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Original Research Article

A Comparison of Attenuation of the Pressor Response to Laryngoscopy and Intubation with Intravenous Fentanyl and Intravenous Butorphanol

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Abstract:

Background: This study was conducted to compare intravenous fentanyl and intravenous butorphanol with regard to the attenuation of the pressor response to laryngoscopy and intubation (systolic pressure, diastolic pressure, mean arterial pressure, mean pulse rate, rate pressure product, post-extubation respiratory rate, and post-extubation sedation score).

Methods: This was a hospital-based randomized prospective study conducted among 60 patients who were scheduled for various elective surgeries, which was conducted in Govt. Kilpauk Medical College and Hospital, Chennai, and Govt. Royapettah Hospital, Chennai, from May 2013 to September 2013 after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Results: There was a significant rise in the heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and rate pressure product when compared to the pre-operative values in both the fentanyl and the butorphanol groups. The rise in hemodynamic parameters following intubation was significantly lower in the butorphanol group than in the fentanyl group. The increase in the heart rate, diastolic blood pressure, mean arterial pressure and rate pressure product was short lived in the butorphanol group when compared to the fentanyl group. Both the butorphanol group and the fentanyl group were comparable with respect to events of intraoperative hypotension and intra operative bradycardia. There was no significant respiratory depression post-extubation in both groups.

Conclusion: Butorphanol could be an effective alternative to fentanyl for attenuating the hemodynamic stress response to laryngoscopy and intubation.

Keywords: Pressor Response, Laryngoscopy, Intubation, Intravenous, Fentanyl, Intravenous Butorphanol

Introduction

In an era where regional anaesthetic techniques are gaining a strong foothold, general anaesthesia still maintains its rank as the technique of choice when securing an

airway is of prime importance and also when regional techniques fail. Hence, it becomes a necessity for every anaesthesiologist to provide general anaesthesia to any patient in the safest manner possible. In spite of several new airway devices emerging in recent times, direct laryngoscopy and tracheal intubation still reign as the gold standard in airway management. Laryngoscopy and the introduction of a tracheal tube are noxious stimuli. The changes in hemodynamics that arise from manipulation of the airway are attributed to the sympathoadrenal discharge that occurs as a result of stimulation of the epipharyngeal and parapharyngeal regions. These changes manifest as a rise in the pulse rate and blood pressure which is variable, transient and unpredictable. A normal healthy person can tolerate this response however, these responses may pose serious challenges in cardiovascular diseases like hypertension, coronary artery disease, and those with decreased intracranial compliance like head injuries with extra or intradural hematoma formation, intracranial tumors or aneurysmal vascular disease. Left ventricular failure, myocardial ischemia, and cerebral hemorrhage can be precipitated by this sudden change in blood pressure. Also, it can precipitate convulsions in pre-eclamptic patients. Numerous attempts have been made in the past to find a suitable drug or technique to suppress this response. The various pharmacological methods are aimed at the efferent, afferent, or both limbs of the response. It involves the use of volatile inhalational agents, [1] lignocaine, [2] opioids, [3] sodium nitroprusside, [4] nitroglycerine, [5] calcium channel blockers, [6] and adrenergic blockers. [7] The non-pharmacological methods aim at smooth and gentle intubation with a shorter duration of laryngoscopy, insertion of LMA in place of endotracheal intubation [8] and blocking of the glossopharyngeal nerve and the superior laryngeal nerves [9]. Since none of the above agents have proven to be the best choice to attenuate this pressor response the quest for the ideal agent still continues. Nevertheless, opioids have been employed for this purpose for quite a long time and pressure has proved to be extremely useful in attenuating the pressor response to laryngoscopy and intubation apart from providing good analgesia. Of the opioids fentanyl is the drug that is employed routinely to attenuate the pressor response. Hence, in this study we decided to compare the effects of the commonly used opioid fentanyl with another opioid drug, butorphanol in attenuating the pressor responses to laryngoscopy and intubation. This study was conducted to compare intravenous fentanyl and intravenous butorphanol with regard to the attenuation of the pressor response to laryngoscopy and intubation (systolic pressure, diastolic pressure, mean arterial pressure, mean pulse rate, rate pressure product, post-extubation respiratory rate, and post-extubation sedation score).

