Bispectral index (Bis) guided comparison of control of haemodynamic responses by fentanyl and butorphanol during tracheal intubation in neurosurgical patients

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Abstract

Introduction
Laryngoscopy and intubation are required for almost all neurosurgical patients undergoing general anaesthesia, which often causes certain undesired haemodynamic changes which may culminate in poor surgical outcome. Fentanyl and Butorphanol are commonly used for suppression of these undesired haemodynamic changes. The aim of the study was to compare haemodynamic responses during intubation and extubation along with Bis changes using equianalgesic doses of butorphanol (30µg/kg) or fentanyl (2µg/kg) as a component of general anaesthesia for neurosurgical patients.

Materials and methods
This was a prospective randomised control study. One hundred and ten patients belonging to the American Society of Anaesthesiology (ASA) grade I and II were randomly allocated into two groups, Fentanyl group (F) and Butorphanol group (B). All Pts were monitored in terms of Heart rate, ECG (Electrocardiogram), Non-invasive blood pressure, End tidal CO2 (ETCO2), Bispectral index (40-60) and oxygen saturation during intubation, 1 min before intubation and at an interval of 1 min till five minutes post intubation. Results were analysed statistically with SPSS 16.0 version using an unpaired t-test. P value <0.05 was considered as significant. Power of the study was 80.

Results
This study revealed that both Fentanyl and Butorphanol attenuated haemodynamic response to tracheal intubation like Mean arterial pressure (MAP) and Heart rate (HR) but there was significant (P<0.05) rise of heart rate and mean blood pressure post-intubation in Butorphanol group than in Fentanyl group.

Conclusion
Therefore Fentanyl is better option for control of haemodynamic responses during tracheal intubation than Butorphanol.

Introduction
Maintenance of optimum cerebral perfusion pressure (CPP) and cerebral oxygenation remain the basics of neuroanaesthesia. Laryngoscopy and intubation are often associated with undesired haemodynamic changes due to reflex sympathetic reaction such as tachycardia or bradycardia and rise in blood pressure. Such effects are deleterious in susceptible individuals culminating in significant rise in intracranial pressure (ICP) and decreased CPP hence anaesthetic management of these patients demands selection of suitable drugs to prevent intubation response. Fentanyl and Butorphanol both are used as adjuncts to balanced general anaesthesia for attenuating haemodynamic response during intubation. Since both have different pharmacodynamic profile, it becomes important to determine which opioid is better to give smooth general anaesthetic induction with minimal adverse effects.

Bispectral index (Bis)² is a statistically based, empirically derived complex parameter, a numerical index of depth of sedation ranging from 100 (awake) to 0 (isoelectric Electroencephalogram).

Combination of propofol with fentanyl may give an average and optimum BIS index for smooth anaesthetic induction, which may be different from propofol and butorphanol combination for the same purpose. Sedative effect of butorphanol may get added to propofol. The emphasis remains on the provision of good operative conditions, assessment and preservation of neurological function, and a rapid, high-quality recovery. This study was based on a hypothesis that fentanyl, being a short acting profound analgesic would be a better alternative to butorphanol as a component of general anaesthesia for attenuating haemodynamic responses after intubation and extubation of trachea in neurosurgical patients.

Materials and methods
This study was conducted in a tertiary care centre located in northern India between October 2009 and March 2011. After obtaining approval from the hospital ethical committee and informed consent from the patients, one hundred and ten patients belonging to ASA grade I and II scheduled for elective neurosurgery were studied. The patients were subjected to detailed clinical examination and routine investigations to exclude any associated systemic disorder.

Patients with systemic disease like respiratory, cardiac, hepatic or renal insufficiency, cervical spondylosis, any hypersensitivity to Propofol, Butorphanol or Fentanyl and requiring emergency neurosurgery, and patients with neuromuscular diseases were excluded from the study. Patients with difficult airway or requiring techniques...
other than direct laryngoscopy and intubation were also excluded.

Patients were randomly (randomization done by draw of lots) allocated to one of the two groups; Group F: 56 Patients receiving 2µg/kg Fentanyl, Group B: 54 Patients receiving 30µg/kg Butorphanol.

On arrival in the operation theatre, standard monitors (Electrocardiograph, Pulse oxymeter, Noninvasive blood pressure, Bispectral index) were attached to the patients. Noninvasive blood pressure was adjusted at one minute interval in auto mode, capnograph attached to circle circuit. In the operating room an arm vein was cannulated and all patients received normal saline 5ml/kg over a 15 minutes period.

All patients received injection Ondensetron 0.1mg/kg Thereafter patients were given injection Fentanyl 2 µg/kg (Group F) or Butorphanol 30 µg/kg (group B) intravenously in respective groups.

