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## Comparison of haemodynamic changes during propofol induction by fentanyl and butorphanol as pre-medication agent

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### Abstract

Propofol decreases systemic blood pressure. This is accompanied by corresponding changes in cardiac output and systemic vascular resistance. Systemic blood pressure reductions of 50% have been seen with 2mg/kg bolus of propofol. A negative inotropic effect of propofol may be due to decrease in intracellular calcium availability secondary to inhibition of transsarcolemmal calcium influx. Base line heart rate, blood pressure, SpO<sub>2</sub>, Respiratory rate and Entropy values was recorded. Patients were randomly allocated into two groups of 70 each using sealed envelope technique. In our study we have found that suppression of intubation response was better with fentanyl 2mcg/kg than butorphanol 20mcg/kg which is statistically significant.

**Keywords:** butorphanol, pre-medication agent, haemodynamic changes

### Introduction

Propofol is one of a group of alkylphenols. The alkylphenols are oils at room temperature and insoluble in aqueous solution, but they are highly lipid soluble. It has pH of 7 and pKa of 11, appears as a slightly viscous, white milky substance. It is stable at room temperature and is not light sensitive. If a dilute solution of propofol is required, it is compatible with 5% dextrose in water<sup>[1]</sup>.

Propofol is presumed to exert its sedative hypnotic effects through interaction with GABA, the principal inhibitory neurotransmitter in the CNS. When the GABA receptor is activated, transmembrane chloride conductance increases, resulting in hyperpolarization of post synaptic cell membrane and functional inhibition of post synaptic neuron. Propofol interacts with specific components of GABA receptor complex, appears to decrease the rate of dissociation of GABA from its receptor. This increases the duration of GABA activated opening of the chloride channel with resulting hyperpolarization of cell membrane<sup>[2]</sup>.

Propofol decreases systemic blood pressure. This is accompanied by corresponding changes in cardiac output and systemic vascular resistance. Systemic blood pressure reductions of 50% have been seen with 2mg/kg bolus of propofol. A negative inotropic effect of propofol may be due to decrease in intracellular calcium availability secondary to inhibition of transsarcolemmal calcium influx. The relaxation of vascular smooth muscle produced by propofol is primarily due to inhibition of sympathetic vasoconstrictor nerve activity. Stimulation produced by direct laryngoscopy & intubation of the trachea reverses blood pressure effect of propofol. This drug is more effective than thiopentone in blunting the magnitude of this pressor response. Propofol also effectively blunts the hypertensive response to placement of laryngeal mask airway.

Fentanyl is a highly selective  $\mu$  receptor agonist, which is mainly responsible for its analgesic properties. It acts by increasing intra-cellular calcium concentration which in turn increases K<sup>+</sup> conductance and hyperpolarization of cell membranes. This decreased membrane conductance decreases pre and post synaptic responses. Analgesia is produced principally through interaction with  $\mu$  receptor at supra spinal sites. It also binds to k receptor causing spinal analgesia, sedation, and anaesthesia<sup>[3, 4]</sup>.

Butorphanol tartrate is a synthetic opioid partial agonist analgesic. Butorphanol is an agonist-antagonist opioid that resembles pentazocine. Compared with pentazocine, its agonist effects

are about 20 times greater, whereas its antagonist actions are 10 to 30 times greater<sup>[5]</sup>.

Heart rate and blood pressure were not significantly altered after butorphanol i.v. in normal volunteers although some studies do indicate some indices of cardiovascular function can be altered. A dose of 25 mcg/kg butorphanol, i.v., increased pulmonary artery pressure, pulmonary wedge pressure, left ventricular end-diastolic pressure, systemic arterial pressure, pulmonary vascular resistance, and cardiac index. As a nasal preparation, hypotension did not occur with any appreciable frequency. No change in cardiac or vital signs were observed in volunteers receiving multiple doses of 1-4 mg for 16 days. Interestingly, butorphanol (1.5-6 mg/70 kg, i.m.) dampened the tachycardic response to cocaine administration<sup>[6]</sup>.

**Methodology**

**Design of Study**

Prospective Randomized control trial

**Sample Size**

To detect a minimum of 20% difference in propofol consumption between fentanyl and butorphanol a minimum of 67 patients was required when alpha error is kept at 0.05 and power of study at 80%

So sample size was 70 patients in each group.

**Inclusion Criteria**

- 18-65 years of age of either sex
- ASA physical status I and II for surgeries under general anaesthesia
- Patients who gave informed written consent

**Exclusion Criteria**

- Patient refusing to participate in the study.
- Patients with history of Neurological, Respiratory, Cardiovascular and Hepatic disorder.
- BMI more than 30 and individuals with difficult airway.
- Allergy to the study drug.
- Patients on opioids, sedatives, anti-psychotics, anti-epileptics.
- Pregnant or lactating mothers.
- Alcoholic

Base line heart rate, blood pressure, SpO<sub>2</sub>, Respiratory rate and Entropy values was recorded.

