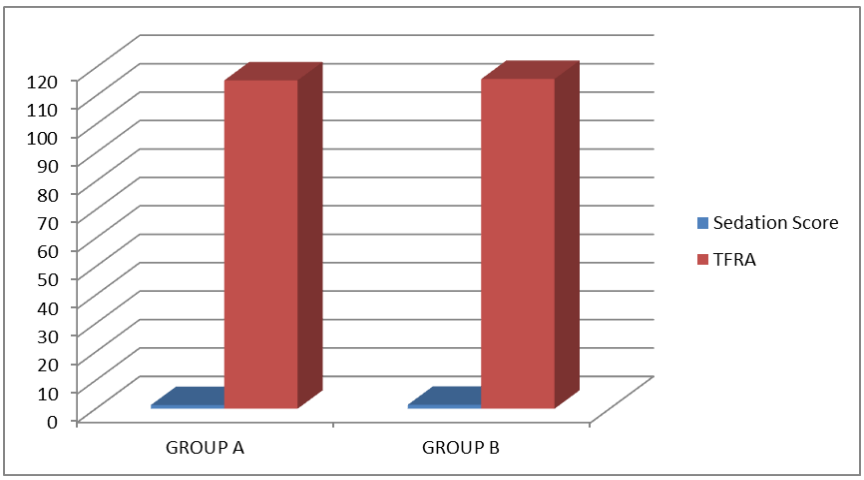

Fig. 2. Showing sedation score and time of first rescue analgesia between the two groups

IV. Discussion

Laryngoscopy and intubation alter cardiovascular physiology as a reflex sympathetic response to the mechanical stimulation of the trachea and larynx. These responses are manifested as various cardiovascular changes such as tachycardia, hypertension, dysrythmias, increased circulatory catecholamines and myocardial ischemias[11]. Studies had found that this changes is due to the reflex symphatho-adrenal stimulation[12].The increase in plasma catecholamine concentration during endotracheal intubation is associated with both non adrenergic and adrenergic responses which suggest an increase in sympathoadrenal activity. In absence of measures to prevent the haemodynamic response, the heart rate can increase from 26% to 66%[13] and arterial pressure can increase from 36% to 45%[14,15] during laryngoscopy and intubation, which peaks in 1-2 min, returning to the baseline by 5 min.[16] This pressure response occurring at laryngoscopy and intubation is due to the augmented sympathetic response provoked by stimulation of epipharynx and laryngopharynx.[14,17] These responses are well tolerated in healthy individuals, but, may increase mortality and morbidity in patients with coronary artery diseases, vascular anomalies and intracranial diseases.[18]

In this present study, the demographic variables of the two groups i.e. Group "A" patients receiving 100µg//kg and Group "B" patients receiving 150µg/kg nalbuphine intravenously were comparable with respect to the age, weight and ASA status ($p>0.05$), with a female gender preponderance.

Dhabi PG et al[19] in their study observed significant rise in heart rate (34.17%) in the Control group at 1 minute after intubation from baseline as compared to 18.75% in nalbuphine group. Similar findings were observed by Tariq AM et al[20] and Chowda PM et al[21] with nalbuphine 0.2mg/kg; however, they found lesser rise in heart rate as compared to the control group (p value >0.05). In another study by Sharma Net al[5], there was 12.5% increase in heart rate during intubation with nalbuphine 0.2µg/kg compared to fentanyl group at 2µg/kg .On the other hand, Bhandari et al[22],in their study found an increase of in heart rate (6%) from baseline value of 89.83±1.48bpm to 95.33±16.99bpm during intubation in nalbuphine group. These findings were comparable with the findings of our study, where we observed an increase in the heart rate(10%) in group A from 89.10±3.58 to 98.46±2.96 bpm and in group B from 86.83±2.83 bpm to 96.63±3.09bpm(11%), which was statistically insignificant($p>0.05$). Moreover, the changes in the heart rate were transient and it came down to the baseline after 2-3 minutes of intubation.

