# ATTENUATION OF CARDIOVASCULAR RESPONSES TO LARYNGOSCOPY AND TRACHEAL INTUBATION

## - Intravenous Sufentanil vs Pethidine -

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## Abstract

**Background:** The study was undertaken to compare the effects of small doses of sufentanil or pethidine on cardiovascular responses induced by tracheal intubation.

**Methods:** Sixty ASA physical status I-II patients, scheduled for elective abdominal surgery under general anesthesia, were randomly allocated in a double blind fashion to receive an intravenous bolus of either sufentanil 0.1 μg/kg (Group S, n = 30) or pethidine 1.5 mg/kg (Group P, n = 30) for induction of anesthesia. The heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP) were measured before induction of anesthesia (baseline), at 1-min intervals for 3 min after the induction of anesthesia, and at 1, 3, 5, and 7 min after start of laryngoscopy.

**Results:** No significant differences in SAP, DAP, and MAP were

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observed between the two groups. Heart rate was significantly increased 2 and 3 minutes after induction of anesthesia and 1 minute after intubation in group P as compared to group S ($P < 0.01$). However, the numbers of patients who developed a heart rate increase more than 20% of basal value were not different between two groups. At the end of the study period, systolic, diastolic, and mean arterial pressure slightly decreased from preinduction values was transient and did not require treatment.

**Conclusions:** If adequate timing in opioid administration is warranted according to the time to peak effect of each opioid drug, small doses of sufentanil or pethidine could provide effective control of the inotropic response induced by laryngoscopy and tracheal intubation.

**Keywords:** Intubation, cardiovascular physiology, opioids, sufentanil, pethidine.

## Introduction

Induction of anesthesia and tracheal intubation may induce profound alteration of the hemodynamic state of the patient subsequent to both the effects of anesthetic drug administered perioperatively, and the adrenergic state of the patient[1].

Tracheal intubation induces clinically relevant neurovegetative responses[2-4]. Plasma concentration of catecholamines is increased[2-4] and there may be associated myocardial ischemia[5] and cerebral hemorrhage[6].

Opioids are widely used to control the neurovegetative response to intubation; a linear relationship exists between increasing opioid dose and cardiovascular response reduction[7-10].

Casati et al.[9] reported that the use of small bolus doses of sufentanil (0.1 μg/kg) effectively blunts the cardiovascular response to intubation. Pethidine or meperidine is a narcotic analgesic similar to morphine. In addition to its strong opiodergic and anticholinergic effects, it has local anesthetic effects related to its interactions with sodium ion channels[11]. Van den Berg and colleagues[12], examined vasomotor responses to

tracheal intubation after pethidine given prior to induction of anesthesia. They showed that pethidine reduces the inotropic response to airway instrumentation.

Few data are available comparing the efficacy of sufentanil or pethidine in controlling hemodynamic variations during the peri-intubation period. We therefore, conducted a randomized double blind study to evaluate any possible blunting of the cardiovascular effects of laryngoscopy and tracheal intubation by the use of small doses of sufentanil or pethidine.

## Methods and Materials

Following Institutional approval and obtaining informed consent from all patients, sixty ASA I and II consequent patients, aged 18-65 years, scheduled for elective abdominal surgery under general anesthesia, were enrolled in this study. Those who had taken drugs that could influence hemodynamic and autonomic function, were excluded from the study. Further exclusion criteria consisted of patients with predictably difficult airways or obesity (body weight > 100 kg), electrocardiographic abnormalities (cardiac rhythm other than sinus, premature ventricular contractions, a heart rate was less than 55/min), congestive heart failure, diabetes mellitus, hypertension, and coronary artery, respiratory, renal, or cerebral disease.

In a double blind fashion and using a sealed envelope technique, patients were randomly allocated to one of two groups according to the agents to be used for the induction of anesthesia: sufentanil (Group S, n = 30) or pethidine (Group P, n = 30).

Syringes containing sufentanil or pethidine were prepared, in a double blind fashion, by a collaborator not involved in data recording. The same collaborator administered drugs while a blind observer collected data.

No premedication was given. In the operating room, an 18 G intravenous cannula was inserted and Ringer's solution was started, at 10 ml/kg per h throughout the study period.

