

# The effect of Propofol Fentanyl and Propofol Butorphanol on the increase in intraocular pressure due to succinylcholine and intubation

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## Abstract

The increase in intraocular pressure (IOP) associated with succinylcholine (Sch) has made its use in patients with open globe injuries controversial. Studies that have examined techniques to prevent the increase in IOP due to Sch have shown a larger increase in IOP from the stimulus of laryngoscopy and endotracheal intubation. We investigated whether butorphanol in combination with propofol could attenuate this increase in IOP during induction of anaesthesia, laryngoscopy and intubation. Sixty patients of either sex, aged 20-50 years undergoing elective non-ophthalmic surgery under general anaesthesia, were randomized blindly to receive either placebo, fentanyl 2µg/kg or butorphanol 1 mg, 15 min before induction of anaesthesia with propofol. Endotracheal intubation was facilitated with succinylcholine 2mg/kg. IOP and hemodynamic variables (HR, SAP and O<sub>2</sub> saturation) measured before induction (baseline), after propofol, after Sch, and at 1 min, 3 min, 5 min and 10 min after intubation. Butorphanol in combination with propofol effectively obtunded the hemodynamic response as well as increase in IOP after Sch and intubation, without any increase in adverse events. Butorphanol 1 mg was found to be equipotent to 2µg/kg fentanyl in this respect.

## INTRODUCTION

Succinylcholine (Sch) is commonly used to facilitate rapid sequence intubation in patients at risk for aspiration of gastric contents. Sch remains unsurpassed in providing ideal intubating conditions<sup>1</sup>. However, an increase in intraocular pressure (IOP) after Sch is one of its undesirable effects, especially in patients with an open globe injury. The intraocular hypertensive effect may be due to a tonic contraction of the extraocular muscles, choroidal vascular dilatation and contraction of orbital smooth muscle<sup>23</sup>, which makes its use controversial in patients with penetrating eye injury<sup>4</sup>. Although larger reviews have pointed safety record of Sch in open globe injury patients with preservation of ocular contents<sup>45</sup>. However, laryngoscopy and endotracheal intubation are bigger culprits to cause an increase in IOP greater than the increase attributed to Sch<sup>678</sup>. Despite many claims with the use of various drugs including propofol<sup>6</sup>, fentanyl<sup>79</sup>, sufentanil<sup>10</sup>, remifentanyl<sup>9</sup>, esmolol<sup>11</sup>, etomidate<sup>12</sup>, diazepam<sup>13</sup> and lignocaine<sup>14</sup> to attenuate this response but to the contrary, none of the drug consistently blunts this IOP response to Sch and intubation.

Butorphanol is a mixed agonist antagonist with intrinsic activity at receptors of the µ opioid type (morphine like). It is also an agonist at kappa opioid receptors. Its interaction with these receptors in the CNS apparently mediates most of its pharmacological effects, including analgesia and sedation. The effect of butorphanol on IOP in humans has not been described till date in literature. This study was undertaken to determine if a bolus of butorphanol given before induction of anaesthesia with propofol can obtund the IOP effects and hemodynamic changes associated with induction of anaesthesia and its comparison with fentanyl.

## MATERIAL AND METHODS

After obtaining Hospital Ethics Committee approval and informed written consent, we studied 60 ASA I and II patients, aged 20-50 years of either sex, who required tracheal intubation as part of the anesthetic technique for elective non-ophthalmic surgery. Patients with ocular, respiratory or cardiovascular disease, known sensitivity to opioids and with anticipated difficult intubation, were excluded.

This was a randomized, double blind, controlled study.

Random allocation of the patients was based on computer generated table of random numbers. All patients were premedicated with midazolam 0.15mg/kg I.V. just after insertion of intravenous cannula inside the operation theater. The patients were allocated to one of the three groups (n= 20 in each group) to receive either normal saline (Group P), 2µg/kg Fentanyl (Group F) or 1 mg Butorphanol (Group B), 15 min before induction of anaesthesia. The drug was prepared in the identical syringe and in equal volume by the technician and the anaesthetist was not aware of the drug given to the patient. One drop of proparacaine 0.5% was placed in each patient's left eye and baseline IOP was measured using a Goldman hand held applanation tonometer. After pre-oxygenation, anaesthesia was induced with 1.5-2 mg/kg of propofol and IOP was measured after loss of verbal response. Succinylcholine (Sch) 2mg/kg was given to facilitate endotracheal intubation and IOP was measured after fasciculations were passed from the face. Thereafter, endotracheal intubation was performed by a single anaesthetist with gentle laryngoscopy and intubation time was recorded. Patient's lungs were ventilated with 60% nitrous in oxygen. The IOP was then measured at 1 min, 3 min, 5 min and 10 min after intubation. At each IOP measurement, heart (HR), systolic arterial pressure (SAP) and oxygen saturation ( $S_pO_2$ ) was recorded. Intravenous vecuronium bromide was given to maintain muscle relaxation and surgery was allowed to begin after the study was completed.