After preoxygenating the patients with 100% oxygen for 3 minutes with a facemask, all patients were induced with injection Propofol, given manually and titrated till response to verbal command wore off and relaxed with injection Vecuronium bromide given 100µg/kg as a bolus. Then patients were manually ventilated with 100% oxygen bag and mask for next three minutes. Intubation was performed with Mc-Intosh laryngoscope and laryngoscopy was limited to <30 seconds. Intubation was done with 7.5mm and 8.0mm endotracheal tubes in females and males respectively. Immediately after induction of anaesthesia, Propofol infusion 50-200µg/kg/min was started and titrated according to Bis values & haemodynamic parameters till the end of surgery. For maintenance of anaesthesia 66%Nitrous oxide in oxygen, intermittent Vecuronium bromide and Fentanyl (in repeat doses of 1mg and 50µg respectively) were used.

Patient's heart rate, electrocardiogram, mean arterial pressure, Bispectral index and ETCO2 were recorded 1 minute before, during (defined as start of laryngoscopy), and after intubation at an interval of 1min till 5 minutes. All the patients were transferred to Post Anaesthesia Care Unit (PACU) for further monitoring after the completion of satisfactory reversal.

Results were analysed statistically with SPSS 16.0 version using unpaired t-test. The critical probability value "p" indicating a significant difference was taken as < 0.05. Power of the study was 80.

Results

In our study we have compared two groups, group1 Fentanyl [F] and group 2 Butorphanol [B]. Patient's age, sex, weight and clinical parameters i.e. heart rate, mean arterial pressure, oxygen saturation, ETCO2 and Bis values were taken as variables during intubation.

The age varied from 3 to 65 between the two groups. Mean age were Figure 1: Statistical comparison of mean heart rate per minute ± SD at different time interval in two groups during intubation and extubation.

Figure 2: Statistical comparison of mean of mean arterial pressure ±SD at different time interval in two groups during intubation and extubation.
34.31±17.38 years in group 1 and 36.27±14.24 years in group 2. The male to female ratios were 66.67: 33.33 in group 1 and 56.7:43.3 in group 2.

Statistical comparison of the mean ages, sex distributions, mean weight did not reveal any significant difference (p>0.05).

Figure 1 shows mean heart rates (±SD) at different time intervals in two groups. In Fentanyl group, the 1 minute before intubation heart rate of 77.6±13.74 changed to 79.38±12.59 during intubation then decreased to 78.76±13.02 at 1 minute post intubation, 76.24±12.31, 75.69±12.64, 75.38±12.78, 75.45±12.74 at 2, 3, 4, 5 minutes post intubation respectively.

In the Butorphanol group, the 1 minute before intubation heart rate of 79.73±13.12 increased to 84.83±14.45 during intubation then increased to 88.50±12.19 at 1 minute post intubation, 83.40±11.45, 80.40±11.97, 79.10±12.10, 77.80±12.55 at 2, 3, 4, 5 minutes post intubation respectively.

Corresponding means of heart rate at each time interval among the two groups have been compared statistically.

Each group was compared to the other using student-t test. 1 minute before and during intubation heart rates were comparable in group F Vs group B i.e. statistically there was no significant difference (p>0.05). There was significant rise in heart rate at 1 minute and 2 minute post intubation in group B as compared to group F. But there was statistically no significant difference in group F and group B in mean arterial pressure at 3 minutes, 4 minutes, and 5 minutes after intubation (p>0.05).

Oxygen Saturation
Corresponding means of oxygen saturation during intubation at each time interval among the two groups have been compared statistically. Each group was compared to the other using student-t test. There was no significant difference (p>0.05) between the groups.

End Tidal CO2
Corresponding means of end tidal CO2 at 1 minute before, during intubation and 1 minute, 2 minutes, 3 minutes, 4 minutes, and 5 minutes post-intubation between the two groups were comparable statistically (p>0.05).

Bispectral Index
Figure 3 shows mean of Bis value ± SD at different time intervals in two groups. Corresponding mean of Bis value at each time interval among the two groups have been compared statistically. Each group was compared to the other using unpaired t test 1 minute before, during intubation and 1 minute, 2 minutes, 3 minutes, 4 minutes, and 5 minutes post intubation Bis values were comparable in group F Vs group B i.e. statistically there was no significant difference (p>0.05).

Discussion
Haemodynamic responses associated with laryngoscopy and endotracheal intubation have long been studied. Multitude of drugs has been used for attenuating this response with variable success. Opioids represent the most common class of drugs that is used for this purpose. Importance of maintaining constant haemodynamics perioperatively in neuroanaesthesia practice has been a vital and well established fact. In this study, post intubation haemodynamic and Bis responses were compared using Fentanyl or Butorphanol in neurosurgical patients. Observations were made at 1 minute before intubation, during intubation and at an interval of 1 minute till five minutes after intubation.

