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# The Study On Comparison Of Haemodynamic Changes During Propofol Induction By Fentanyl And Butorphanol As Pre-Medication Agent

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**Abstract**

**Introduction**: Propofol is used for induction and maintenance of anaesthesia, as well as for sedation in and outside the operating room. Opioids are given as a pre-medication agent during induction of anesthesia to provide analgesia in various surgical procedures. It is also known to potentiate hypnotic effect of propofol, thus reducing the requirement of propofol and subsequent hypotension due to propofol.

**Aims**: This study aims to compare the propofol requirement by fentanyl and butorphanol as pre-medication agent using clinical end points.

**Methodology**: The study was conducted on inpatients of hospitals attached to our institute for a duration of 18 months. This is a Prospective Randomized control trial that that included two groups, namely group B included patients on Butorphanol [20 µg/kg] and group F included patients on Fentanyl [2 µg/kg]. Seventy patients were randomly selected for each group, thus a total of 140 patients were included in the study.

**Results**: In the present study, heart rate, blood pressure, MAP and respiratory rate were comparable among the two groups.

**Discussion**: Reduction in the requirement of induction dose reduces the hemodynamic effects of propofol. Because of dose sparing effect of induction dose of propofol by opiods, haemodynamic effects of propofol are reduced.

**Conclusion**: The findings of the current study conclude that butorphanol 20µg/kg reduces the induction requirement of propofol comparable to that of fentanyl 2µg/kg and confers hemodynamic stability.

## Introduction

Propofol is now widely used in clinical practice because of its favorable recovery profile and low incidence of side effects. In 1977, Kay & Rolly confirmed the potential of propofol as an anesthetic induction agent. Propofol was initially prepared with Cremaphor EL. Because of anaphylactoid reactions associated with cremaphor, the drug was reformulated as emulsion. Propofol is used for induction and maintenance of anaesthesia, as well as for sedation in and outside the operating room. Propofol inhibits acetyl choline release in hippocampus and prefrontal cortex through acting on

GABA A receptors producing sedation. Propofol produces central nervous system effects by inhibiting NMDA sub- type of glutamate receptor through modulation of sodium channel gating. [1]
Among the various induction agents, propofol has become increasingly popular in last two decades for induction of anesthesia. Major drawbacks of propofol are a greater degree of hypotension [25-40%], compared with other hypnotic agents and inadequate attenuation of hypertensive response to intubation, respiratory depression, apnoea & blunts hypoxic-hypercapnic drive, allergic reactions, pain & thrombophlebitis of the vein into which propofol is injected [2]
Opioids are given as a pre-medication agent during induction of anesthesia to provide analgesia in various surgical procedures. It is also known to potentiate hypnotic effect of propofol, thus reducing the requirement of propofol and subsequent hypotension due to propofol. It is also known to reduce the hypertensive response to intubation, unwanted vagal reflexes & stress response to surgery [3]
Propofol decrease cerebral metabolic rate for oxygen, cerebral blood flow and intracranial pressure. Large doses of propofol may decrease systemic blood pressure sufficiently to decrease cerebral perfusion 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. Heart rate remains unchanged inspite of decreased systemic blood pressure during induction with propofol. Apnoea occurs after an induction dose of propofol, the incidence and duration appear to depend on dose, speed of injection and concomitant premedication. A maintenance infusion of propofol decreases tidal volume and frequency of breathing. [4-6]
**Aims**: This study aims to compare the propofol requirement by fentanyl and butorphanol as pre-medication agent using clinical end points.

