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RESEARCH ARTICLE
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COMPARATIVE STUDY OF INTRAVENOUS BOLUS DOSES OF NALBUPHINE WITH FENTANYL IN ATTENUATING HEMODYNAMIC RESPONSE TO LARYNGOSCOPY IN PATIENTS UNDERGOING NASAL INTUBATION FOR ORAL AND MAXILLOFACIAL SURGERY UNDER GENERAL ANAESTHESIA

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ABSTRACT

BACKGROUND: Nasotracheal intubation is the commonly performed technique in patients undergoing surgeries on head and neck surgeries. Laryngoscopy for guiding the endotracheal tube into trachea induces significant hemodynamic pressor response.

AIM: To compare the efficacy of nalbuphine and fentanyl in attenuation of hemodynamic pressor response in patients undergoing nasal intubation under general anaesthesia for oral and maxillofacial surgeries.

MATERIAL AND METHODS: This prospective, randomized, double blinded study was conducted at Trauma centre, Sir Sunder Lal Hospital, IMS, BHU, Varanasi, India and included 300 ASA I and II patients aged 18-60 years who underwent oral and maxillofacial surgeries. They were randomly divided into two groups of 150 each: Group N (Nalbuphine 0.2mg/kg) and Group F (Fentanyl 2mcg/kg). We assessed hemodynamic changes in two groups during laryngoscopy for nasal intubation. Secondary outcomes were sedation and postoperative pain assessment.

RESULTS: In Group F patients the pressor response was blunted better in comparison to Group N. There was statistically significant difference in postoperative pain (Visual Analogue scale 2) at 2 hours postoperatively ($p<0.0001$). There was significant difference in Ramsay sedation scale at 0, 1, 2, 3 hours postoperatively ($p<0.05$).

CONCLUSION: Fentanyl was superior in blunting the pressor response to laryngoscopy and intubation as well as better analgesia but Nalbuphine provided better endotracheal tube tolerance in postoperative period.

KEYWORDS: Fentanyl, Hemodynamic pressor response, Nalbuphine, Nasotracheal intubation.

INTRODUCTION

The hemodynamic pressor response to laryngoscopy believed to be initiated by a sympathetic reflex triggered by mechanical stimulation of upper airway which leads to a surge in catecholamines levels in bloodstream.[1] Along with this response there is also elevation in intracranial, intraocular pressure which can be detrimental in patients with head or globe injury.[2] A number of drugs had been used to attenuate the cardiovascular response such as nicardipine, lignocaine, esmolol, labetalol etc.[3]
Nasotracheal intubation is done to keep the endotracheal tube out of the surgical field in patients undergoing oral and maxillofacial surgeries (OMFS).[4]

MATERIAL AND METHODS

This prospective, randomized, double-blinded, interventional study was conducted at Trauma Centre, Sir Sunder Lal Hospital, Banaras Hindu University, India. Patients were recruited from August 2023 to February 2024. After approval from Institutional Ethical Committee and informed written consent patients were allocated into two Groups of 150 each. The study patients between the ages of 18-60 years of either sex, belonging to American Society of Anesthesiologists physical status (ASA) I or II who were scheduled to undergo nasal intubation for OMFS were included in the study. Patients with history of hypertension, coronary artery disease, hemodynamic instability, nasal bone fractures, restricted mouth opening and obesity were excluded from the study.
Patients were randomly divided into two groups using computer-generated random numbers. The interventional drugs were loaded in a 5-milliliter syringe with the total volume of 5 milliliter by a nurse not involved in the study.

Group N: received nalbuphine 0.2 mg/kg intravenously.
Group F: received fentanyl 2 mcg/kg intravenously.

