Role of IV Nalbuphine in attenuation of haemodynamic response to laryngoscopy and endotracheal intubation

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Abstract

Background: Laryngoscopy and endotracheal intubation evoke a haemodynamic response leading to increased heart rate and blood pressure. Purpose of present study was to evaluate the efficacy of Nalbuphine for attenuation of haemodynamic response to laryngoscopy and intubation.

Methods: 120 patients belonging to ASA Grade I and II, posted for elective laparoscopic surgery under general anaesthesia were included in this double blind prospective randomised study. Patients were randomly allocated in two groups to receive either injection Nalbuphine IV 0.2mg/kg diluted to 5 ml with normal saline (Group N) or 5 ml normal saline (Group C), five minutes before induction. Monitoring of heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure was done at laryngoscopy and endotracheal intubation and 1, 3, 5, 7 and 10 minutes after laryngoscopy and endotracheal intubation.

Results: Increase in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure in Group N was lower than in Group C.

Conclusion: Intravenous Nalbuphine in the dose of 0.2 mg/kg appears to be a promising drug which can be used to attenuate the haemodynamic response to laryngoscopy and intubation.

Keywords: Nalbuphine, Haemodynamic response, Laryngoscopy, Intubation, Heart Rate and Mean arterial blood pressure.

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Introduction

Laryngoscopy and endotracheal intubation plays a pivotal role in the field of anaesthesiology. Laryngoscopy and endotracheal intubation is associated with various complications like increased heart rate and blood pressure. These effects were first described by Reid and Brace[1] in 1940. Pharyngolaryngeal stimulation augments sympathetic activity in the efferent fibres of heart. This explains the increase in plasma level of norepinephrine and epinephrine which occur during airway instrumentation[2]. Usually these transient changes have no deleterious effects in healthy individuals[3] but in patients with hypertension and ischaemic heart disease, laryngoscopy and intubation can cause serious complications[4].

Number of methods are used to attenuate the haemodynamic response to laryngoscopy and intubation that include various techniques[5], equipment[6,7,8] and drugs like B blockers[9,10], vasodilators[11,12,13], α2 agonists[14,15], opioids[16,17] and lignocaine[18]. Nalbuphine is agonist antagonist opioid acting on μ receptors as antagonist and on κ receptors as agonist with analgesic potency equal to morphine and antagonist potency is approximately one-fourth of nalorphine[19]. Onset of action is rapid when given intravenously (2 to3 minutes) with plasma half-life of 4 to 5 hours. Nalbuphine undergoes hepatic metabolism to pharmacologically inactive conjugates. The aim of this study was to evaluate the efficacy of Nalbuphine for attenuation of haemodynamic response to laryngoscopy and intubation.

Methods

After obtaining institutional ethical committee approval and written informed consent, 120 patients between 18 to 60 years of age, ASA Grade I and II undergoing elective laparoscopic surgery under general anaesthesia were included in the study. Patients with history of allergy to opioids, difficult intubation, cardiovascular disease, on antihypertensive drugs were excluded from the study. Patients with unanticipated difficult laryngoscopy and intubation were excluded from the study. Preanesthetic check-up included history, general examination, systemic examination, investigations like blood grouping, complete blood count, blood sugar, kidney function test, electrocardiogram, chest x-ray and liver function test.

All patients were randomly allocated to two groups(60 patients in each group) to receive either injection Nalbuphine 0.2 mg/kg diluted to 5 ml with normal saline (Group N) or 5 ml Normal saline (Group C) intravenously. On arrival in the operation theatre, multipara monitor with facility of ECG, non-invasive blood pressure, SPO_2 was attached. Baseline heart rate, systolic, diastolic, mean arterial blood pressure was recorded. Intravenous line was established. Premedication was done with intravenous midazolam