**Materials and methods**
The study was conducted on inpatients of hospitals attached to our institute for a duration of November 2015 to May 2017, accounting to 18 months of the study duration. This is a Prospective Randomized control trial that included a minimum of 67 patients to detect a minimum of 20% difference in propofol consumption between fentanyl and butorphanol, when alpha error is kept at 0.05 and power of study at 80%. So sample size was 70 patients in each group. This was derived using the formula: $n = 2 \times [(\text{alpha error} + \text{beta error})^2 \times \text{Standard deviation}^2] / \text{Difference between two group}$. GROUP B included patients on Butorphanol [20 µg/kg] and GROUP F included patients on Fentanyl [2 µg/kg]. Thus, a total of 140 patients were included in the study. We included patients belonging to 18-65 years of age of either sex , ASA physical status I and II for surgeries under general anaesthesia and Patients who gave informed written consent. We excluded the patients refusing to participate in the study. The 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 and Alcoholics were excluded from the study.
Following approval of institutional ethical committee, 140 patients were taken up for the study. A routine pre anaesthetic checkup was done in the evening before the surgery assessing for the History and general condition of the patient, Airway assessment by Mallampati grading, Nutritional status, height and weight of the patient. A detailed examination of the cardiovascular system, Respiratory system and Central nervous system & other systems, examination of the spine was done. The routine investigations were done in all patients and written informed consent was obtained. All patients were kept nil per oral for 8 hours prior to surgery. Base line heart rate, blood pressure, $SpO_2$, and Respiratory rate were 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 and Group B: Inj.Butorphanol 20mcg/ kg. Study drug dose was calculated per kg body weight and diluted to 5ml with normal saline and given as pre-medication 5minute before the procedure.Heart rate, blood pressure, $SpO_2$, and Respiratory rate was recorded @ 1 & 5 minutes after pre-medication. Patient was pre-oxygenated with 100% oxygen for 3minutes prior to induction of anaesthesia.

Patients were induced with Inj. Propofol 30mg/10seconds till loss of response to verbal commands and loss of response to eyelash reflex and Heart rate, blood pressure, SpO2, Respiratory rate was recorded for 2 minutes after induction. Inj. Succinyl choline 2 mg/ kg was given. After adequate relaxation, endotracheal intubation was performed. Heart rate, blood pressure, SpO2, Respiratory rate was recorded for 5 minutes after intubation. To ensure blinding, the parameters were recorded by anesthetist not involved in the study. The Haemodynamic parameters such as Heart rate, BP, SpO2, Respiratory rate were measured in the study.

Statistical Methods: Descriptive and inferential statistical analysis had been carried out in the present study. Results on continuous measurements were presented on Mean ± SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5 % level of significance. The assumptions on data such as,dependent variables should be normally distributed, the samples drawn from the population should be random, and the Cases of the samples should be independent Student t test (two tailed, independent) had been used to find the significance of study parameters on continuous scale between the two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test had been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. *Significant figures were divided into* significant (P value: $0.05<P<0.10$), moderately significant (P value: $0.01<P \leq 0.05$) and strongly significant (P value: $P \leq 0.01$). The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

**Results**

The present study is a clinical randomized double blinded study with 140 patients randomly divided into two groups of 70 each using sealed envelope technique. GROUP F included Fentanyl 2 µg/kg I.V and GROUP B included Butorphanol 20 µg/kg I.V. Demographic data suggests that most of the patients belonged to age group of 31-40 years in both the groups (50% in group F and 47% in group B). The Age group was comparable between two groups with P=0.189 (Table 1). Similarly, the number of patients of either sex was comparable between two groups with P=0.499 (Figure 1). Height, Weight, and BMI were measured among the two groups and the results were comparable between the two groups (Table 2).

**Table 1: Age distribution of patients studied**

| Age in years | Group F | Group B | Total |
|---|---|---|---|
| <20 | 2(2.9%) | 1(1.4%) | 3(2.1%) |
| 20-30 | 7(10%) | 5(7.1%) | 13(9.3%) |
| 31-40 | 35(50%) | 33(47.1%) | 68(48.6%) |
| 41-51 | 22(31.4%) | 22(31.4%) | 44(31.4%) |
| 61-71 | 4(5.7%) | 8(11.4%) | 12(8.6%) |
| Total | 70(100%) | 70(100%) | 140(100%) |
| Mean ± SD | 37.97±9.27 | 40.04±9.31 | 39.01±9.31 |