Patients were randomly allocated into two groups of 70 each using sealed envelope technique.

Premedicated with Inj. Glycopyrrolate 0.2mg plus

Group F: Inj.Fentanyl 2mcg/ kg

Group B: Inj.Butorphanol 20mcg/ kg

**Results**

**Table 1:** Comparison of Heart rate (bpm) in two groups of patients studied

Heart rate (bpm)	Group F	Group B	Total	P value
Baseline	86.86±6.24	85.80±6.91	86.32±6.58	0.344
1 Minute after Premedication	86.94±6.16	84.56±7.50	85.75±6.94	0.042*
5 Minute after premedication	82.71±5.76	83.16±5.92	82.94±5.82	0.654
At Induction	83.20±5.43	82.56±6.01	82.88±5.72	0.508
1 Minute after induction	82.06±5.80	81.80±6.72	81.93±6.25	0.809
2 Minute after induction	80.59±7.43	80.71±6.80	80.65±7.10	0.915
1 Minute after intubation	90.51±9.33	93.20±7.21	91.86±8.42	0.059+
2 Minute after intubation	87.97±7.28	88.91±6.02	88.44±6.68	0.405
3 Minute after intubation	85.16±6.58	86.51±6.10	85.84±6.36	0.208
4 Minute after intubation	82.59±6.25	85.47±6.27	84.03±6.40	0.007**
5 Minute after intubation	81.49±6.11	84.27±6.11	82.88±6.25	0.008**

Student t test

- Heart rate was found to be within normal limits in both the groups.
- Significant difference in heart rate is observed 1 minute after pre-medication where heart rate is slightly less in Group B compared to Group F
- Significant difference in heart rate @ 4 & 5 minutes after intubation is observed where heart rate is slightly high in Group B than Group F

**Table 2:** Comparison of SBP (mm Hg) in two groups of patients studied

SBP (mm Hg)	Group F	Group B	Total	P value
Baseline	128.13±8.65	127.91±8.46	128.02±8.52	0.882
1 Minute after Premedication	128.07±8.49	127.20±8.23	127.64±8.34	0.539
5 Minute after premedication	124.50±8.16	124.57±7.81	124.54±7.96	0.958
At Induction	124.03±7.73	124.76±7.34	124.39±7.52	0.568
1 Minute after induction	117.23±6.52	115.63±7.74	116.43±7.17	0.188
2 Minute after induction	106.26±8.17	107.81±8.63	107.04±8.41	0.275
1 Minute after intubation	130.04±8.45	129.47±9.34	129.76±8.88	0.705
2 Minute after intubation	127.20±7.63	131.07±8.00	129.14±8.03	0.004**
3 Minute after intubation	125.17±8.07	128.76±8.42	126.96±8.42	0.011*
4 Minute after intubation	121.86±7.30	126.69±8.41	124.27±8.21	<0.001**
5 Minute after intubation	117.36±8.96	123.00±8.49	120.18±9.14	<0.001**

Student t test

Statistically significant increase in SBP is seen in Group B minutes compared to Group F especially @ post-intubation 2,3,4,5

**Table 3:** Comparison of DBP (mm Hg) in two groups of patients studied

DBP (mm Hg)	Group F	Group B	Total	P value
Baseline	81.30±6.36	80.99±6.38	81.14±6.35	0.771
1 Minute after Premedication	81.14±6.33	81.03±6.17	81.09±6.23	0.914
5 Minute after premedication	78.47±5.90	78.77±6.10	78.62±5.98	0.768
At Induction	79.09±6.53	78.94±6.41	79.01±6.45	0.896
1 Minute after induction	74.41±5.49	73.53±6.91	73.97±6.24	0.403
2 Minute after induction	69.29±8.08	68.46±8.21	68.87±8.13	0.548
1 Minute after intubation	84.40±6.91	83.54±6.71	83.97±6.80	0.458
2 Minute after intubation	80.36±6.73	85.00±6.1	82.68±6.81	<0.001**
3 Minute after intubation	79.76±7.40	83.61±5.61	81.69±6.82	0.001**
4 Minute after intubation	78.56±7.17	82.51±5.35	80.54±6.61	<0.001**
5 Minute after intubation	75.53±6.97	81.27±6.00	78.40±7.09	<0.001**

Student t test

Statistically significant increase in DBP is seen in Group B minutes compared to Group F especially @ post-intubation 2,3,4,5

**Table 4:** Comparison of MAP (mm Hg) in two groups of patients studied

MAP (mm Hg)	Group F	Group B	Total	P value
Baseline	96.93±6.46	96.64±6.48	96.79±6.45	0.794
1 Minute after Premedication	96.79±6.34	96.41±6.22	96.60±6.26	0.727
5 Minute after premedication	93.79±5.84	94.00±5.91	93.89±5.85	0.829
At Induction	94.03±6.03	94.21±5.97	94.12±5.98	0.855
1 Minute after induction	88.67±4.85	87.56±6.70	88.11±5.86	0.262
2 Minute after induction	81.61±7.72	81.53±8.17	81.57±7.92	0.949
1 Minute after intubation	99.49±6.52	98.89±6.70	99.19±6.60	0.592
2 Minute after intubation	95.99±6.34	100.37±5.94	98.18±6.51	<0.001**
3 Minute after intubation	94.89±6.88	98.67±5.67	96.78±6.56	0.001**
4 Minute after intubation	93.03±6.52	97.24±5.50	95.14±6.37	<0.001**
5 Minute after intubation	96.93±6.46	96.64±6.48	96.79±6.45	<0.001**