In our study, we observed a rise in systolic blood pressure during laryngoscopy and intubation in both the groups compared to the baseline value ($p=0.01$). In group A, the systolic blood pressure rose from the baseline value of 129.20±2.73 to137.13±2.86 mm Hg(6%)as compared to group B from 131.90±3.25 to 139.70±3.55mm Hg(6%; $p>0.05$). It came down to baseline from 1 minute after intubation. These findings are comparable with the findings of Nath R et al.[8] , who compared nalbuphine 0.1mg/kg and 0.2mg/kg and found that the systolic blood pressure and diastolic blood pressure increased in both the groups just after intubation but the increase was not significant($p>0.05$).

Sharma Net al[5] in their study found that the increase in blood pressure was more in nalbuphine group than in the fentanyl group. Here, in our study, there was transient rise in systolic blood pressure in both group A (100µgm/kg) and group B (150µgm/kg) during laryngoscopy and intubation but it came down to the baseline value after 1minute of intubation.

In our study, the mean arterial pressure(MAP) dropped from 95.55±2.43 to 87.60±2.46 mmHg(8%) in group A as compared to group B from 95.33±2.40 to 84.53±2.77mm Hg(11%) during intubation ($p>0.05$) but was significantly decreased when compared to the baseline in both the groups($p=0.02$). This is in agreement to the study of Ahsan et al,[23] where MAP decreased by 10.5% in the nalbuphine group.

A non-significant fall ($p>0.05$) in the heart rate(HR) and all the three parameters of blood pressure(SBP, DBP and MAP) were observed with both doses of nalbuphine, which could be attributed to the predominant kappa receptor agonistic action of nalbuphine.[24,25]In contrast to our findings, where there was a fall in all the hemodynamic parameters compared with the baseline, Kay B et al[26] observed that the responses were reduced after nalbuphine, however, a tachycardia still occurred and concluded that nalbuphine 0.3mg/kg is only partially effective in reducing the cardiovascular responses to laryngoscopy and intubation. The inadequate effect of nalbuphine in attenuating the hemodynamic responses in their study could be due to the fact that it was administered only two minutes before the intubation, and this short interval may not have allowed sufficient time to obtain the maximum effect. The two groups had almost equal duration of postoperative analgesia period (115.50±2.88 and 115.97±2.4 min ($p=0.9$) and a sedation score of 1.27±0.08 versus 1.37±0.09($p=0.4$) with no incidence of opioid side effects especially respiratory depression and pruritus.

V. Conclusion

It may be concluded from the present study that nalbuphine in the two low doses i.e. intravenous 100µg//kg and150µg//kg administered 5 minutes before induction of anaesthesia effectively reduced tachycardia, hypertension associated with laryngoscopy and intubation.

The findings were comparable in both the groups without any statistically significant difference; however, there was statistically significant attenuation of haemodynamic response at various time intervals in both the groups when compared to the baseline. It also provided good intra operative haemodynamics and adequate postoperative analgesia.

Limitations and future directions

There are some limitations to our study: we did not compare the use of the drug in emergency cases or in more prolonged surgeries i.e.in ASA III and IV and emergency procedures. There is need for more studies to assess the benefit and drawback, if any, or its use in various facets of pain, and also administration of the different doses of the drug at different time intervals for attenuation of haemodynamic responses during laryngoscopy and intubation.