**Figure 1 showing Gender wise distribution among the study population**

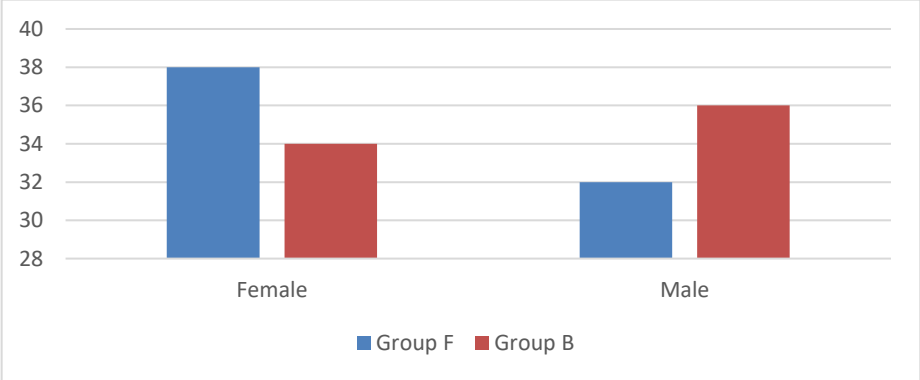


**Table 2: Comparison of weight, Height and BMI in two groups of patients studied**

| | Group F | Group B | Total | P value |
|---|---|---|---|---|
| Weight (kg) | 57.43±7.77 | 57.07±5.49 | 57.25±6.71 | 0.754 |
| Height (cm) | 158.94±6.51 | 159.69±6.67 | 159.31±6.58 | 0.506 |
| BMI (kg/m$^2$) | 22.69±2.38 | 22.40±1.90 | 22.54±2.15 | 0.425 |

The 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 at 4 & 5 minutes after intubation is observed where heart rate is slightly high in Group B than Group F (Table 3 and Figure 2). Systolic blood pressure was compared and showed statistically significant increase in SBP in Group B compared to Group F especially at post-intubation 2,3,4,5 minutes (Figure 3). Diastolic blood pressure was compared and showed statistically significant increase in DBP in Group B compared to Group F especially at post-intubation 2,3,4,5 minutes (Figure 4).

