ORIGINAL RESEARCH PAPER

Anaesthesiology

A CLINICAL COMPARATIVE STUDY BETWEEN INTRAVENOUS NALBUPHINE VERSUS INTRAVENOUS DEXMEDETOMIDINE IN ATTENUATING THE HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND INTUBATION

KEY WORDS: Nalbuphine, Dexmedetomidine, Endotracheal Intubation, Haemodynamic response, VAS Score.

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ABSTRACT

Background:-The haemodynamic stress during laryngoscopy and intubation may have detrimental effects in high risk patients.The objective of this study is to compare the analgesic potential, any side effects and the attenuation of haemodynamic response by Nalbuphine and Dexmedetomidine to laryngoscopy and endotracheal intubation.

Methods:-80 patients, aged 18–60 years,of ASA grade I and II were randomly divided into two groups of 40 each. Group A received Inj.Nalbuphine 0.2mg/kg body weight slow i.v. and Group B received Inj.Dexmedetomidine 1µg/kg body weight in 100ml Normal saline (NS) i.v. over 10 min, at 3 min prior to intubation. The baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) & SpO2% were recorded. Thereafter, haemodynamic parameters and post-operative complications were recorded at various intervals. Postoperative analgesia was assessed by VAS score.

Results:-Intraoperatively there was no significant difference in the heart rate, SBP and DBP of patients of both the groups (P-value > 0.05). However, there was a transient rise in SBP and DBP, and a fall in HR at just immediately after the administration of Dexmedetomidine in Group B (P-value < 0.05). The mean duration of analgesia in Nalbuphine group was 5hours 15min and that of Dexmedetomidine group was 2hours 50min and with minimal side effects in both the groups.

Conclusion:-Both the study drugs - Nalbuphine 0.2mg/kg and Dexmedetomidine 1µg/kg were effective in attenuating the haemodynamic response to laryngoscopy and intubation. Duration of analgesia and post operative analgesia were better in Nalbuphine group in our study and with minimal side effects in both the study groups.

INTRODUCTION

The process of laryngoscopy and intubation, a noxious stimulus, constitutes a period of extreme haemodynamic stress and is associated with intense sympathetic activity marked by tachycardia and hypertension which is described as reflex sympathoadrenal stimulation (King et al., 1951 (1). The pressor response and heart rate increases by 36% and 19% respectively from pre-induction control levels with the act of tracheal intubation (Shribman et al. 1987 (2)

An opioid agonist-antagonist, Nalbuphine, a kappa (κ) agonist and partial mu (µ) antagonist, is used for attenuation of circulatory response to endotracheal intubation. Nalbuphine is equal in potency as an analgesic to morphine and one fourth potent as nalorphine as an antagonist, with cardiovascular stability, longer duration of analgesia, minimal respiratory depression, lesser nausea and vomiting and potential safety in overdose (Fragen et al.1977 (3) Lake et al. 1984 (4) Klepper et al. 1986 (5). The alpha-2 agonists like Clonidine (Kulka et al. 1995 (6) and Dexmedetomidine (Getler et al. 2001 (7) have also been used for attenuating the sympathetic response to laryngoscopy and intubation. The intravenous Dexmedetomidine as premedicant in the anaesthesia setting provides advantages of sedation, analgesia, anxiolysis and improved haemodynamic stability (Hall et al. 2000 (8)

The objective of this study is to compare the analgesic potential, any side effects and the attenuation of haemodynamic response by Nalbuphine and Dexmedetomidine to laryngoscopy and intubation.

Materials and Methods

The study was undertaken in Silchar Medical College and Hospital, Silchar, Assam, from June 1st, 2017 to May 31st, 2018, after obtaining Institutional Ethical Committee clearance and written informed consent from the patients. A randomized single blinded prospective study involving 80 patients of both sexes requiring endotracheal intubation and general anaesthesia for various elective surgical procedures belonging to ASA grade I and II were included in the study.

Inclusion criteria:

1) Patients aged between 18-60 years,
2) Patients of either sex,
3) Patients with ASA grade I and II,
4) Patients scheduled for elective surgical procedure under general anaesthesia.