The patients were monitored every minute for first 3 minutes, thereafter every 3 minutes for next 12 minutes, thereafter every 15 minutes till 90 minutes, thereafter every 30 minutes till 180 minutes. The level of sedation was evaluated using the Ramsay Sedation Score [5], which classified patients as alert and calm, drowsy, or sedated based on the level of sedation. The study has defined sedation as a state in which the patients was asleep and responded to verbal commands.
The primary outcome was to assess the efficacy of nalbuphine and fentanyl in blunting the hemodynamic pressor response to laryngoscopy. The secondary outcomes were to compare the post-operative sedation and post-operative pain.

Sample Size Calculation

The sample size calculation was performed using Krejcie Morgan formula which came out to be 300 (150 in each group).
$n = X^2 Np(1-p)/e^2(N-1) + X^2p(1-p)$

- n = sample size
- N = population size
- e = acceptable sampling error
- X^2= chi-square of degree of freedom 1 and confidence 95%
- p = proportion of population (if unknown,0.5)

Statistical Methods

The data management and statistical analysis were performed using SPSS version 28. Quantitative data were analyzed using the Mann Whitney and t-test. Quantitative data were presented as mean and standard deviations, while categorical data were presented as numbers and percentages. Categorical data were compared using Chi-square test and quantitative data using one-way ANOVA test. A p value less than 0.05 were considered significant.

RESULTS

All 300 patients completed the study successfully (figure 1). The study groups were comparable in terms of age and ASA status but there was statistically significant difference in terms of sex and weight of the patients as the road traffic accidents are more common in males than females (Table 1).

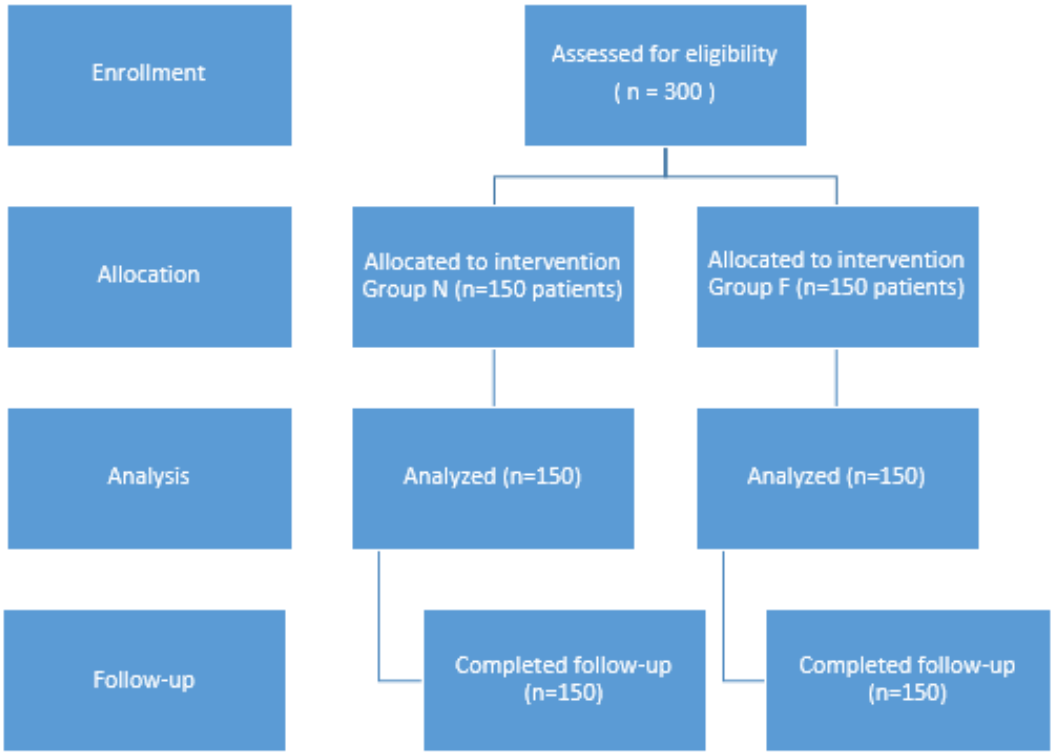

Figure 1. Consort flow diagram of the study population and their allocated groups

Table 1. General characteristics of the studied groups.

