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Observations On Haemodynamic Effects Of Sevoflurane – Propofol Co-Induction.

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ABSTRACT

Background: Both Propofol and Sevoflurane have been seen to decrease the haemodynamic stress response obtained with oro-tracheal instrumentation. But they are also associated with significant depression of cardiovascular system. With the aim to gain benefit from both these agents but lessen the cardiovascular depressive manifestations, we induced the patients using both the agents in decreased dosages and observed the effects there upon on haemodynamic parameters. **Methods:** 30 patients were given to inhale Sevoflurane(4%) in Oxygen and were also administered intravenous Propofol (1mg/kg) for induction of general anaesthesia. Aided by IV SuccinylCholine(1mg/kg), trachea was intubated under direct laryngoscopy. **Results:** The Systolic , Diastolic, Mean Blood Pressure values and Pulse rates were noted before and after induction and following intubation and the observations were analysed. **Conclusion:** .Anaesthesia induction with Propofol and Sevoflurane combination blunts the haemodynamic stress response.

Keywords: Sevoflurane, Propofol, Co-induction, Haemodynamic response.

INTRODUCTION

Induction of anaesthesia comes at a cost of airway compromise along with several haemodynamic changes. Anaesthesiologists should be well versed not only with airway management, but also on ways to mitigate the physiologic changes that follows. Since 1879, when William Macevan first performed elective intubation,[1] anaesthesia has come a long way in airway management with many options like fibreoptic and supraglottic airway devices being available. But endotracheal intubation is considered still the gold standard for securing the airway.

Instrumentation of larynx and trachea produces intense noxious stimulus that is reflected as sympathoadrenal stress response. Mechanoreceptors present in the airway mucosa are primarily responsible for the stress response seen during laryngoscopy and intubation. To attenuate this response, the most popular technique employed is inducing anaesthesia with agents that centrally suppress the airway reflexes.

Anaesthesia can be induced using either intravenous or inhalational induction agents. Among the intravenous induction agents, Propofol in doses of 2-2.5mg/kg is most preferred as it suppresses the airway reflexes, causes antiemesis and has short context-sensitive half-life but in this dosage, Propofol can produce deep hypotension, myoclonus and pain during injection. On the other hand, inhalational induction of anaesthesia is needle-free and painless. The halogenated inhalational agents Halothane and Sevoflurane are popular on account of sweet agreeable odor, smooth and rapid induction of anaesthesia. Sevoflurane is preferred over Halothane because it has relatively high blood-gas partition coefficient, long induction period and does not produce Hepatitis. Sevoflurane has proven itself as a potent induction agent especially for laryngeal mask airway (LMA) insertion. But for endotracheal intubation, deep levels of Sevoflurane anaesthesia is required because the MAC bar of Sevoflurane is over 8%; which is almost 4 MACim.[2] At this level of anaestheisa, hypotension and bradycardia is greatly potentiated warranting use of adjuvants such as opioids, muscle relaxants, Propofol and/or Ketamine.[3]

In this study we observed the haemodynamic response obtained upon induction and intubation when patients were co-induced with Sevoflurane (4%) as well as Propofol (1mg/kg).

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MATERIALS AND METHODS

It was a prospective randomized observational study. After obtaining approval of institutional ethical committee and informed written consent, 30 adult patients of ASA grade I & II posted for elective surgery with endotracheal intubation were included randomly. Patient refusal, evidence of difficult airway and history of malignant hyperthermia were taken as exclusion criteria. On the day of surgery, after base line reading of haemodynamic parameters- Pulse rate, Systolic blood pressure, Diastolic blood pressure and Mean arterial pressure were recorded, all the patients were premedicated intravenously with Inj.Glycopyrrolate(0.2mg), Inj.Midazolam (1mg) and Inj.Butorphanol(1mg). Each patient was pre-oxygenated with 100% oxygen for 3min.