Exclusion criteria:

1. Refusal to informed consent,
2. Anticipated difficult airway,
3. ASA grade III and IV,
4. Allergy to study drugs,
5. Patients with cardiovascular, respiratory, renal, hepatic and neuromuscular system disorders.
6. Pregnant and lactating women.

On the day prior to the scheduled date of proposed surgery, the General Physical Status & Systemic examination, ASA Grading, Airway assessment and routine investigations were performed in all patients.

80 patients were randomly divided into 2 groups and each group consisted of 40 patients.

1) Group A - Nalbuphine Group – received Nalbuphine 0.2mg/kg body weight i.v. slowly, 3minutes before induction.

2) Group B - Dexmedetomidine Group – received Dexmedetomidine 1µg/kg body weight diluted in 100ml normal saline i.v. over 10minutes, 3minutes before induction.

The baseline pulse rate, SBP, DBP & SpO2 % were recorded (T0) and an IV line was secured. Patients were pre-medicated with Inj. Ondansetron 4mg, Inj. Ranitidine 50mg and Inj. Glycopyrrolate 0.2mg. The study drugs were administered and the patients were pre-oxygenated with 100% oxygen for 3minutes. Induction of anaesthesia was done with inj. Propofol 2mg/kg body wt. i.v. and muscle relaxation was achieved with inj. Succinylcholine 1mg/kg body wt. i.v. Patients were intubated with appropriate sized cuffed endotracheal tube following standard laryngoscopy, which was accomplished within 15-20seconds. Anaesthesia was maintained

with mixture of N2O and O2 with Sevoflurane and muscle relaxation was maintained with intermittent dosage of Inj. Atracurium. After the commencement of the surgical procedure, infusion Paracetamol 15mg/kg body wt. was also infused to the patients. Hemodynamic parameters such as pulse rate, SBP, DBP and SpO2% were recorded in all patients after injecting the study drug (T) and just after induction (T1). Then all patients were observed for pulse rate, SBP, DBP, EtCO2 & SpO2% at 1min (T2), 5min (T3) and at 10min (T4) after laryngoscopy & intubation, and thereafter at every 30min interval till completion of the surgery.

At the end of surgery, when patients had respiratory efforts, residual neuromuscular blockade was reversed with Inj. Neostigmine 0.05mg/kg & Inj. Glycopyrrolate 0.01mg/kg i.v. Recovery assessement & extubation were done after thorough laryngeal suction. The patients were shifted to the post op. ward, and the pulse rate, SBP, DBP, Ramsay sedation score, Visual analogue score (VAS), post op. nausea and vomiting (PONV) and other side effects (if any) were recorded at every 30min interval till 120min and thereafter at 1hr interval till 12hr post op. or till requirement of analgesia (VAS ≥ 4), whichever was the earlier.

STATISTICAL METHOD EMPLOYED

All data were presented as Mean ± SD (Standard Deviation). All Quantitative data were assessed using Student's t - test to analyze changes over a period of time. Qualitative data were assessed using Fisher exact Test or Chi- square test. The P-value <0.05 was considered Statistically Significant (S). The statistical software Graphpad Insat-3 ® was used for the analysis of data and Microsoft Word ® and Microsoft Excel ® had been used to generate graphs, tables, etc.

RESULTS

The mean age, weight, height and duration of surgery of both the groups were comparable. There was no significant difference amongst the groups with regard to demographic variables (P-value > 0.05).

Although immediately after drug administration, the heart rate increased in Group A and decreased in Group B (P-value < 0.0001), the heart rate gradually stabilized at near or below the baseline value during the intra operative period in both the groups. Intraoperatively, there was no significant difference in the heart rate of both the groups (P-value >0.05).

There was an increase in SBP in Group B and a decrease in the SBP in Group A (P-value < 0.0001) immediately after study drug administration. Thereafter, there was no significant difference in the SBP of both the groups (P-value > 0.05) during the intra operative period.

There was also an increase in DBP in Group B and a decrease in DBP in Group A (P-value < 0.0001) immediately after the drug administration. Thereafter, there was no significant difference in DBP of both the groups during the intra operative period (P-value > 0.05), except at 70min after intubation (T6) there was a quite significant difference in DBP in both the groups (P-value < 0.05).