			Group N (n = 150)	**Group F (n = 150)**	**P-value**
Age (years)		**Mean ± SD**	**31.24 ± 10.90**	**31.88 ± 10.25**	**0.6**
Sex	Males	n (%)	99 (66)	76 (50.67)	0.007
	Females	n (%)	51 (34)	74 (49.33)	
ASA	ASA I	n (%)	123 (82)	117 (78)	0.38
	ASA II	n (%)	27 (18)	33 (22)	
	Weight (kg)	Mean ± SD	63.9 ± 8.11	60.94 ± 11.11	0.008
ASA: American Society of Anesthesiologists					

The table 2 presents the mean heart rate in beats per minute (bpm) at different time intervals for two groups. At baseline, Group N exhibits a mean heart rate of 82.08 bpm, slightly higher than Group F's 80.98 bpm. As time progresses, both groups undergo fluctuations in heart rate. At the earliest measured interval of 1 minute, Group N's heart rate spikes to 107.11 bpm, while Group F's remains notably lower at 93.77 bpm. This trend continues until the 3-minute mark, where Group N records a peak of 120.91 bpm compared to Group F's 87.84 bpm. Subsequently, both groups experience a decline in heart rate, with intermittent fluctuations, showcasing the dynamic nature of physiological responses over time.

Table 2. Comparison of heart rate between the two groups.					
Heart rate (beats per minute)	**Group N Mean ± SD**		**Group F Mean ± SD**		**P value**
0 min (baseline)	82.08	12.32	80.98	9.75	0.39
1 min	107.11	14.5	93.77	10.05	<0.0001
2 min	108.07	18.77	88.76	12.25	<0.0001
3 min	120.91	13.02	87.84	12.65	<0.0001
6 min	102.89	15.3	84.92	12.92	<0.0001
9 min	98.82	16.09	84.34	14.19	<0.0001
12 min	90.88	17.13	86.94	14.64	0.03
15 min	89.95	19.33	82.53	16.60	0.0004
30 min	85.14	18.51	81.8	17.84	0.11
45 min	84.95	16.14	79.97	17.51	0.01
60 min	84.38	16.53	81.77	16.42	0.17
90 min	85.57	14.21	79.54	10.76	<0.0001
120 min	81.14	12.86	77.01	12.05	0.004
150 min	80	11.61	76.43	13.00	0.01
180 min	86.46	11.91	76.39	14.04	<0.0001
210 min	87.31	20.45	87.00	11.93	0.8
240 min	84.56	14.1	78.00	13.9	0.6

The table 3 illustrates the mean systolic blood pressure (SBP) in millimeters of mercury (mmHg) at various time intervals for two distinct groups. Initially, at baseline, Group N displays a mean SBP of 123.4 mmHg, slightly higher than Group F's 121.26 mmHg. As time progresses, significant fluctuations in SBP are observed, particularly evident within the first few minutes. At the earliest recorded interval of 1 minute, Group N shows a notable increase in SBP to 140.19 mmHg, surpassing Group F's 128.2 mmHg. This trend continues until the 6-minute mark, where Group N records 125.19 mmHg, contrasting with Group F's 113.34 mmHg. Thereafter, both groups demonstrate a gradual decline in SBP with intermittent fluctuations, showcasing the dynamic physiological responses over time. Notably, significant differences in SBP between the two groups persist throughout the observation period, with varying p-values indicating the statistical significance of these differences. For instance, at the 3-minute mark, the p-value is less than 0.0001, indicating a highly significant difference between the groups.