0.02 mg/kg, glycopyrrolate 4 microgram/kg, ranitidine 1 mg/kg. Five minutes before induction of general anaesthesia, patient received either intravenous Nalbuphine 0.2 mg/kg (Group N) or 5ml Normal saline (Group C). Before induction, Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial blood pressure (MAP) was recorded. After preoxygenation, patients were induced with intravenous propofol 2 mg/kg. Suxamethonium was administered intravenously at a dose of 2 mg/kg to achieve muscular relaxation for intubation. After laryngoscopy, trachea was intubated with appropriate size endotracheal tube. Intubation was done by anaesthesiologist having more than two years of experience in laryngoscopy and endotracheal intubation. After securing airway anaesthesia was maintained in both the group with oxygen 50 %, nitrous oxide 50%, sevoflurane (1.8%) and titrated doses of intravenous vecuronium bromide as muscle relaxant. Patient ventilation was controlled on closed circuit with circle absorber. $ETCO_2$ was monitored after intubation. Surgery was started 10 minutes after intubation. HR, SBP, DBP and MAP were recorded at the following time points:

T0: Baseline
T1: Before induction
T2: At laryngoscopy and intubation
T3: 1 minute after endotracheal intubation
T4: 3 minutes after endotracheal intubation
T5: 5 minutes after endotracheal intubation
T6: 7 minutes after endotracheal intubation
T7:10 minutes after endotracheal intubation

10 minutes after intubation, patients in Group C received injection pentazocine 0.5 mg/kg intravenously for intraoperative analgesia. After completion of surgical procedure, neuromuscular blockade was reversed with injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.01 mg/kg and patients were extubated after thorough oropharyngeal suction and shifted to post anaesthesia care unit.

Mean and standard deviation for all values were calculated and compared within the group with the baseline values as well as intergroup comparison was done. One way repeated measure ANOVA, Unpaired T test and Chi square test were used for statistical analysis. P value < 0.05 was considered statistically significant. Statistical software STATA VERSION 10.0 was used for data analysis.

Results

Patients in both the groups were statistically comparable in demographic characteristics like sex, age, weight and preoperative vital parameters.

Table 1: Gender wise comparison of groups

Gender	Group-C	Group-N
Male	41	43
Female	19	17
Total	60	60

Table 2: Comparison of demographic profile of patients

Parameters	Group-C	Group-N	P-Value
Age in years	41.3±10.04	42.16±10.58	0.6462,NS
Weight in Kg	53.03±12.16	53.41±11.56	0.8001,NS

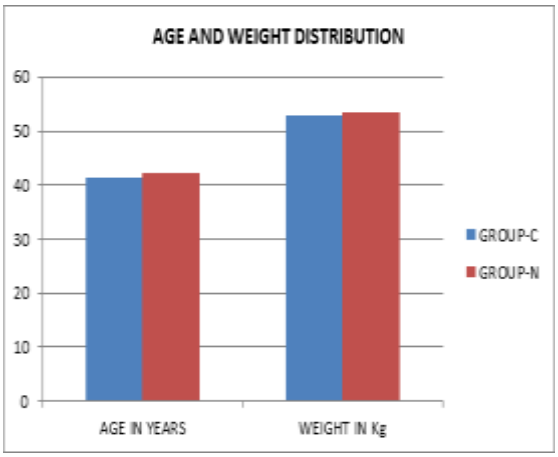


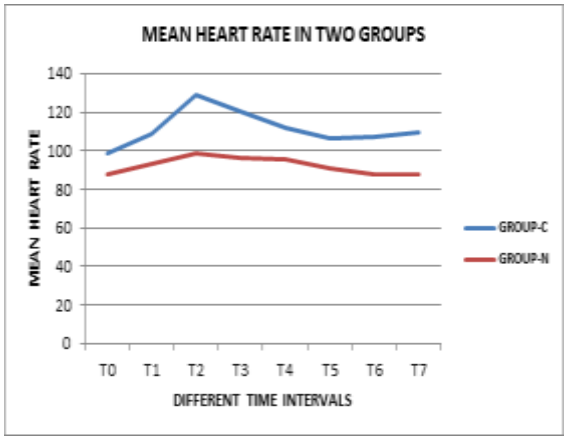
Table 3: Mean heart rate in group-C and group-N at different time points

Time	Group-C	Group- N
T0	98.68±11.56	87.86±19.22
T1	108.51±16.85	93.13±18.41
T2	128.65±11.98	98.35±18.47
T3	120.46±15.27	96.63±14.44
T4	112.23±16.06	95.76±15.74
T5	106.55±18.05	91.03±17.16
T6	107.06±18.61	87.73±15.96
T7	109.38±26.04	87.93±15.28
F-Value	91.79	32.68
P-Value	<0.0001,HS	<0.0001,HS