Results are being expressed as mean  $\pm$ SD. A paired t test and two way analysis for repeated measurements (ANOVA with treatment group and time as between-and within-group) were used to analyse the changes in IOP, HR, and SAP using SPSS for Windows computer software. Gender and ASA class of the patients were analysed using chi-square test. A two-tailed probability of  $<0.05$  was the criterion for statistical significance.

Sixteen patients per group represents a sample size with 80% power to detect a difference, based upon an assumption of standard deviation of 3.75 for changes in IOP at  $\alpha=0.05$ . To increase the power of the study, we have recruited twenty patients in each group.

## RESULTS

There were no significant differences among groups in terms of patient's age, sex distribution, weight, ASA classification and intubation time (Table-I).

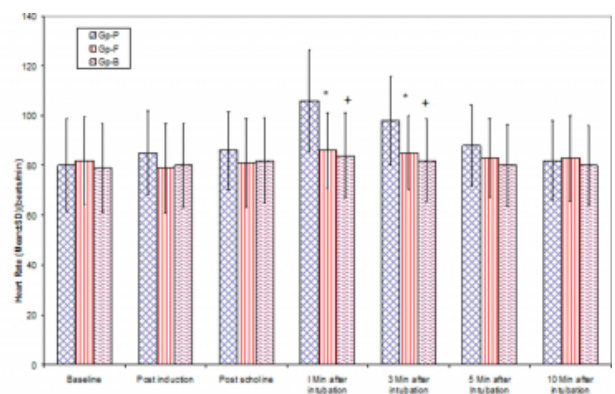
Table 1: Patient Characteristic

Figure 1

	Group P	Group F	Group B
Age( in years)	36 $\pm$ 6	38 $\pm$ 5	35 $\pm$ 8
Male: Female	9:11	8:12	10:10
Weight (in kg)	75 $\pm$ 16	72 $\pm$ 13	74 $\pm$ 15
Intubation time(in Sec)	41 $\pm$ 20	42 $\pm$ 18	40 $\pm$ 19
ASA I : II	8:12	10:10	7:13

Figure 1: Changes in heart rate in the groups

Figure 2



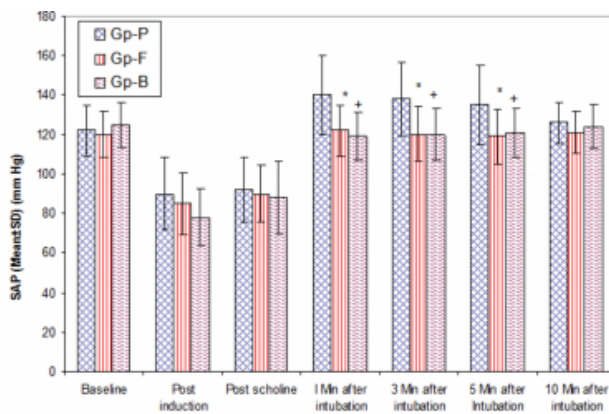
\*  $p<0.05$  (Group P vs Group F)

+  $p<0.05$  (Group P vs Group B)

There was significant increase in heart rate from baseline in placebo group at 1 and 3 min after intubation than in fentanyl and butorphanol group ( $p<0.05$ ) (figure – 1).

There was significant increase in SAP from baseline in placebo group at 1 min, 3min, and 5 min after intubation than in fentanyl and butorphanol group ( $p<0.05$ ) (figure – 2).

**Figure 3**



\*  $p < 0.05$  (Group P vs Group F)

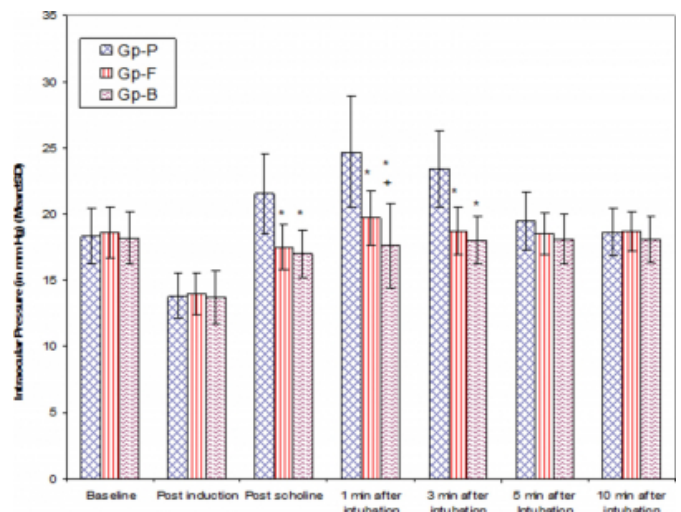
+  $p < 0.05$  (Group P vs Group B)