Table 3. Comparison of Systolic Blood Pressure between the two group

Systolic Blood Pressure (mm of Hg)	**Group N Mean ± SD**		**Group F Mean ± SD**		**P value**
0 min	123.4	9.31	121.26	8.78	0.05
1 min	140.19	13.93	128.2	15.23	<0.0001
2 min	128.93	13.74	121.01	15.18	<0.0001
3 min	125.18	13.87	117.96	14.69	<0.0001
6 min	125.19	16.7	113.34	13.57	<0.0001
9 min	121.52	16.4	112.52	12.69	<0.0001
12 min	116.16	14.23	112.58	13.78	0.02
15 min	115.96	17.64	109.57	13.60	0.0005
30 min	111.58	16.47	110.51	15.67	0.56
45 min	113.40	12.78	112.12	15.09	0.42
60 min	113.56	13.06	113.45	13.6	0.7
90 min	113.61	11.10	108.77	10.30	0.0001
120 min	113.24	9.10	107.19	11.94	<0.0001
150 min	115.32	11.02	110.43	11.24	0.0002
180 min	126.14	15.12	114.37	7.96	<0.0001
210 min	122.89	18.6	114.15	9.81	<0.0001
240 min	103.93	10.71	113.6	5.36	<0.0001

The table 4 depicts the mean diastolic blood pressure (DBP) in millimeters of mercury (mmHg) at various time intervals for two distinct groups. Initially, at baseline, Group N exhibits a mean DBP of 78.48 mmHg, slightly higher than Group F's 76.56 mmHg, with a corresponding p-value of 0.01, indicating a statistically significant difference between the groups. As time progresses, both groups demonstrate fluctuations in DBP, particularly noticeable within the first few minutes. At the earliest recorded interval of 1 minute, Group N shows a substantial increase in DBP to 91.58 mmHg, while Group F records a lower DBP of 84.05 mmHg, with a highly significant p-value of less than 0.0001.

This trend continues until the 6-minute mark, where Group N displays a DBP of 76.78 mmHg, contrasting with Group F's 71.92 mmHg, indicating a statistically significant difference with a p-value of 0.001. Following this, both groups exhibit varying degrees of fluctuation in DBP over time, with some intervals demonstrating statistically significant differences between the groups, as evidenced by the p-values.

Table 4. Comparison of Diastolic Blood Pressure between the two group

Diastolic Blood Pressure (mm of Hg)	**Group N Mean ± SD**		**Group F Mean ± SD**		**P value**
0 min (baseline)	78.48	6.18	76.56	7.54	0.01
1 min	91.58	9.55	84.05	11.43	<0.0001
2 min	83.14	9.82	77.07	11.20	<0.0001
3 min	77.74	13.03	76.10	10.87	0.23
6 min	76.78	14.18	71.92	12.08	0.001
9 min	73.82	11.79	71.37	11.35	0.06
12 min	69.22	10.93	72.32	12.39	0.02
15 min	70.48	12.20	69.87	12.49	0.66
30 min	66.52	11.99	70.74	13.22	0.004
45 min	68.65	10.01	69.60	12.49	0.46
60 min	69.63	11.17	71.82	9.87	0.07
90 min	71.52	7.91	68.73	8.02	0.002
120 min	73.08	7.67	66.00	9.74	<0.0001
150 min	72.09	5.83	69.51	9.40	0.004
180 mi sn	83.25	16.27	69.85	8.40	<0.0001
210 min	79.15	20.10	68.61	13.20	<0.0001
240 min	65.81	7.22	76.00	4.47	<0.0001

The table 5 showcases the mean arterial pressure (MAP) in millimeters of mercury (mmHg) at various time intervals for two distinct groups. Initially, at baseline, Group N exhibits a mean MAP of 93.5 mmHg, slightly higher than Group F's 90.89 mmHg, with a corresponding p-value of 0.002, indicating a statistically significant difference between the groups. As the observation period progresses, both groups demonstrate fluctuations in MAP, particularly noticeable within the first few minutes. At the earliest recorded interval of 1 minute, Group N displays a significant increase in MAP to 107.63 mmHg, while Group F records a lower MAP of 98.01 mmHg, with a highly significant p-value of less than 0.0001.