Table 4: Percentage change in mean heart rate in group-C and group-N at different time point from baseline value

Time	Group-C	Group- N	P-Value
T1	+9.96	+5.46	0.0547,NS
T2	+30.37	+11.93	<0.0001,HS
T3	+22.07	+9.98	<0.0001,HS
T4	+13.73	+8.99	0.0054,HS
T5	+7.95	+3.60	0.0482,S
T6	+8.49	-0.14	0.0008,HS
T7	+10.84	+0.08	0.0005,HS

+ = increase; - = decrease



Increase in HR in Group C (+30.37%) was highly significant compared to Group N (+11.93%) at T2. Then there was gradual decrease in HR in both the groups.

Table 5: Mean systolic blood pressure in group-C and group-N at different time points

Time	Group-C	Group- N
T0	119.81±11.78	123.63±14.89
T1	121.56±16.08	122.6±16.43
T2	148.75±17.66	121.78±11.93
T3	133.38±14.31	120.03±21.65
T4	107.71±16.16	105.46±15.11
T5	110.36±12.51	103.06±18.38
T6	104.65±10.58	101.46±15.61
T7	106.88±11.81	98.96±15.31
F-Value	90.46	43.78
P-Value	<0.0001,HS	<0.0001,HS

Table 6: Percentage change in mean systolic blood pressure in group-C and group-N at different time point from baseline value

Time	Group-C	Group-N	P-Value
T1	+1.46	-0.83	0.1370,NS
T2	+24.15	-1.49	<0.0001,HS
T3	+11.32	-2.91	<0.0001,HS
T4	-10.09	-14.69	0.0418,S
T5	-7.88	-16.63	0.0017,HS
T6	-12.65	-17.93	0.0480,S
T7	-10.79	-19.95	0.0324,S

+ = increase; - = decrease

There was significant increase in SBP (+24.15%) in Group C. Fall in blood pressure was observed in Group N (-1.49%) at laryngoscopy and intubation (T2).Thereafter fall in SPB was observed in both the group till T7.

Table 7: Mean diastolic pressure in group-C and group-N at different time points

Time	Group-C	Group-N
T0	69.16±11.43	72.43±7.79
T1	74.06±14.73	73.95±9.71
T2	97.06±20.44	78.11±8.39
T3	92.3±15.81	74.38±15.0
T4	69.33±9.22	59.20±8.55
T5	72.46±13.46	59.33±7.66
T6	72.33±10.33	60.98±7.38
T7	68.96±9.96	58.81±7.63
F-Value	46.70	50.84
P-Value	<0.0001,HS	<0.0001,HS

Table 8: Percentage change in mean diastolic blood pressure in group-C and group-N at different time point from baseline value

Time	Group-C	Group-N	P-Value
T1	+7.08	+2.09	0.1450,NS
T2	+40.34	+12.94	<0.0001,HS
T3	+33.45	+7.54	<0.0001,HS
T4	+0.24	-14.61	<0.0001,HS
T5	+4.77	-14.21	<0.0001,HS
T6	+4.58	-11.82	<0.0001,HS
T7	-0.28	-18.79	<0.0001,HS

+ = increase; - = decrease

When baseline value of DBP compared with value at laryngoscopy and intubation, there was significant increase in Group C (+40.34%) in relation to Group N (+12.94%).

Table 9: Mean arterial blood pressure in group-C and group-N at different time points

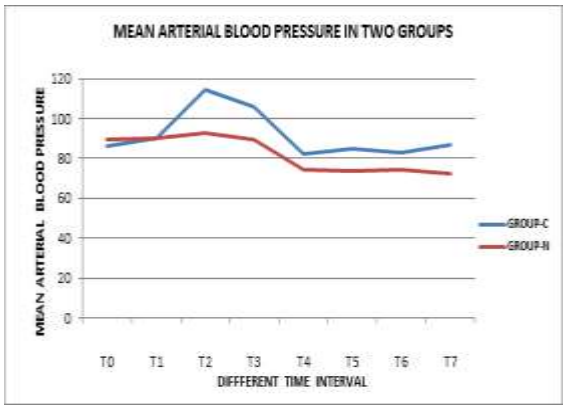
Time	Group-C	Group-N
T0	86.03±11.53	89.49±6.24
T1	89.91±15.11	90.30±9.57
T2	114.18±18.93	92.68±7.21
T3	105.97±14.56	89.60±15.86
T4	82.11±11.37	74.44±9.68
T5	85.08±13.05	73.92±10.07
T6	83.10±10.12	74.48±9.74
T7	87.01±12.16	72.20±9.59
F-Value	59.53	62.09
P-Value	<0.0001,HS	<0.0001,HS