Methods

This was a hospital-based randomized prospective study conducted among 60 patients who were scheduled for various elective surgeries, which was conducted in Govt. Kilpauk Medical College and Hospital, Chennai, and Govt. Royapettah Hospital, Chennai, from May 2013 to September 2013 after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Inclusion Criteria

ASA class I

20 – 49 years

Both sexes

Elective procedure under general anaesthesia

MPC class I and II airway.

Exclusion Criteria

Valvular heart disease

Ischemic heart disease

Hypertension

Endocrine disorders

Metabolic disorders

Respiratory disease

Anaemic patients

Allergic diathesis

Unanticipated difficult airway

Patients who failed to give consent

Statistical Methods

The results were systematically analyzed using a paired 't' test for variables within the group and an unpaired 't' test for variables between the two study groups. A p–value of less than 0.05 was considered to be statistically significant.

Results

Table 1 Comparison of Pre-Operative Parameters (PRE OP 2)

Parameter	Group B		Group F
Pre op1 HR	81.4±4.65		80.4±4.59
Pre op1 SBP	122.53±5.72		123.53±4.83
Pre op1 DBP	81.33±5.47		81.4±3.48
Pre op1 MAP	95.06±5.02		95.44±2.35
Comparison of Pre-Operative Parameters (PRE OP 1)			
Parameter	Group B	Group F	P-Value
Pre op2 HR	80±5.14	77.67±4.95	0.2846
Pre op2SBP	120.96±6.36	122.03±4.99	0.2365
Pre op2 DBP	79.83±5.83	80.73±3.44	0.235
Pre op2 MAP	92.94±5.52	94.5±2.40	0.082
RR P1	11.46±0.97	11.53±1.04	0.3993

The pre-operative 1 (pre-op 1) parameters are comparable between the two groups.
The pre-operative 2 (pre-op 2) heart rate, systolic and diastolic blood pressures, mean arterial pressure, and respiratory rate are comparable between the two groups.

Table 2: Diastolic BP (in mmHg)

Heart Rate (beats/min)	Group B	Group F	P-Value between B and F
Mean Pre-op1	81.4±4.65	80.4±4.59	0.2031
Mean Pre-op2	80±5.14	77.67±4.95	0.2846
Mean PI	77.13±5.30*	74.8±11.63	0.1609
Mean T1	88.93±4.63*	89.8±3.40*	0.2062
Mean T2	84.73±4.97*	87.87±3.03*	0.0023
Mean T3	80.87±5.17	84.7±3.09*	<0.001
Mean T4	77±5.38*	81.33±2.94*	<0.001
Mean T5	73.07±4.40*	77.63±2.55	<0.001
Mean T10	68.17±2.72*	71.9±2.39*	<0.001
Heart Rate (in beats/min)			
Systolic BP (mmHg)	Group B	Group F	P-Value between B and F
Mean Pre-op1	122.53±5.72	122.53±4.83	0.2340
Mean Pre-op2	120.967±6.36	122.03±4.99	0.2365
Mean PI	118.1±6.18*	119.13±15.31	0.2452

Mean T1	128.73±4.90*	130.33±2.55*	0.0592
Mean T2	125.6±5.51*	128.33±2.41*	0.0079
Mean T3	122.36±6.15*	124.46±2.75*	0.0467
Mean T4	119.7±6.24	121.26±2.80	0.1076
Mean T5	116.86±5.92	117.73±3.07*	0.2399
Mean T10	112.17±6.012*	113.06±2.92*	0.2341
Systolic Blood Pressure (in mmHg)			
Diastolic BP (mmHg)	Group B	Group F	P-Value between B and F
Mean Pre-op1	81.33±5.47	81.4±3.48	0.4776
Mean Pre-op2	79.83±5.83	80.73±3.44	0.2350
Mean PI	77.3±5.01*	79.53±2.93	0.0197
Mean T1	86.23±4.56*	89.8±1.82*	<0.001
Mean T2	82.2±3.88*	88.26±1.85*	<0.001
Mean T3	78.93±4.31	86.06±1.46*	<0.001
Mean T4	75.36±4.01	84.67±1.24	<0.001
Mean T5	71.9±3.82	81.7±1.49	<0.001
Mean T10	68.68±2.49*	77.3±2.74*	0.0033

P-value < 0.05 → significant

* → P-value < 0.05 within group

The heart rate was significantly lower in group B when compared to group F at the second, third, fourth, fifth and tenth minutes after intubation.