Vital capacity induction(VCI) technique was employed for Sevoflurane induction. Prior to induction, all the patients were taught and made to practice the technique i.e., to exhale fully, then inhale fully and hold the breath as long as possible. After the anaesthesiologist was convinced of the patient's understanding of the vital capacity induction technique, patients were asked to inhale deeply following full exhalation from a circuit primed with Sevoflurane. Priming was done with Sevoflurane vaporizer dial set to 4% with oxygen flow of 8L/min, till the gas analysis in inspired limb measured 3%. It typically required three fill/empty cycles with the circuit occluded. The pre-oxygenation mask was removed at end-expiration, and this primed circuit with mask was applied to the face. Patients were encouraged to hold the breath as long as possible. Following the vital capacity breaths, InjPropofol (1mg/kg)was given IV over 20sec. This was followed by Inj.Succinylcholine (1mg/kg) and orotracheal intubation was done under direct laryngoscopy. Anaesthesia was maintained with N2O:O2 = 3:2 along with Isoflurane @ 0.6-1% v/v. Adequate muscle relaxation was maintained with intermittent intravenous bolus Inj. Vecuronium. Pulse rate(PR), Systolic blood pressure(SBP), Diastolic blood pressure(DBP), Mean arterial pressure(MAP) and Oxygen saturation(SpO2) were recorded at the following periods: pre-induction, post-induction, and, 2min, 5min, 10min, 15min following induction.

Vital parameters were monitored throughout peri-operative period. At the end of surgery, all anaesthetics were withdrawn. Residual muscle paralysis was reversed with Inj.Neostigmine (0.05mg/kg) and Inj. Glycopyrolate (0.04mg/kg) and awake extubation was done.

RESULTS

Gender and weight distribution being comparable, we had more patients in 20-30 years age-group and in ASA category I.

Table 1: Demographic Variables (n=30)

Variables	Age(years)		Gender		Weight (Kg)			ASA Grade	
	20-30	30-40	Male	Female	41-50	51-60	61-70	I	II
No. of Patients	18	12	16	14	11	10	9	27	3
Percentage of Total	60%	40%	53.33%	46.67%	36.66%	33.33%	30.00%	90%	10%

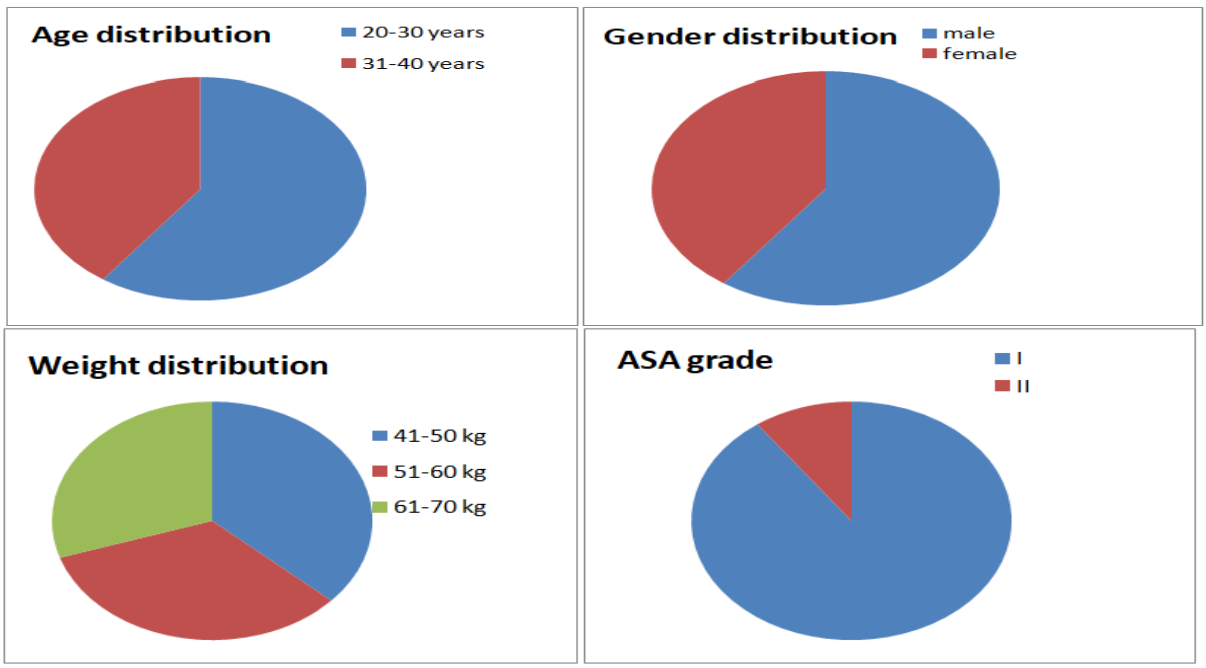
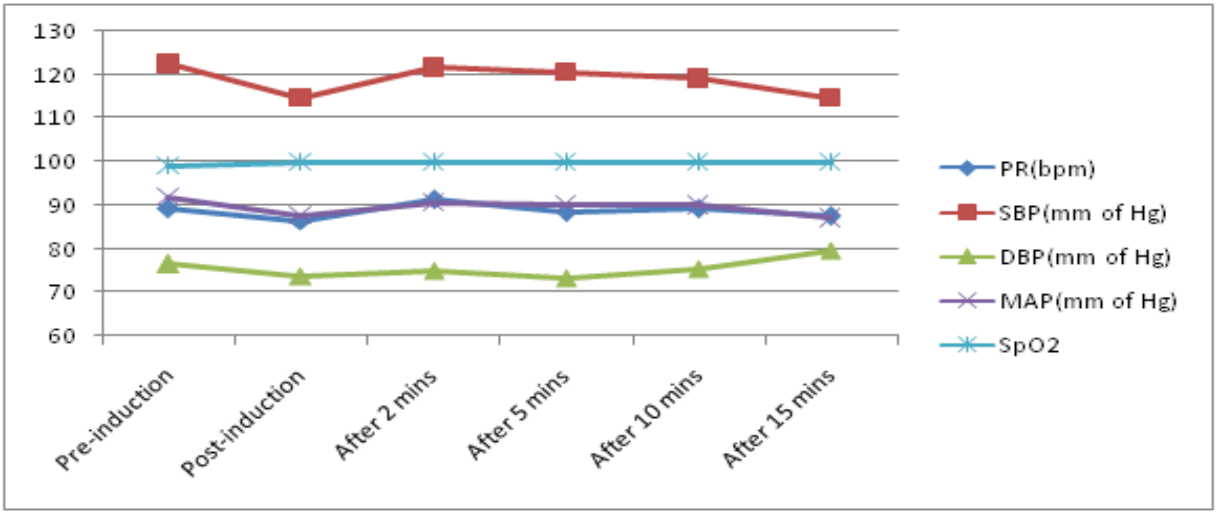