Student t test

Statistically significant increase in MAP is seen in Group B minutes compared to Group F especially @ post-intubation 2,3,4,5

**Table 5:** Comparison of SpO2% in two groups of patients studied

SpO2%	Group F	Group B	Total	P value
Baseline	98.66±0.81	98.69±0.79	98.67±0.80	0.833
1 Minute after Premedication	98.63±0.75	98.66±0.68	98.64±0.71	0.813
5 Minute after premedication	95.94±0.88	96.37±1.13	96.16±1.03	0.014
At Induction	96.43±1.37	96.84±1.49	96.50±0.147	0.005
1 Minute after induction	99.96±0.20	99.97±0.17	99.96±0.19	0.652
2 Minute after induction	99.94±0.29	99.93±0.31	99.94±0.30	0.779
1 Minute after intubation	99.97±0.17	99.97±0.17	99.97±0.17	1.000
2 Minute after intubation	99.99±0.12	99.99±0.12	99.99±0.12	1.000
3 Minute after intubation	99.96±0.27	99.96±0.27	99.96±0.26	1.000
4 Minute after intubation	99.97±0.17	99.97±0.17	99.97±0.17	1.000
5 Minute after intubation	99.99±0.12	99.99±0.12	99.99±0.12	1.000

Student t test

SpO2 is comparable between group F and Group B without significant difference

**Discussion**

Suppression of intubation response was better with fentanyl 2mcg/kg group than butorphanol 20mcg/kg group which shows statistically significant difference especially at 2,3,4,5 minutes post-intubation

Pandit SK *et al.* [7] measured perioperative vital signs during laparoscopy using butorphanol 40mcg/kg and fentanyl 2mcg/kg. They found that the patients who received

butorphanol experienced lesser increases in heart rate and systolic blood pressure two minutes after intubation compared to fentanyl group.

In our study, patients who received butorphanol 20mcg/kg had higher heart rate and blood pressure compared to fentanyl 2mcg/kg group which could be possibly explained because of higher dose of butorphanol [40mcg/kg] used in Pandit SK *et al.* Study.

Philip BK *et al.* [8] study measured vital signs in laparoscopic surgeries under general anaesthesia and demonstrated post intubation lower pulse rate & blood pressure in butorphanol

20mcg/kg group than fentanyl 1mcg/kg group.

In our study, patients who received butorphanol 20mcg/kg had higher heart rate and blood pressure compared to fentanyl 2mcg/kg group which could be possibly explained because of lower dose of fentanyl[1mcg/kg] used in Philip BK *et al.* Study.

Jasleen kaur *et al.* [9] study measured post-intubation response by using pre-medication with fentanyl 2mcg/kg, butorphanol 20mcg/kg and 40mcg/kg respectively. Study showed all the three groups had a comparable increase in HR in the post-intubation period, which returned to baseline within 5 minutes.

In our study we have found that suppression of intubation response was better with fentanyl 2mcg/kg than butorphanol 20mcg/kg which is statistically significant.

This is in contrast to the study of Jasleen kaur *et al.* Which demonstrated suppression of intubation response was comparable between butorphanol and fentanyl.

The major drawback of propofol is reduction in blood pressure with the standard induction dose of propofol. A typical induction dose of propofol (2 mg/kg) results in an approximate 30% reduction in SBP. Reduction in the requirement of induction dose reduces the hemodynamic effects of propofol [10].

Because of dose sparing effect of induction dose of propofol by opioids, haemodynamic effects of propofol is reduced.

The hemodynamic stability with butorphanol was comparable to fentanyl without any statistical significance.

Jasleen kaur *et al.* [9] study demonstrated changes in vital parameters at induction with propofol using fentanyl 2mcg/kg, butorphanol 20mcg/kg and 40mcg/kg respectively. MAP at induction was  $82.50 \pm 4.53$  in Group F,  $85.80 \pm 9.04$  in Group B20 and  $84.60 \pm 7.35$  in Group B40 where the incidence of fall in blood pressure is <30% in all three groups.

Our study is in consistent with the previous study of Jasleen kaur *et al.* Which demonstrated <30% reduction in blood pressure in all three groups

## Conclusion

We conclude that butorphanol 20µg/kg reduces the induction requirement of propofol comparable to that of fentanyl 2µg/kg and confers hemodynamic stability.

It is therefore an acceptable alternative opioid to fentanyl as an adjuvant to balanced general anesthesia.

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