Monitoring consisted of an automated BP cuff. Electrocardiography and pulse oximetry.

Measurements of pre-induction: systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP) and heart rate (HR), were used as baseline values.

For induction patients received either sufentanil 0.1 μg/kg iv (Group S) or pethidine 1.5 mg/kg (Group P) followed 60s later by thiopental 4 mg/kg. Atracurium 0.6 mg/kg was given as an intravenous bolus to facilitate tracheal intubation, which was performed 5 min after induction. Patients' lungs were manually ventilated for 4 minutes with 100% oxygen before orotracheal intubation was performed. Direct laryngoscopy was carried out using a Macintosh blade at peak effects of iv sufentanil or pethidine (at 6 min after injection), and tracheal intubation was accomplished within 30s. The patients' lungs were then mechanically ventilated with a tidal volume of 10 ml/kg and a respiratory rate of 12/min to maintain end-tidal PaCO2 at around 38 mmHg. Anesthesia was maintained with isoflurane 1.2% and 50% nitrous oxide in oxygen.

In each patient, the BP (SAP, DAP, MAP) and HR. were measured at three time-points: baseline (3 min before induction), preintubation (at 1-min intervals for 3 min after induction), and postintubation (at 1, 3, 5, and 7 min after start of laryngoscopy).

Statistical analysis was performed using SPSS version 11.0. Mean blood pressure (MBP) was taken as diastolic blood pressure (DBP) plus ⅓ × (systolic blood pressure [SAP]-DAP). Statistical comparisons among the groups were performed using two-way analysis of variance (ANOVA), followed by an unpaired *t*-test with Bonferroni's correction. Hemodynamic responses to induction and intubation in a given group were analyzed using a repeated-measurements ANOVA (one-way ANOVA) followed by a paired *t*-test with Bonferroni's correction. The Mann Whitney test was used to compare continuous variables. Continuous variables are presented as mean ± SD. Ordinal variables are presented as numbers (%). A value of $P < 0.05$ was considered the minimum level of statistical significance.

**Results:** Demographic characteristics, induction time (time from administration of induction drugs till start of laryngoscopy), apnea duration (since removal of mask ventilation till start of mechanical ventilation), and duration of laryngoscopy, were comparable in the two groups (Table 1). There was no significant difference between the two groups in Cormack-Lehane grades (Table 2).

*Table 1*

*Demographic characteristics and peri-intubation measured data of patients (mean ± SD or number).*

| | Group S (Sufentanil) | Group P (Pethidine) |
|---|---|---|
| No. of patients | 30 | 30 |
| Sex (female/male) | 9/21 | 11/19 |
| ASA (I/II) | 23/7 | 21/9 |
| Age (yrs) | 31.0 ± 4.9 | 29.97 ± 5.9 |
| Weight (kg) | 64.5 ± 6.6 | 65.4 ± 4.8 |
| Height (cm) | 167.6 ± 6.1 | 165.8 ± 6.3 |
| Induction time (sec) | 111.1 (3.1) | 113.3 (2.8) |
| Apnea duration (sec) | 11.1(2.3) | 11.4 (1.9) |
| Duration of laryngoscopy (sec) | 8.6 (1.1) | 9.1 (1.2) |

No significant difference among groups.

*Table 2*

*Cormack-Lehane grades encountered during direct laryngoscopy (number)*

| | Group S (Sufentanil) | Group P (Pethidine) |
|---|---|---|
| No. of patients | 30 | 30 |
| Cormack-Lehane 1 | 15 | 13 |
| Cormack-Lehane 2a | 12 | 15 |
| Cormack-Lehane 2b | 3 | 2 |

No significant difference among the two groups.

The preoperative arterial pressure and heart rate values were comparable in the two groups (Fig. 1). Systolic, diastolic, and mean arterial pressure were not significantly different between the two groups 1-3 min after induction with the administration of either drug and 1-7 min after intubation (Fig. 1). Heart rate significantly increased 2 and 3 minutes after induction and 1 minute after intubation in group P compared with group S ($P < 0.01$) (Fig. 1). Compared with preoperative values, changes

in systolic, diastolic, and mean arterial pressure values observed after induction and intubation were not statistically significant in either group; while at the end of the study period, systolic, diastolic, and mean arterial pressure, slightly decreased from preinduction values (Fig. 1). However, the observed decreases in blood pressure were transient in both groups and did not require treatment. In comparison with the preoperative values, heart rate significantly increased 3 minutes after induction and 1-3 minutes after intubation in group P ($P < 0.05$); while in group S, heart rate changes after induction and intubation were not significant compared with the preoperative values.