The study groups were comparable demographically (age, sex, weight). Butorphanol is mixed agonist-
antagonist with low intrinsic activity at morphine-like (μ) receptors. It is also an agonist at kappa (k) receptors. Its interactions with these receptors in the central nervous system apparently mediate its pharmacologic effects, including analgesia. Fentanyl is a strong μ-receptor agonist and causes profound analgesia. Fentanyl also binds to the kappa (k) opioid receptors located within the spinal cord. Fentanyl has a shorter half-life, time of onset and peak effect time than Butorphanol.

Although the exact mechanisms by which tracheal intubation causes haemodynamic changes remain as yet to be elucidated. Tracheal intubation produces a profound but short, uniform stimulation in the anesthetized patient.

After thorough analysis of our observations we found Fentanyl was more effective than Butorphanol in optimally controlling heart rate responses during tracheal intubation. Fentanyl was more effective in controlling pressor response during tracheal intubation than Butorphanol. In our single blind controlled prospective study we found that the intubation techniques, oxygen saturation, Bis values and end tidal CO2 were comparable in both the groups before and after induction of anaesthesia but there was transient but significant rise in the heart rate post intubation in Butorphanol group in comparison to Fentanyl group.

These observations are in accordance with Dahlgren et al, who reported that Fentanyl 15mg/kg administered IV in conjunction with thiopental 5mg/kg three and a half minutes prior to laryngoscopy significantly attenuated the BP and HR responses. However such a high dose of Fentanyl is rarely used in clinical conditions. We too used only 2µg/kg in our Fentanyl group patients. In normotensive patients Kauto et al reported that Fentanyl 2mg/kg significantly, and 6mg/kg completely, attenuated the BP and HR responses when it was given three and one-half minutes before laryngoscopy. These findings are in contrast to observations reported by Pandit et al.

and Beverly K Philip et al, who reported significantly higher post-intubation heart rate in Fentanyl group as compared to Butorphanol group. In our study, we found that the mean arterial pressure significantly increased in Butorphanol group as compared to Fentanyl group at 1 minute post-intubation, rest of the readings were comparable in both the groups. This is in contrast to the findings reported by Pandit et al, who reported that patients receiving Butorphanol were having post intubation blood pressures values almost similar to pre intubation values, but they reported that Butorphanol (40µg/kg) used as part of a standard balanced general anaesthetic for outpatient procedures was not superior to Fentanyl (2µg/kg) used in the same fashion. Our findings are also in contrast with Philip et al, who conducted a study in which Butorphanol was compared with Fentanyl as the narcotic component of general anaesthesia for ambulatory laparoscopic surgery. They found that Butorphanol is an acceptable alternative analgesic in general anaesthesia for ambulatory laparoscopy.

In another study done by Singh et al, Butorphanol in combination with Propofol effectively obtunded the haemodynamic response as well as increase in IOP after giving Succinylcholine and after intubation, without any increase in adverse events. Butorphanol 1 mg was found to be equipotent to 2µg/kg Fentanyl in this respect. In contrast to this, in our study Butorphanol in combination with Propofol could not effectively obtund haemodynamic response. We have seen that in Butorphanol group, during intubation both heart rate and pressor response are not controlled well. Driessenet al, found lack of significant correlation between the Bispectral index values and the haemodynamic responses. Similarly we also couldn’t find any correlation between the Bispectral index values and the haemodynamic responses. Wei-Dong Mi et al. found that 2µg/kg Fentanyl intravenous, in conjunction with Propofol was effective in blunting the haemodynamic responses to intubation at a given Bis. We also found that Fentanyl 2µg/kg with Propofol was effective in blunting the haemodynamic responses to intubation at a given Bis in comparison to Butorphanol. Our study clearly shows that haemodynamic response to tracheal intubation was attenuated by both the drugs, but the response was significantly more after Fentanyl in comparison to Butorphanol.

After tracheal intubation, the arterial pressure and HR in patients receiving IV Butorphanol increased significantly compared with the preintubation values, whereas in patients receiving injection Fentanyl were maintained at the level of preintubation values, which resulted in the significant difference in arterial pressure between these groups. From where does this difference come? This may be explained as Fentanyl has known sympatho-inhibitory effect, which activates vagal efferent fibres (through M3 receptors) causing bradycardia thereby counter acting the tachycardia response of endotracheal intubation.

Conclusion
The above results proves that our hypothesis is true as we have observed that Fentanyl is overall better at controlling intubation response than Butorphanol. In our study we have taken only haemodynamic parameters in account, and observations have been made using the maintenance doses of analgesics only. While Butorphanol does not give good control of haemodynamic response after intubation, it will be safer to use Butorphanol with some additional drug which can attenuate haemodynamic responses both during intubation. Further research needs to be done on drugs and techniques to prevent adverse tracheal intubation outcomes.

Authors' contribution
The review is the product of the collaboration of Sunit Kumar, Ajeet Singh, LD Mishra, Manoj Giri, each one contributed of his knowledge and
expertise. All authors read and approved the final manuscript.

References