Post-operatively, rescue analgesia was given when the VAS score was > 4 after the completion of the surgery. In our study, the mean time of first rescue analgesia was earlier in Group B in comparison to the Group A. The mean duration of analgesia was 5 hours 15 min (approx) in Group A and 2 hours 50 min (approx) in Group B.

In our study, 5 patients had PONV in Group A, and 3 patients had bradycardia, 2 had hypotension and 3 had PONV in Group B. On comparison of the side effects, no significant differences were found between both the groups (P-value > 0.05). Other side effects like respiratory depression, muscle rigidity, pruritus and dryness of mouth were not seen in both groups.

Table-1:- Demographic characteristics

Sl. No.	Particulars	Group A	Group B	P – Value
		Mean + SD	Mean + SD	
1	Age (in years)	39.27 + 10.56	39.47 + 11.80	0.9366
2	Sex (Male/Female)	18/22	16/24	0.8213
3	ASA (I/II)	33/7	35/5	0.7555
4	Weight (kg)	62.85 + 7.87	63.77 + 6.99	0.5803
5	Height (cm)	164.60 + 3.54	163.98 + 3.41	0.4243
6	Types of Surgery			
	Open Cholecystectomy	10	8	
	Lap. Cholecystectomy	6	9	
	Appendicectomy	4	3	
	Fibroadenoma Excision	4	6	
	Hernioplasty	5	6	
	Tonsillectomy	4	3	
	Diagnostic Laparoscopy	7	5	
7	Duration of Surgery (min)	80.13 + 9.23	76.25 + 9.39	0.0665

Table-2:- Comparison of mean heart rate in between two groups.

Study Period	Heart Rate (beats/min)				P-value
	Group A		Group B		
	Mean	SD	Mean	SD	
T0	82.07	3.72	83.15	4.81	0.2673
T	83.70	2.71	75.30	7.70	<0.0001
T1	85.47	3.28	84.22	3.79	0.1194
T2	81.75	3.16	83.15	4.09	0.0914
T3	82.15	3.77	82.30	5.16	0.8825
T4	81.05	2.23	82.20	4.85	0.1775
T5	80.97	3.73	81.47	5.36	0.6298
T6	81.80	4.15	81.87	3.37	0.9296
Just after extubation	84.95	5.52	85.65	3.69	0.5073
30 min after extubation	83.77	4.78	84.77	3.46	0.2875
60 min after extubation	82.02	2.92	83.05	4.52	0.2323
90 min after extubation	82.52	2.89	83.52	4.98	0.2759
120 min after extubation	81.40	2.65			
3 hours after extubation	81.55	2.61			
4 hours after extubation	81.67	2.30			

Table-3:- Comparison of mean systolic blood pressure in between two groups.

Study Period	Systolic BP (mm Hg)		P value
	Group A	Group B	

	Mean	SD	Mean	SD	
T0	130.33	3.71	129.78	2.62	0.4464
T	127.13	3.16	138.05	7.68	< 0.0001
T1	127.05	2.36	127.08	2.86	0.9661
T2	129.83	2.98	131.28	4.21	0.0796
T3	126.03	3.13	126.20	4.09	0.8305
T4	125.38	2.43	126.20	2.77	0.1616
T5	124.33	2.74	124.15	5.17	0.8507
T6	123.05	2.70	121.63	7.21	0.2459
Just after extubation	127.93	4.00	125.80	3.47	0.0132
30 min after extubation	125.60	3.46	124.50	6.39	0.3418
60 min after extubation	125.75	3.59	124.25	4.33	0.0958
90 min after extubation	126.33	2.99	124.73	5.04	0.0883
120 min after extubation	127.18	2.59			
3 hours after extubation	127.30	2.55			
4 hours after extubation	127.75	2.29			

Table 4:- Comparison of mean diastolic blood pressure between the two groups.