This trend continues until the 6-minute mark, where Group N shows a MAP of 91.82 mmHg, contrasting with Group F's 85.4 mmHg, indicating a statistically significant difference with a p-value of less than 0.0001. Following this, both groups exhibit varying degrees of fluctuation in MAP over time, with some intervals demonstrating statistically significant differences between the groups, as evidenced by the p-values.

Table 5. Comparison of Mean Blood Pressure between the two groups

Mean Arterial Pressure (mm of Hg)	Group N Mean ± SD		Group N Mean ± SD		P value
0 min (baseline)	93.50	6.53	90.89	8.10	0.002
1 min	107.63	10.7	98.01	13.00	<0.0001
2 min	97.88	11.84	90.77	13.16	<0.0001
3 min	92.48	13.05	89.06	12.43	0.02
6 min	91.82	13.30	85.40	12.56	<0.0001
9 min	89.60	11.50	85.14	11.34	0.0008
12 min	85.41	11.13	84.81	12.86	0.66
15 min	85.74	13.00	82.26	12.77	0.02
30 min	81.96	13.62	83.53	13.76	0.32
45 min	83.54	9.95	84.12	12.23	0.65
60 min	83.65	10.74	85.25	10.00	0.1
90 min	84.40	9.34	81.72	8.74	0.01
120 min	83.49	7.21	78.60	9.90	<0.0001
150 min	83.37	8.36	79.98	12.17	0.005
180 min	94.28	13.20	83.74	7.58	<0.0001
210 min	89.10	15.55	82.76	10.21	<0.0001
240 min	76.87	7.90	88.80	4.91	<0.0001

The table 6 presents the postoperative pain levels assessed through the Visual Analogue Scale (VAS) for two distinct groups. Initially, at hour zero, both groups exhibit similar distributions across pain severity categories, with no statistically significant differences observed (P-value = 0.97). However, as time progresses, variations emerge in pain levels between the groups. Notably, at the 2-hour mark, Group N reports significantly fewer patients experiencing no pain compared to Group F (P-value < 0.0001). This trend persists across subsequent time intervals, with Group N consistently reporting a higher proportion of patients experiencing mild or moderate pain compared to Group F, albeit without significant statistical differences.

Table 6. Comparison of Visual Analogue scale between the two group

Postoperative pain (Visual analogue scale)		Group N Number of patients	Percentage	Group F Number of patients	percentage	P value
0 hour	Moderate pain	11	7.33	10	6.67	0.97
	Mild pain	19	12.67	19	12.67	
	No pain	120	80.00	121	80.67	
1 hour	Moderate pain	48	32	42	28.00	0.59
	Mild pain	96	64	99	66.00	
	No pain	6	4	9	6.00	
2 hour	Moderate pain	83	55.33	79	52.67	<0.0001
	Mild pain	61	40.67	62	41.33	
	No pain	6	4	9	6	
3 hour	Moderate pain	78	52.00	71	47.33	0.63
	Mild pain	60	40.00	61	40.67	
	No pain	6	4	9	6	
4 hour	Moderate pain	71	47.33	70	46.67	0.52
	Mild pain	66	44	62	41.33	
	No pain	5	3.33	9	6	
5 hour	Moderate pain	67	44.67	70	46.67	0.42
	Mild pain	70	46.67	62	41.33	
	No pain	5	3.33	9	6	
6 hour	Moderate pain	76	50.67	79	52.67	0.45
	Mild pain	69	46	62	41.33	
	No pain	5	3.33	9	6	

The table 7 provides an overview of postoperative sedation levels assessed using the Ramsay Sedation Scale for two groups, labeled as Group N and Group F, across different time intervals following surgery. At hour zero, significant differences are evident between the groups, with Group N having a higher proportion of patients in sedation grades 5, and 6 compared to Group F (P-value < 0.0001). As time progresses, these differences persist, with Group N consistently showing higher sedation levels compared to Group F across all time intervals.