The heart rate in group B after intubation becomes comparable to the pre-operative heart rate at the third minute after intubation and it becomes significantly lower than the pre-operative heart rate from the fourth minute after intubation onwards.

The heart rate in group F after intubation becomes comparable to the pre-operative heart rate at the fifth minute after intubation and it becomes significantly lower than the pre-operative pulse rate at the tenth minute after intubation.

P-value < 0.05 → significant

* → P-value < 0.05 within group

The systolic BP was significantly lower in group B when compared to group F at the second and third minutes after intubation.

The systolic BP in group B after intubation becomes comparable to the pre-operative systolic BP at the fourth minute after intubation and it becomes significantly lower than the pre-operative systolic BP at the tenth minute after intubation.

The systolic BP in group F after intubation becomes comparable to the pre-operative systolic BP at the fourth minute after intubation and it becomes significantly lower than the pre-operative systolic BP at the fifth minute after intubation.

P-value < 0.05 → significant

* → P-value < 0.05 within group

The diastolic BP was significantly lower in group B when compared to group F from immediately before induction until the tenth minute after intubation.

The diastolic BP in group B after intubation becomes comparable to the pre-operative diastolic BP at the third minute after intubation and it becomes significantly lower than the pre-operative diastolic BP at the tenth minute after intubation.

The diastolic BP in group F after intubation becomes comparable to the pre-operative diastolic BP at the fourth minute after intubation and it becomes significantly lower than the pre-operative diastolic BP at the tenth minute after intubation.

Table 3:

Mean Arterial Pressure (mmHg)	Group B	Group F	P-Value between B and F
Mean Pre-op1	95.07±5.02	95.44±2.35	0.3555
Mean Pre-op2	92.94±5.52	94.5±2.40	0.082
Mean PI	90.9±4.83*	92.73±2.45*	0.0346
Mean T1	100.4±4.19*	103.31±1.52*	<0.001
Mean T2	96.67±4.07*	101.62±1.68*	<0.001
Mean T3	93.41±4.60	98.86±1.71*	<0.001
Mean T4	90.14±4.27*	96.82±1.53	<0.001
Mean T5	86.89±4.02*	93.71±1.54	<0.001
Mean T10	80.41±15.54*	89.22±1.90*	0.002
Mean Arterial Pressure (mm/Hg)			
Rate Pressure Product	Group B	Group F	P-Value between B and F
Mean Pre-op1	9988.03±913.21	9943.67±855.9	0.4003
Mean Pre-op2	9550.96±1002.83	9489.9±855.9	0.4003
Mean PI	9124±945.37*	8909.7±1487.18*	0.254
Mean T1	11459.1±888.94*	11706.83±564.61*	0.101
Mean T2	10657.6±962.02*	11278.43±496.34*	0.001
Mean T3	9915.96±1023.89*	10546.27±533.07*	0.002
Mean T4	9237.56±1008.60	9864.73±461.28*	0.002
Mean T5	8553.96±836.23*	9140.26±389.94	<0.001
Mean T10	7400.67±1525.76*	8127.63±289.26*	0.0065
Rate Pressure Product			
RR	Group B	Group F	P-Value between B and F
P1	11.467±0.9732	11.533±1.041	0.3993
P2	12.4±1.734	12.2±0.8469	0.2862
Respiratory Rate			
SS	Group B	Group F	P-Value between B and F
P1	1	1	NA
P2	2.3±0.46	1.2±0.40	<0.001
Sedation Rate			

P-value < 0.05 → significant

* → P-value < 0.05 within group

The mean arterial pressure was significantly lower in group B when compared to group F from immediately before induction until the tenth minute after intubation.

The mean arterial pressure in group B after intubation becomes comparable to the pre-operative mean arterial pressure at the third minute after intubation, and it becomes significantly lower than the pre-operative mean arterial pressure at the fourth minute after intubation.

The mean arterial pressure in group F after intubation becomes comparable to the pre-operative mean arterial pressure at the fourth minute after intubation, and it becomes significantly lower than the pre-operative mean arterial pressure at the tenth minute after intubation.