Table 2: Haemodynamic Parameters (Mean±SD)

Variables	PR (bpm)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	SpO2 (%)
Pre-induction	89.13±8.35	122.40±7.32	76.53±7.90	91.73±7.31	99.10±0.66
Post-induction (0 minute)	86.50±7.06	114.63±6.33	73.80±7.66	87.77±6.16	99.90±0.30
After 2 mins	91.23±6.36	121.53±5.79	74.97±7.43	90.50±6.44	99.93±0.25
After 5 mins	88.30±5.21	120.43±5.68	73.43±7.63	90.13±6.84	99.90±0.30
After 10 mins	89.10±6.14	119.00±5.57	75.47±6.56	90.00±5.94	99.97±0.18
After 15 mins	87.37±4.00	114.60±8.48	79.73±2.40	87.00±3.36	99.97±0.18



Graph of Haemodynamic Parameters

DISCUSSION

Multimodality approach in balanced anaesthesia aims at obtaining the desired effect while minimizing undesirable side effects. In our study we analysed the haemodynamic fluctuations of induction and tracheal intubation when anaesthesia was induced using both Sevoflurane and Propofol in reduced dosages.

In the year 1940, Reid & Brace first reported the incidence of tachycardia and rise in blood pressure following intubation.[4]King BD et al in 1950 observed that haemodynamic changes upon laryngoscopy and intubation was significantly higher in light plane of anaesthesia, and concluded that deepening the plane of anaesthesia attenuates this response.[5]

The review article by Blanc and Trembley on complications of endotracheal intubation published in 1974, stated that laryngo-tracheal stimulation induces tachyarrhythmia and hypertension. They linked this phenomenon to increase in plasma Nor Adrenaline as a result of laryngosympathetic reflex.[6] Russel et al in 1981,[7] Derbyshire DR et al in 1983[8] and Pyres Roberts et al in 1986,[9] also observed independently the rise in plasma NAdr level following laryngoscopy and intubation. Their studies also supported that conducted by King BD et al; concluding that these sympathetic responses are readily precipitated by light plane of anaesthesia, hypoxia and hypercarbia.

Currently employed halogenated inhalational agents provide the desired plane of anaesthesia for laryngoscopy and intubation. Among the available agents, Sevoflurane is the most popular agent for inhalational induction. It has a blood: gas partition coefficient of 0.67 at 37° C, which is 2nd lowest among the modern volatile agents. This permits a rapid induction of anaesthesia.