Table 7. Comparison of Ramsay sedation scale between the two group

Postoperative sedation (Ramsay Sedation Scale)		Group N		Group F		P value
		No of patients	Percentage	No of patients	Percentage	
0 hour	Grade 3	6	4	39	26	<0.0001
	Grade 4	60	40	78	52	
	Grade 5	30	20	16	10.67	
	Grade 6	54	36	17	11.33	
1 hour	Grade 3	34	22.67	70	46.67	<0.0001
	Grade 4	86	57.33	74	49.33	
	Grade 5	26	17.33	6	4	
	Grade 6	4	2.67	0	0	
2 hour	Grade 2	101	67.33	83	55.33	<0.0001
	Grade 3	21	14	0	0	
	No sedation	28	18.67	67	44.67	
3 hour	Grade 2	27	18	9	6	0.001
	No sedation	123	82	141	94	
4 hour	Grade 2	7	4.67	2	1.33	0.09
	No sedation	143	95.33	148	98.67	
5 hour	No sedation	150	100	150	100	
6 hour	No sedation	150	100	150	100	

DISCUSSION

The process of intubation, preceded by laryngoscopy, acts as an intense nociceptive stimulus that triggers a sympathetic response, leading to tachycardia, hypertension, and arrhythmias [6]. These changes peak one minute after intubation and typically persist for approximately five to ten minutes.[7] Nalbuphine, a synthetic mixed opioid agonist/antagonist, belonging to the phenanthrene series. The appeal of agents with partial antagonist activity lies in them potential to reduce abuse risk and limit side effects, particularly respiratory depression. Nalbuphine, for instance, has analgesic potency equal to morphine on a milligram basis, with the advantage of a ceiling effect on respiratory depression compared to pure opioid agonists. Nath et al.[8] compared two doses of nalbuphine (group 1: 0.1 mg/kg and group 2: 0.2 mg/kg), finding better hemodynamic control with the higher dose. Chawda et al.[9] showed that nalbuphine at a dose of 0.2 mg/kg, administered five minutes before laryngoscopy, effectively prevented thehemodynamic response associated with intubation.

Fentanyl attenuates the cardiovascular response by acting on opioid receptors and decreasing sympathetic outflow.[10] Fentanyl is approximately 100 times more potent than morphine as an analgesic, it functions as a mu-opioid receptor agonist with high lipid solubility, rapid onset and a brief duration of effects.

Fentanyl appears to be a superior agent than nalbuphine in attenuating the pressor response to laryngoscopy and intubation. A study by Kautto U M et al.[11] indicated that supplementing anesthetic induction with fentanyl at a dose of 2 µg/kg significantly attenuated the increase in heart rate, arterial pressure, and rate pressure product after laryngoscopy and intubation, and fentanyl at a dose of 6 µg/kg completely abolished these pressure responses. Fentanyl being more potent analgesic as compared to nalbuphine, patients in group F have more patients with mild or no pain as analyzed by visual analogue scale than group N. Patients receiving nalbuphine demonstrated a notably higher proportion of patients in sedation grades 5 and 6 compared to group F (p value <0.001). An additional point is noted that tube tolerance in postoperative period in nasal intubation is better with nalbuphine group as compared to fentanyl group. This better tube tolerance can be attributed to increased sedative

property of nalbuphine. In a similar study conducted by Akheela L K et al,[12] utilizing the RASS Score (Richmond Agitation-Sedation Scale), the findings align, with significant distinctions observed in sedation levels between the nalbuphine and fentanyl groups, particularly post-extubation period.

Limitations

Visual analogue scale and Ramsay sedation scale, the primary measurement tool are subjective scales and can vary between patients with same degree of pain and sedation.

CONCLUSIONS

We conclude that fentanyl is better in attenuating the hemodynamic pressor response as compared to nalbuphine. Nalbuphine being a longer duration of action and having more sedation activity, patients tolerate the nasotracheal tube better in the postoperative period.

Source of Funding

None.

Conflict of Interest

None declared by the authors.

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