Table 10: Percentage change in mean arterial blood pressure in group-C and group-N at different time point from baseline value

Time	Group-C	Group-N	P-Value
T1	+4.51	+0.90	0.1329,NS
T2	+32.72	+3.56	<0.0001,HS
T3	+23.17	+0.12	<0.0001,HS
T4	-4.55	-16.81	<0.0001,HS
T5	-1.10	-17.39	<0.0001,HS
T6	-3.40	-16.77	<0.0001,HS
T7	-5.59	-19.32	<0.0001,HS

+ = increase; - = decrease

Increase in MAP in Group C (+32.72%) was statistically highly significant compared to Group N (+3.56%) P value < 0.0001 at laryngoscopy and intubation



Discussion

Increase in heart rate and blood pressure has always been a matter of concern during laryngoscopy and intubation. Haemodynamic response to laryngoscopy and intubation has deleterious effects in patients suffering from hypertension, ischemic heart disease. Various techniques, equipment and drugs are used to attenuate the haemodynamic response of laryngoscopy and endotracheal intubation, but none is ideal. Most of the drugs used for this purpose are having their own side effects; some are costly and are not easily available.

Therefore present study was planned to evaluate the efficacy of Nalbuphine for attenuation of haemodynamic response to laryngoscopy and endotracheal intubation.

Nalbuphine is agonist antagonist opioid. Priti M Chawada et al[20] in their study used Nalbuphine in dose of 0.2mg/kg IV for attenuation of haemodynamic response to laryngoscopy and intubation. In our study we used Nalbuphine in dose of 0.2mg/kg IV safely.

The present study shows statistically significant increase in heart rate in both the groups when compared to baseline heart rate. There was statistically significant difference even when intergroup comparison was done. The baseline heart rate was 98.68±11.58 in Group C and 87.86±19.22 in group N. At T1 i.e. five minutes after premedication, percentage rise in heart rate was 9.96 in Group C and 5.46 in Group N. This rise in heart rate was compared and found statistically insignificant (p value 0.0547). Increase in heart rate in both groups can be attributed to injection glycopyrrolate administered in premedication. At laryngoscopy and intubation, percentage rise in heart rate was significantly high in Group C (+30.37%) as compared to Group N (+11.96%). Increased heart rate was transient in group N which returned to normal after 5 minutes of endotracheal intubation. But in Group C, increase in heart rate remained higher till 10 minutes after endotracheal intubation and did not return to baseline.

There was significant rise of SBP in control group (+24.15%) at laryngoscopy and intubation as compared to Nalbuphine group. Nalbuphine group showed slight fall (-1.49%) in SBP from premedication to 10 minutes after laryngoscopy and intubation. This difference was significant and was present till 10 minutes of observation. Slight fall in SBP in Group-N may be due to synergistic action of induction agent and Nalbuphine.

Increase in DBP at laryngoscopy and intubation was observed in both the group but the increase was significantly more in control group (+40.34%) as compared to Nalbuphine group (+12.94%).

Minimal rise in mean arterial blood pressure was observed in Nalbuphine group (+3.56%) and significant rise in control group (+32.72%) at laryngoscopy and intubation. Similar observations were found in some studies made by Priti M Chawada et al[20] and Muhammad Ahsan- Ul- Haq et al[21]. No significant side effects like allergy, respiratory depression were observed in our study. Limitation of our study was that Nalbuphine was not compared with other conventional drugs used for attenuation of pressor response[22]. Primary objective of this study was to test the efficacy of Nalbuphine to attenuate pressor response of laryngoscopy and intubation. Secondly we found no significant side effects as observed with other drugs used for attenuation of pressor response[23]. Easy availability and cost effectiveness is an added advantage of Nalbuphine.

Thus, from our study it is concluded that intravenous Nalbuphine in dose of 0.2mg/kg, five minutes before induction of anaesthesia effectively attenuated haemodynamic response to laryngoscopy and endotracheal intubation.

Conflict of interest: None

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