References

[1]. Kitamura T, Yamada T, Chine M, Du HL, Hamaoka K. Attenuation of hemodynamic response to tracheal intubation by StyletScope. Br. J Anaesth 2001; 86:275-7.
[2]. Derbyshire DR, Chmielewski A, Fell D, Vater M, Achola K, Smith G.Plasma catecholamine responses to tracheal intubation. Br J Anaesth 1983; 55(9):855-60.
[3]. Kanchi M, Nair HC, Banakal S, Murthy K, Murugesan C. Haemodynamic response to endotracheal intubation in coronary artery disease: Direct versus video laryngoscopy Indian J Anaesth 2011; 55(3): 260–5.
[4]. Singhal S, Neha. Haemodynamic response to laryngoscopy and intubation: comparison of McCoy and Macintosh laryngoscope. The Internet J Anesth 2007; 17:1-5.
[5]. Sharma N, Parikh H. A comparative study of hemodynamic responses to intubation: fentanyl versus nalbuphine. Guj Med Jour 2014; 69(2):48-53.
[6]. Klepper ID, Rosen M, Vickers MD, Mapleson WW. Respiratory function following nalbuphine and morphine in anesthetized man. Br J Anaesth 1986; 58:625-9.
[7]. Lake CL, Duckworth EN, Difazio CA, Magruder MR. Cardio respiratory effects of nalbuphine and morphine premedication in adult cardiac surgical patients. ActaAnaesthesiolScand 1984; 28:305-9.
[8]. Nath R, Dutta S, Khandelwal A. Attenuation of hemodynamic response during laryngoscopy and intubation with low dose intravenous nalbuphine. J HematolTransfus 2015; 3(1):1036-9.
[9]. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol 2011; 27:339-43.
[10]. Gomaa HM, Mohamed NN, Zoheir HAH, Ali MS. A comparison between post-operative analgesia after intrathecalnalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after caesarean section. Egyptian J Anaesth.2014; 30:405–10.
[11]. Kavoc AL Controlling hemodynamic response to laryngoscopy and endotracheal intubation. JClinAnesth. 1996; 8(1):63-79.
[12]. McCoy EP, Mirakhur RK, McCloskey BV. A comparison of the stress response to laryngoscopy. The Macintosh versus the McCoy blade.1995; 50(11) : 943-6.
[13]. Malde A, Sarode V. Attenuation of hemodynamic response to endotracheal intubation: fentanyl versus lignocaine. The Internet Journal of Anaesthesiology.2006; 12(1). Available from http://ispub.com/IJA/12/1/10964. Last accessed on 12 June 2017
[14]. Prys Roberts C, Greene LT, Meloche R, Foex P. Studies of anaesthesia In relation to hypertension II: Hemodynamic consequences of induction and endotracheal intubation. Br J Anaesth 1971; 43:531-46.
[15]. Chung KS, Sinatra RS, Halevy JD, Paige D, Silverman DG. A comparison of fentanyl, esmolol and their combination for blunting haemodynamic responses during rapid sequence induction. Can J Anaesth. 1992; 39(8):774-9.
[16]. Handerson J. Airway management in the adult. In. Miller RD, Eriksson LI ,Flieisher LA, Wiener-Kronish JP, Young WL, editors. Miller's anesthesia.7th ed. Philadelphia: Churchill Livingstone; 2009. p .1573-1610.
[17]. Burstein CL, Lopinto FJ, Newman W. Electrographic studies during endotracheal intubation: Effects during usual routine techniques. Anaesthesiology 1950; 11:224.
[18]. Low JM, Harvey JT, Prys- Roberts C, Dangio J. Studies of anaesthesia in relation to hypotension.VII: Adrenergic responses to laryngoscopy. Br J Anaesth 1986;58(5):471-7
[19]. Dabhi PG, Mehta S , Golwala MP, Upadhyay MR, BumiyaRG.Effect of intravenous nalbuphine on haemodynamic response to laryngoscopy and intubation. Int. J Res Med. 2014; 3(4):24-7.
[20]. Tariq AM, Iqbal Z, Qadirullah. Efficacy of nalbuphine in preventing haemodynamic response to laryngoscopy and intubation. J Postgrad Med Inst 2014; 28(2):211-6.
[21]. Chawda PM, Pareek MK, Mehta KD. Effect of Nalbuphine on Haemodynamic Response to Orotracheal Intubation. J AnaesthesiolClinPharmacol. 2010; 26(4): 458–60.
[22]. Bhandari R, Rastogi S, Tyagi A, Joshi A, Malik N, Sachdeva A, Shomik. Attenuation of haemodynamic response to endotracheal intubation with nalbuphine and fentanyl: A comparative study. J Evol Med Dental Sci 2015; 4(64): 11172-181.
[23]. Ahsan-ul-HaqM, Kazmi EH, Rao ZA. Nalbuphine prevents haemodynamic response to endotracheal intubation. J Col PhysSurg Pak 2005; 15(11):668-70.
[24]. 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; 7(3): 326–30.
[25]. Singh M. Stress response and Anesthesia, Altering the peri and post-operative management. Indian J Anaesth 2003;47:427-34.
[26]. Kay B , Healy TE, Bolder Pm .Blocking the circulatory response to direct laryngoscopy and intubation, comparison of fentanyl and nalbuphine. Anaesthesia 1985; 40(10):960-3.

Dr. Dr. Takhelmayum Hemjit Singh. "Low Dose Nalbuphine in Attenuation of Hemodynamic Responses to Laryngoscopy and Intubation – A Study." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 1, 2019, pp 32-37.