Study Period	Diastolic BP (mm Hg)				P- value
	Group A		Group B		
	Mean	SD	Mean	SD	
T0	78.47	5.38	78.87	5.50	0.7435
T	78.27	4.74	86.35	3.78	< 0.0001
T1	77.97	5.29	79.05	3.18	0.2746
T2	79.05	4.88	80.65	3.90	0.1096
T3	77.82	4.46	78.15	4.01	0.7331
T4	77.77	4.36	78.87	2.53	0.1720
T5	78.27	2.67	78.52	4.26	0.7542
T6	78.22	2.42	79.47	2.13	0.0166
Just after extubation	82.17	2.34	83.32	3.78	0.1063
30 min after extubation	80.47	1.72	80.85	2.27	0.4081
60 min after extubation	80.20	1.72	80.77	2.22	0.2005
90 min after extubation	79.35	2.57	79.95	2.53	0.2968
120 min after extubation	79.47	2.52			
3 hours after extubation	79.67	2.49			
4 hours after extubation	79.62	2.59			

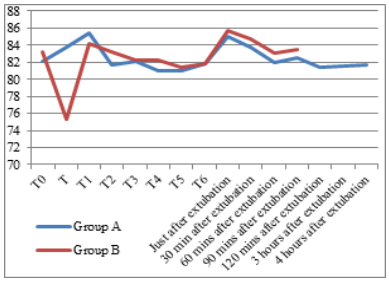

Figure 1 – Line diagram showing comparison of mean heart rate between the two groups.

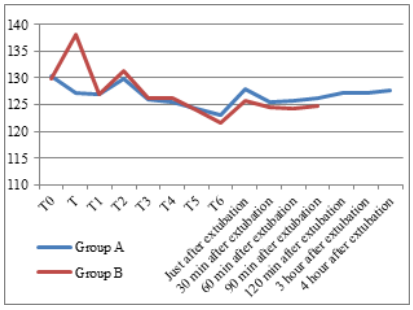

Figure 2 – Line diagram showing comparison of mean systolic blood pressure between two groups.

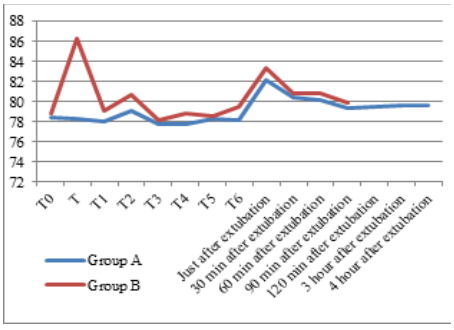

Figure 3 – Line diagram showing comparison of mean diastolic blood pressure between the two groups.

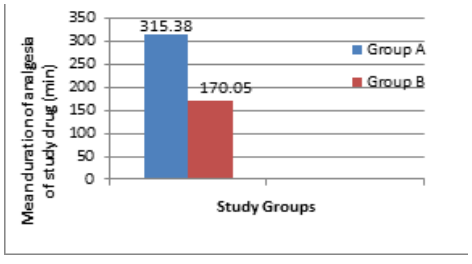

Figure 4 - Bar diagram showing the mean duration of analgesia of the study drug between the two groups.

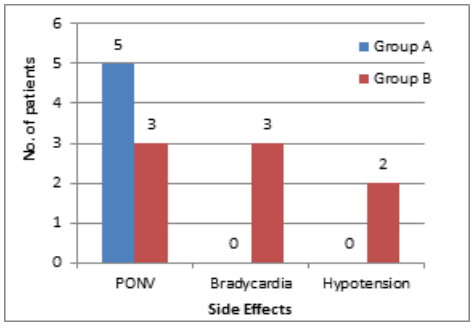

Figure 5 - Bar diagram showing side effects in between two groups.

DISCUSSION

Although the elevation in blood pressure and heart rate due to laryngoscopy and intubation are brief, they may have detrimental effects in high risk patients including myocardial infarction, cardiac failure, intracranial haemorrhage and increase in intracranial pressure (Prys-Roberts et al. 1971 (9) Shapiro et al. 1972 (10) Attempts have been made to suppress the circulatory response using various pharmacological agents aimed at afferent, efferent or both limbs of response.