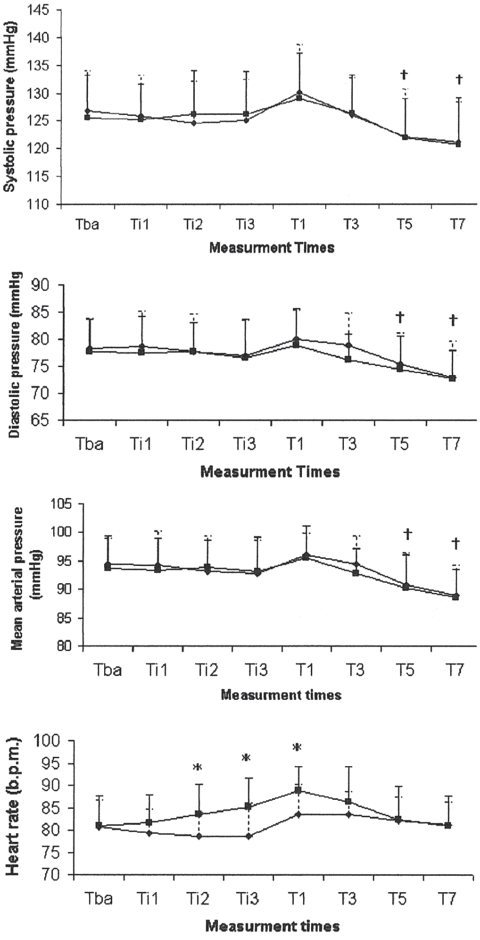


*Fig. 1*
*The hemodynamic changes during intubation period in the two groups. Data are mean ± sd. ◆ = group S (sufentanil); ● = group P (pethidine); Tba = preoperative; Ti1-3 = 1-3 min after induction; T1-7 = 1-7 min after intubation. † P < 0.05 vs. Tba; * P < 0.01 = P vs. S.*

The number of patients who developed a heart rate increase more than 20% of preoperative value were not different between the two groups 3 minutes after induction, and 1-3 minutes after intubation (Fig. 2). There was no case of arrhythmia or hypotension among groups. No ST segment depression was noted in either group.

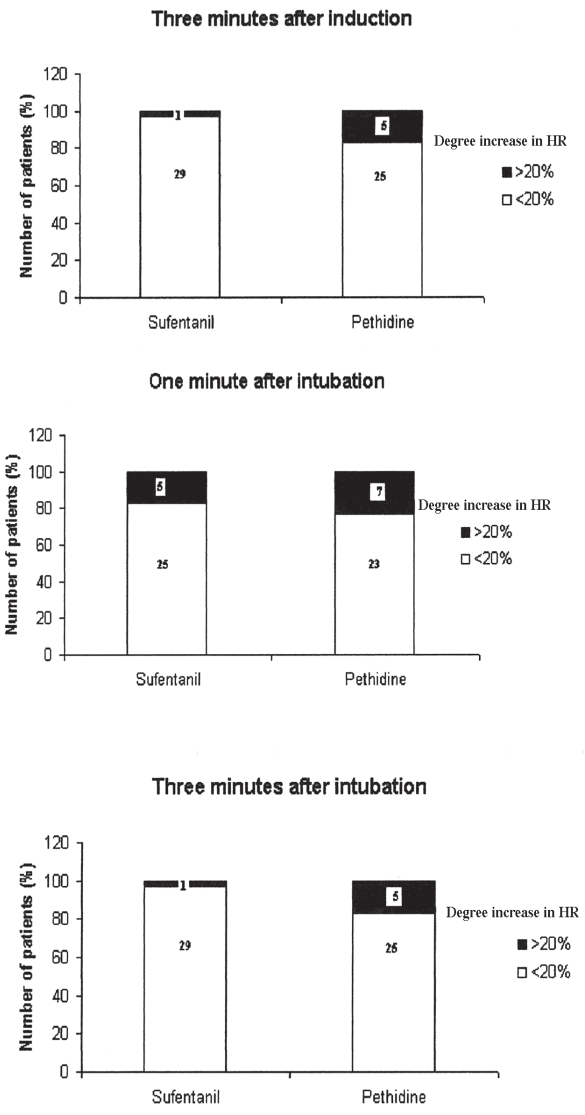


*Fig. 2*
*The number of patients who developed a heart rate increase more than 20% of the value before the induction of anesthesia for each group. There was no significant difference between two groups in any time. HR = Heart rate.*