**Figure 2: Changes in systolic arterial pressure in the groups**

There were no significant differences in baseline (awake) IOP values among the groups and there was a non-significant decrease in IOP in all groups with induction of anaesthesia. Sch caused a consistent increase in IOP, but this was not significant compared with that of awake baseline values. The most significant finding was the increase in IOP immediately after intubation (1 min and 3 min) in placebo group than in fentanyl and butorphanol group ( $p < 0.05$ ). After the initial decrease with induction of anaesthesia, the mean IOP in fentanyl and butorphanol group never increased above baseline throughout the study period (figure – 3).

**Figure 4**

**Figure 3: Changes in intraocular pressure in the groups**



\*  $p < 0.05$  Group P vs Group F and Group B)

+  $p < 0.05$  (Group F vs Group B)

## DISCUSSION

Succinylcholine (Sch) is the drug of choice for rapid induction despite its effects on IOP because of the short onset time and effect allow endotracheal intubation in 30 – 60 s. Its short half-life also allows fast recovery of muscle power if the airway conditions are difficult.

As demonstrated in our study, fentanyl and butorphanol prevents the increase in IOP from Sch as well as laryngoscopy and endotracheal intubation. Rocuronium, a new non-depolarizing neuromuscular blocking drug, which provides a rapid onset of action, has been found not to increase IOP [[15. ]] Unfortunately, it does not provide a rapid and predictable intubating conditions as Sch unless doses of three times of  $ED_{95}$  are used <sup>16</sup>. Although, induction of anaesthesia with propofol caused a statistically non-significant decrease in IOP in our study but it did not attenuated the IOP response to Sch and intubation.

On reviewing literature, maintenance of anaesthesia with propofol infusion was equally effective to sevoflurane <sup>17</sup>, desflurane <sup>18</sup> and isoflurane <sup>18</sup> to maintain IOP at reduced level. In a study various combination of drugs have been used to obtund the increase in IOP due to intubation and it was concluded that IOP did not increase significantly after Sch, but only anaesthesia induced with propofol and alfentanil prevented the increase in IOP due to intubation <sup>19</sup>. Likewise we also found that Sch did not cause significant

increase in IOP in any of the patient in all the three groups but addition of fentanyl and butorphanol effectively and equally blunted the IOP response to laryngoscopy and intubation.

In our study, fentanyl 2µg/kg attenuated the increase in IOP. In contrast, Ng HP and colleague failed to demonstrate attenuation of increase in IOP with fentanyl 2µg/kg<sup>9</sup>. Although in another study author demonstrated 2.5µg/kg dose of fentanyl to attenuate the increase in IOP associated with Sch and endotracheal intubation<sup>7</sup>. In a recent study fentanyl 2µg/kg was found to be comparable to remifentanyl infusion (0.25-0.5µg/kg/min) to maintain IOP at a reduced level<sup>20</sup>.

In our study, we administered Sch in the doses of 2 mg/kg and none of our patients coughed or gagged during intubation and none of the patient was excluded from the study because of this reason. In the study by Alexander and colleagues<sup>21</sup>, Sch 1mg/kg was used and few patients either gagged or coughed due to low dose of Sch used. So apart from the various drugs to be used to attenuate the hemodynamic response or increase in IOP to Sch and intubation, depth of anaesthesia should be maintained with the adequate doses of the induction agent and Sch.

We chose propofol as an induction agent instead of thiopentone sodium as it causes more decrease in IOP<sup>17</sup> than thiopentone but it has been seen that it causes significant hypotension<sup>22</sup>. In our study none of the patient had significant hypotension in any of the group because the patients chosen for our study were middle aged belonging to ASA class I or II with no cardiovascular disease.

The limitation of this study was that it was conducted in patients with normal eyes rather than on patients with open globe injuries. The sequence of IOP changes in patients with open globe or penetrating injuries may not be similar to those in patients with normal eyes. In an open globe, IOP is atmospheric and any increase in pressure results in further loss of ocular contents rather than increase in IOP. Another limitation of this study is that we have used butorphanol 1 mg and fentanyl 2µg/kg and we were not sure at the start of our study whether we have used equipotent doses of butorphanol to that of fentanyl.

In summary, our findings support the claim that Sch as well as endotracheal intubation cause an increase in IOP that can be prevented by achieving adequate depth of anaesthesia

with the combination of butorphanol-propofol likewise the fentanyl-propofol combination. We conclude that 1 mg bolus of butorphanol obtunded the increase in IOP associated with Sch and tracheal intubation without any unwanted hemodynamic effects.

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