Nalbuphine, a kappa-agonist and partial μ-antagonist, is used for attenuation of haemodynamic response to endotracheal intubation. Nalbuphine produces analgesia with a ceiling effect on sedation and respiratory depression. Its cardiovascular stability, longer duration of analgesia, minimal respiratory depression with an ability to antagonize μ-agonist induced respiratory depression, less nausea and vomiting, low abuse potential and potential safety in overdose makes it suitable as a component in balanced anaesthesia.

Various studies like Ahsan et al. 2005 (11) Chawda et al. 2010 (12) and Kothari et al. 2013 (13)have found that Nalbuphine 0.2mg/kg prevented a marked rise in heart rate and mean arterial pressure associated with laryngoscopy and endotracheal intubation which was comparable to our study in attenuation of haemodynamic response by Nalbuphine to intubation.

Recently alpha-2 agonists like Clonidine and Dexmedetomidine have been tried for suppressing the haemodynamic response to intubation without any of the side effects like respiratory depression or increased incidence of PONV. Clonidine is less potent (alpha-1 : alpha-2=1:220) as compared to Dexmedetomidine (alpha-1 : alpha-2=1:1620) in its agonism to alpha-2 receptors (Yildiz et al. 2006 (14). Dexmedetomidine has been found by various authors like Jaakola et al.1992 (15) and Keniya et al.2011 (16) to blunt the haemodynamic response to laryngoscopy and intubation. However, a biphasic effect (Bloor et al 1992 (17) on blood pressure with higher doses (1–4 mcg/kg) of Dexmedetomidine is seen which is characterized by an initial increase and followed by a decrease. This attributes to the initial hypertensive response after the drug administration via the alpha-2B receptors stimulation present in vascular smooth muscles which settles once there is decrease in central sympathetic outflow (Sudheesh et al. 2011)[18].

In our study, we have found that although there was an initial fall in heart rate and a transient rise in SBP and DBP in patients receiving Dexmedetomidine immediately after drug administration, it was observed that the degree of haemodynamic response to laryngoscopy and endotracheal intubation was significantly lower in both Nalbuphine and Dexmedetomidine Group. This was comparable to the study of Patel CR et al. 2016 (19) The biphasic response of Dexmedetomidine 1μg/kg with a transient increase in blood pressure and a reflex decrease in heart rate observed in our study was also comparable to the study of Hall JE et al.[8]

Rescue analgesia was given when the VAS score was > 4 after the completion of the surgery. In our study, the mean time of first rescue analgesia was earlier in Group B than that of Group A. The duration of analgesia was calculated from just after the time of study drug administration to the time of first rescue analgesia. The mean duration of analgesia was 5 hours 15 min (approx) in Group A and 2 hours 50 min (approx) in Group B which is comparable to the results of other studies (Patel CR et al. 2016 (19) Badheka et al. 2016 (20). The study of Jaakola et al 1992 (15) found that Dexmedetomidine had a moderate analgesic effect and found that the use of fentanyl supplements during anaesthesia was less frequent in Dexmedetomidine group.

In our study, 5 patients had PONV in the Nalbuphine group and in Dexmedetomidine group, 3 patients had bradycardia, 2 had hypotension and 3 had PONV in the post op. period which has been reported in other study (Patel CR et al. 2016 (19). The PONV was treated with inj. Ondansetron 0.1mg/kg, bradycardia with inj. Atropine 0.6mg and hypotension with i.v crystalloids. Other side effects like respiratory depression, muscle rigidity, pruritus and dryness of mouth were not seen in our study in both the groups.

CONCLUSION

In this study, although, immediately after administration of Dexmedetomidine, there was a transient rise in SBP and DBP and fall of heart rate, it was observed that the degree of haemodynamic response to laryngoscopy and endotracheal intubation was significantly lower in both Nalbuphine and Dexmedetomidine Group. Hence, both the study drugs-Nalbuphine 0.2mg/kg and Dexmedetomidine 1μg/kg were effective in attenuating the haemodynamic response to laryngoscopy and intubation. Duration of analgesia was found to be longer and better post operative analgesia in Nalbuphine group in our study. There were minimal side effects with no significant difference in both the groups.

Financial support and sponsorship- Nil
Conflicts of interest- There are no conflicts of interest.

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