**Table 3: 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** |

**Figure 2: showing comparison of heart rate among the two groups**

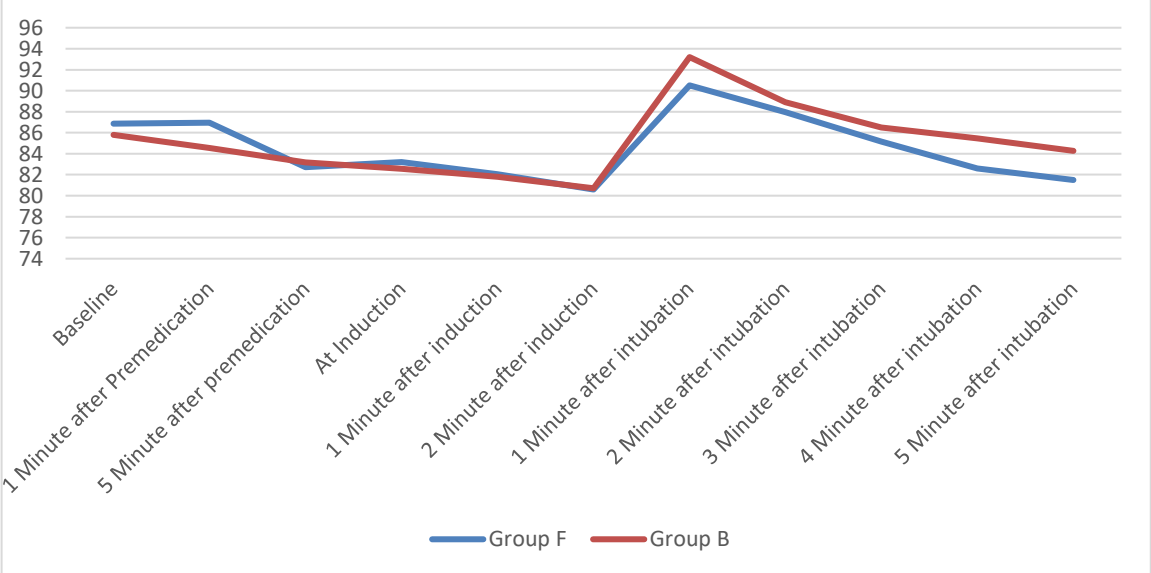


**Figure 3: showing comparison of systolic blood pressure among the two groups**

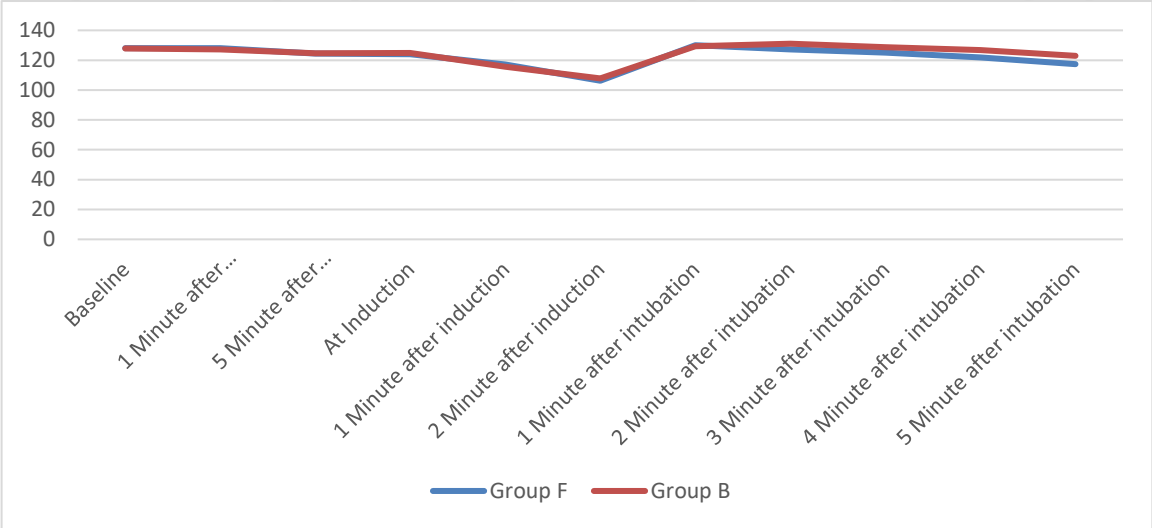
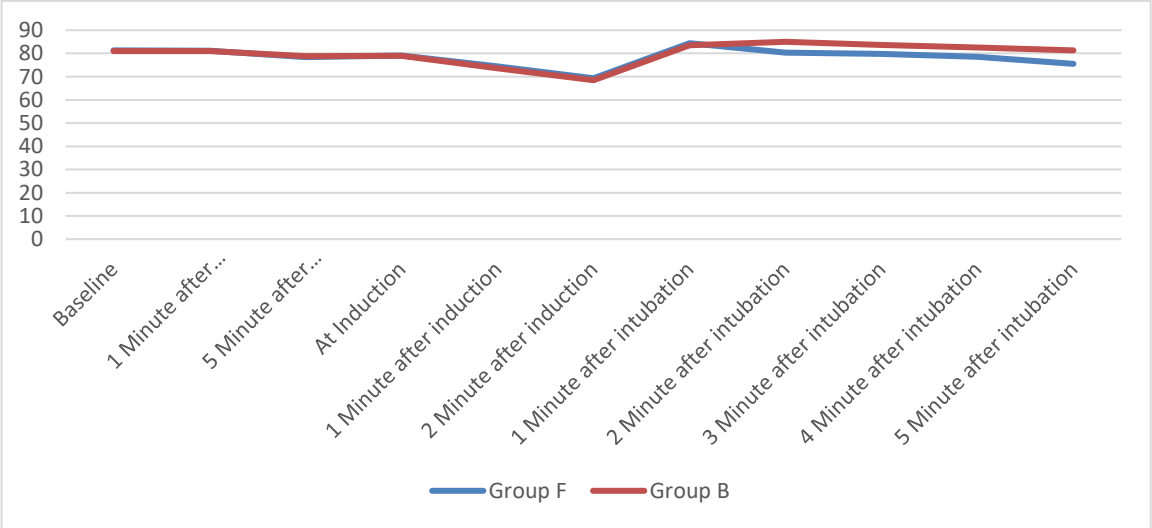



**Figure 4: Comparison of DBP (mm Hg) in two groups of patients studied**




In the present study, the comparison of mean arterial pressure (MAP), respiratory rate (RR) and SpO2 was done. Statistically significant increase in MAP was seen in Group B compared to Group F especially at post-intubation 2,3,4,5 minutes (Table 4). Respiratory rate was comparable between group F and Group B without significant difference (Table 5). SpO2 was comparable between group F and Group B without significant difference (Figure 5)