P-value < 0.05 → significant

* → P-value < 0.05 within group

The rate pressure product was significantly lower in group B when compared to group F in the second minute after intubation.

The rate pressure product in group B after intubation becomes comparable to the pre-operative rate pressure product at the fourth minute after intubation, and it becomes significantly lower than the pre-operative rate pressure product at the fifth minute after intubation.

The rate pressure product in group F after intubation becomes comparable to the pre-operative rate pressure product at the fifth minute after intubation and it becomes significantly lower than the pre-operative rate pressure product at the tenth minute after intubation.

P-value < 0.05 → significant

There was no significant difference between groups B and F with regard to the pre-operative and post-extubation respiratory rates.

P-value < 0.05 → significant

While the sedation score was zero in both groups pre-operatively, the post extubation sedation score was significantly higher in group B than in group F.

Table 4:

			Intraoperative Hypotension		Total
			Yes	No	
Group	Group B	No. of Patients	3	27	30
		% within Group	10%	90%	100.0%
	Group F	No. of Patients	2	28	30
		% within Group	6.7%	93.3%	100.0%
Total		No. of Patients	5	55	60
		% of Study Population	8.3%	91.7%	100.0%
Intraoperative Hypotension Distribution					
			Intraoperative Bradycardia		Total
Group	Group B	No. of Patients	3	27	30
		% within Group	10%	90%	100.0%
	Group F	No. of Patients	1	29	30
		% within Group	3.3%	96.7%	100.0%
Total		No. of Patients	4	56	60
		% of Study Population	6.7%	93.3%	100.0%
Intraoperative Bradycardia Distribution					

P-value: 0.1869

P-value < 0.05 → significant

P-value: 0.2592

P-value < 0.05 → significant

There was no significant difference in the occurrence of intra-operative bradycardia between the two groups.

Table 5:

			Postoperative Shivering		Total
			Yes	No	
Group	Group B	No. of Patients	2	28	30
		% within Group	6.7%	93.3%	100.0%
	Group F	No. of Patients	6	24	30
		% within Group	20%	80%	100.0%
Total		No. of Patients	8	52	60
		% of Study Population	13.3%	86.7%	100.0%
Postoperative Shivering Distribution					
			Post-Operative Nausea and Vomiting		Total
			Yes	No	
Group	Group B	No. of Patients	5	25	30
		% within Group	16.7%	83.3%	100.0%
	Group F	No. of Patients	6	24	30
		% within Group	20%	80%	100.0%
Total		No. of Patients	11	49	60
		% of Study Population	18.3%	81.7%	100.0%
Post-Operative Nausea and Vomiting					

P-value: 0.0051

P-value < 0.05 → significant

The incidence of post-operative shivering was significantly higher in the fentanyl group than in the butorphanol group.

P-value: 0.1704

P-value < 0.05 → significant

The occurrence of post-operative nausea and vomiting was comparable between the two groups.

Discussion

Even in a well anaesthetized individual with no comorbid conditions, reflex tachycardia and hypertension on laryngoscopy and intubation occur quite frequently. [10] Many different opioid drugs in varying combinations and dosages have been studied in the past for their effect on obtunding the pressor response that invariably occurs during laryngoscopy and intubation in all patients. Fentanyl is routinely used intravenously before induction of anaesthesia to serve the purpose of providing analgesia and also to suppress the cardiovascular responses that occur during the process of laryngoscopy and intubation. In our study, we compared the effects of Inj. Fentanyl at a dose of 2 g/kg IV with Inj. Butorphanol at a dose of 40 g/kg IV on the attenuation of the hemodynamic stress response associated with laryngoscopy and intubation. Sixty patients were enrolled in the study. Each group consisted of thirty patients. King et al. (1951) [11] observed a transient but marked increase in blood pressure during laryngoscopy. Similarly, in our study also, in both the Fentanyl group and the butorphanol group, we observed increases in systolic and diastolic pressures following laryngoscopy that lasted for a short duration but were significantly elevated when compared to the baseline values of the same parameters. We also observed a significant increase in mean arterial pressures from the pre-operative values following intubation in both study groups. Corbett and Kerr (1969) [12] and Forbes and Dally (1970)[26] had also observed similar significant increases in mean arterial pressure after intubation that gradually regressed with