## Discussion

This study compared the efficacy of sufentanil 0.1 mg/kg iv and pethidine 1.5 mg/kg iv for controlling cardiovascular responses to laryngoscopy and tracheal intubation. Comparable to sufentanil, pethidine attenuated the increase in systolic, diastolic, and mean arterial blood pressure after intubation.

Direct laryngoscopy and tracheal intubation cause increase in blood pressure and heart rate[13]. Mechanism of cardiovascular response to intubation is assumed to be a reflex sympathetic reaction to the mechanical stimulation of larynx and trachea. Reflex changes in the cardiovascular system after laryngoscopy and intubation lead to an average increase in blood pressure by 40-50% and 20% increase in heart rate[14]. Significant elevations in serum levels of norepinephrine and epinephrine following laryngoscopy, with and without tracheal intubation, have been demonstrated[2,3].

The cardiovascular response to intubation may be attenuated by several methods, including administration of vasodilators[15], β-blockers[16], calcium channel blockers[17], *iv* lidocaine[18] or by deepening the level of anesthesia. Yet, narcotic administration has been the most extensively used strategy[19,7,20,21]. Opioids, in moderate to high dose, have been suggested as a means of blunting this response[21]. In a study done by Iannuzzi et al[1], the use of a small dose of sufentanil proved to be an effective strategy to blunt the cardiovascular response to intubation in healthy normotensive patients. These effects of sufentanil were also documented by Casati et al[9].

Currently, pethidine is used for pre-anesthesia and the relief of moderate to severe pain, particularly in obstetrics and post-operative situations. Pethidine exerts its analgesic effects by the same mechanism as morphine, by acting as an agonist at the μ-opioid receptor. In Van den Berg A and colleagues[12] study, the investigators compared efficacy of equipotent doses of tramadole, nalbuphine, pethidine (3.0, 0.3 mg/kg, 1.5 mg/kg, respectively) and placebo given prior to induction of anesthesia, on the pressor responses after tracheal intubation, and showed that pethidine and nalbuphine blunted the inotropic response to intubation. In another study

by Flacke JW and colleagues[22], intraoperative plasma epinephrine levels were lowest in patients receiving sufentanil and pethidine.

It has been demonstrated that, when small doses of opioids are used before tracheal intubation, physician must accurately consider the time to peak effect in order to maximize the advantages of opioid administration[23]. Sufentanil is a synthetic opioid analgesic drug has an immediate onset of action (1-3 min), with a distribution of 0.72 minutes, time to peak effect of 5-6 min and redistribution of 13.7 minutes[24]. When pethidine is given intravenously, the onset of analgesia is noted within 1 minute and the time to peak effects is 5-7 minutes[11]. This strategy (similar time to peak effect) could account for efficacy of such small doses of opioids[25]. Even though arterial pressure significantly decreased from baseline values at the end of the study period, a small proportion of patients experienced a decrease in systolic pressure to < 90 mmHg after induction of general anesthesia. The observed decreases in arterial pressure values were transient in both groups and did not require treatment. In addition, the small doses of opioid used in this study were not associated with opioid-related side effects such as bradycardia or chest wall rigidity.

In our study, heart rate significantly increased 3 minutes after induction and 1-3 minutes after intubation in patients receiving pethidine. However, incidence of increases in heart rate to greater than 20% above basal values was not significantly different between the two groups. Increase in heart rate during peri-intubation period is most likely due to anticholinergic effect of pethidine[26].

In conclusion, results of this prospective, randomized, double blind study demonstrated that adequate timing in opioid administration is warranted. The time to peak effect of each opioid drug and small doses of sufentanil or pethidine, provide similar effective control of the inotropic response induced by laryngoscopy and tracheal intubation.

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