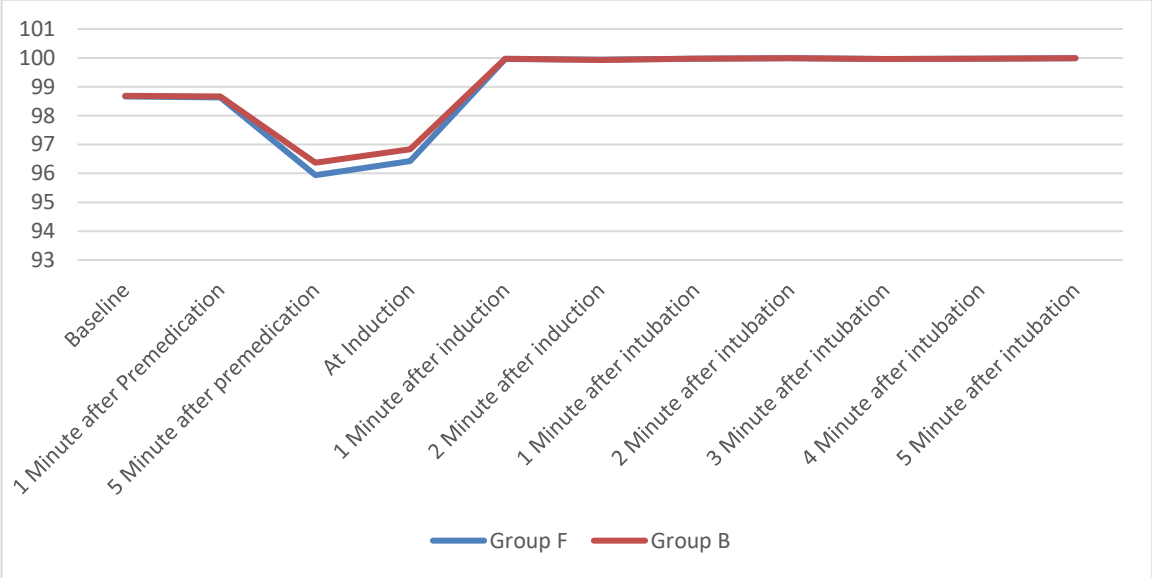
**Table 4: Comparison of MAP (mm Hg) in two groups of patients studied**

| 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** |

**Table 5: Comparison of RR in two groups of patients studied**

| RR | Group F | Group B | Total | P value |
|---|---|---|---|---|
| Baseline | 16.24±1.15 | 16.17±0.88 | 16.21±1.02 | 0.681 |
| 1 Minute after Premedication | 16.11±1.27 | 16.06±0.90 | 16.09±1.10 | 0.759 |
| 5 Minute after premedication | 15.90±1.30 | 15.86±0.98 | 15.88±1.15 | 0.826 |
| At Induction | 15.84±1.29 | 15.59±2.05 | 15.71±1.71 | 0.376 |
| 1 Minute after induction | 12.17±0.56 | 12.17±0.56 | 12.17±0.56 | 1.000 |
| 2 Minute after induction | 12.23±0.64 | 12.17±0.56 | 12.20±0.60 | 0.576 |
| 1 Minute after intubation | 12.17±0.56 | 12.17±0.56 | 12.17±0.56 | 1.000 |
| 2 Minute after intubation | 12.17±0.56 | 12.17±0.56 | 12.17±0.56 | 1.000 |
| 3 Minute after intubation | 12.17±0.56 | 12.17±0.56 | 12.17±0.56 | 1.000 |
| 4 Minute after intubation | 12.17±0.56 | 12.17±0.56 | 12.17±0.56 | 1.000 |
| 5 Minute after intubation | 12.17±0.56 | 12.17±0.56 | 12.17±0.56 | 1.000 |

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




## Discussion

Propofol is the most convenient induction agent in recent days. 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 [7, 8] Reduction in the requirement of induction dose reduces the hemodynamic effects of propofol. Because of dose sparing effect of induction dose of propofol by opiods, haemodynamic effects of propofol is reduced. In our study, MAP (mm Hg) in both group F and group B is as follows: 1 minute after induction in Group F was 88.67±4.85 and 87.56±6.70 in Group B. 2minutes after induction in Group F was 81.61±7.72, and 81.53±8.17 in Group B. The hemodynamic stability with butorphanol was comparable to fentanyl without any statistical significance.

Jasleen kaur et al [ 9 ] [ 2013 ] 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±4.53 in Group F, 85.80±9.04 in Group B and 84.60±7.35 in Group B 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.

Pandit SK et al [8] [1987] 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 [10] [1991] study measured vital signs in laparoscopic surgeries under general anesthesia 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] [2013] 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.

## Conclusion

The findings of the current study 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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