time. When the heart rate following intubation was recorded at various intervals between the fentanyl and the butorphanol groups, we observed that there was a rise in heart rate in both groups. But the increase in heart rate in patients in the butorphanol group was significantly lower than that observed in the patients in the fentanyl group. This was similar to the observations made by Philip BK et al. [13] in their study. We recorded an increase in both systolic and diastolic blood pressure in both butorphanol and fentanyl groups following intubation. The increase in systolic blood pressure was significantly lower in the butorphanol group when compared to the fentanyl group, but only for a short duration during the second and third minutes after intubation. During the rest of the study period the systolic blood pressure was comparable between the two groups. In contrast, butorphanol produced a significant lowering of the diastolic blood pressure from the time prior to induction until the end of the study period of ten minutes when compared to fentanyl. Nevertheless, an increase in diastolic blood pressure was observed in both the study groups following intubation. These observations are consistent with the observations made by Philip BK et al., and Vikramjeet Arora et al. [14] in their respective studies. The mean arterial pressure and the rate pressure product in both the groups increased following intubation. However, the increase was significantly lower in the butorphanol group when compared to the fentanyl group. The mean arterial pressure which is a derived value is important for the maintenance of the auto-regulatory functions of the heart, brain and kidney. The rate pressure product is defined as the product of the heart rate and systolic blood pressure. It is a measure of the myocardial energy requirement and the myocardial oxygen demand. The myocardial oxygen demand is directly proportional to the rate-pressure product. The occurrence of intraoperative hypotension and bradycardia, 10% and 6.7% in the butorphanol and fentanyl groups respectively, was not found to be significant between the two groups. Thus, both drugs provided stable hemodynamics throughout the intraoperative period. Philip BK et al., in their study comparing these two drugs also found the maintenance phase of anaesthesia to be uneventful in both the groups. In our study, there was no significant difference with regard to the post-operative respiratory rate in both the groups. Vikramjeet Arora et al., in their study comparing the recovery characteristics of fentanyl (2 ug/kg) and butorphanol (40 ug/kg) however, found that the respiratory rate was lower in the butorphanol group than that of the fentanyl group. Nevertheless, respiratory depression (respiratory rate <8/min) was not seen in either groups in this study or in our study.

Post-operative sedation was the most prominent side effect observed in the patients who received butorphanol. The sedation score was significantly lower in the Fentanyl group ($p < 0.001$). This finding is similar to that observed by Vikramjeet Arora et al. and Pandit SK et al. [15] Post-operative nausea and vomiting are two of the most frequent side effects observed with opioids, whether they are used in the intra-operative or post-operative period. The dose of the opioid used is more significant than the type of opioid in causing post-operative nausea and vomiting. [16] In our study, post-operative nausea and vomiting occurred in 16.7% of patients in the butorphanol group and in 20% of patients in the fentanyl group. Neither group was superior to the other with regard to the incidence of post-operative nausea and vomiting. Post-operative shivering is an extremely common occurrence, with a high incidence of 65%, especially with the administration of general anaesthesia. [17] The incidence of post-operative shivering was significantly lower in the butorphanol group (6.7%) when compared to the fentanyl group (20%). The side effect

profiles of these two drugs as compared by Vikramjeet Arora et al. also had similar observations. The dose of fentanyl that can effectively suppress the circulatory response to manipulation of the airway can be as high as 11-15 g/kg [18] But as the dose of fentanyl goes higher, it begins to act like a long-acting drug and the possibility of an increased duration of respiratory depression in the postoperative period is also very likely. [19] Similarly, the effect of a dose of butorphanol that can effectively suppress the circulatory response to airway manipulation needs to be studied further. In our study, we saw that at the doses at which the study drugs were used, both drugs could not prevent the hemodynamic response that occurred following laryngoscopy and intubation. However, butorphanol had a significant advantage over an equipotent dose of fentanyl in the sense that the increase in the stress response was comparatively less and of shorter duration.

Conclusion

With this study, we conclude that administration of intravenous butorphanol prior to induction of anaesthesia helps in better attenuation of the hemodynamic response to laryngoscopy and intubation than an equipotent dose of intravenous fentanyl. Neither of the drugs was associated with any adverse hemodynamic events. Hence, we conclude that butorphanol could be an effective alternative to fentanyl for attenuating the hemodynamic stress response to laryngoscopy and intubation.

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