Inhalational anaesthesia can be induced by either of the two methods of inhalational induction i.e., tidal breath or vital capacity method. In both methods, patient needs to inspire from a circuit that is primed by the volatile agent to be used. In tidal breath induction, patient maintains his/her normal basal respiratory rate and tidal volume during induction. Our study employed vital capacity induction technique for Sevoflurane induction. This was first described by J G Bourne in 1954 for Cyclopropane induction.[10] Here patients were asked to inhale from the primed circuit after full exhalation and hold the breath as long as possible. Bourne's technique is superior to tidal breath induction due to shorter induction time and lesser complication during induction as evidenced by Yurino M et al in 1993.[11] MACEI is the minimum alveolar concentration of volatile agent required to obtain an acceptable condition for endotracheal intubation. In the year 1994, Kimura T et al determined the MACEI for Sevoflurane to be 4.52% which is 2.8 times the MACIM.[12] In order to achieve the MACEI patients should be mask ventilated with a circuit primed with 6-7% Sevoflurane for 4-6 minutes.[13] This potentially increases the risk of hemodynamic compromise, as Sevoflurane is known to cause

decrease in cardiac output and systemic vascular resistance in a dose dependent manner.[14,15] Another major drawback of Sevoflurane induction is the patient excitement during induction. Such a case was first reported by Adachi M et al in 1992.[16] They reported a case of tonic clonic seizure-like movements in the extremities of a young girl during Sevoflurane induction. Two years later, Komatsu et al reported two more such incidences.[17] In 2001, Vakkuriet al investigated the effect of induction with Sevoflurane 8% on brain electrical activity. They found evidence of seizure on EEG, especially during controlled ventilation. They also concluded that these abnormal EEG discharges alter the autonomic nervous system outflow leading to hyperdynamic circulatory changes.[18] Wappler F et al published a review article and questioned the immediate administration of Sevoflurane 8% for induction. They reported that the high concentration might be the cause of EEG change. So they advocated for lower concentration of Sevoflurane for induction and to avoid hyperventilation by controlled ventilation.[19]

With the introduction of barbiturate group of drugs, intravenous anaesthesia gained popularity over inhalational route for quick, predictable smooth and pleasant induction. The potent intravenous hypnotic Propofol, is popular as it suppresses the airway reflexes better than other agents - as concluded by Mackenzie and Grant in 1985 and McKeating et al in 1988.[20,21] Stress hormone levels are also considerably lower with Propofol induction. In the year 1995 Mustola ST et al found that plasma adrenaline levels were significantly lower after induction with Propofol and remained below baseline throughout the procedure.[22] Plasma NAdr level also did not increase following Propofol induction as evidenced by S Coley et al.[23] Vasilerou et al in 2009 summarised the non-anaesthetic but beneficial actions of Propofol as follows:[24] stimulates constitutive nitric oxide production, inhibits inducible nitric oxide production, anxiolytic, antioxidant, antiemetic, immunomodulatory, neuroprotective, inhibits both platelet aggregation and intracellular calcium increases in response to thrombin or ADP. It exerts inhibitory effects on recombinant cardiac sarcolemmal KATP channels. Despite these advantages, injection-pain, hypotension and drug hypersensitivity are some major drawbacks of Propofol.

Combination of Propofol with Sevofluranefor induction of anaesthesia have been studied and reported. Harris RS et alin 2006 studied the combined effect of Sevoflurane and Propofol on loss of consciousness and movement to skin incision during general anaesthesia on 36 elective surgical patients and found that both the agents interact in simple additive manner suggesting a common mechanism or site of action. They concluded that these observations were consistent with single site action i.e. GABA-A receptor.[25]

Luke E Sebelet alalso in 2006 did a similar study and observed that either Propofol or Sevoflurane alone enhance the amplitude of GABA-A receptor responses to submaximal concentration of GABA in a dose dependent manner. Co-application of both anaesthetics further enhances the affinity of GABA. Response surface modeling revealed that two of them modulate the receptor function in an additive manner. In their opinion, Propofol and Sevoflurane have separate binding sites and converging pathways of action on the GABA-A receptor.[26]

In the year 2008 Hendrickx et al reviewed various articles on anaesthetic interactions that produce hypnosis and immobility. Their review of both intravenous and inhalational agents found that Sevoflurane and Propofol interact additively.[27]

In order to minimize the untoward haemodynamic effects seen with employment of either Sevoflurane or Propofol as independent sole anaesthetic agents, but take advantages of their anaesthetic properties, we decreased the concentration of Sevoflurane to 4% and supplemented it with intravenous InjPropofol 1mg/kg for induction of anaesthesia and observed the results.

In this observation on 30 patients at our institute, the mean pulse rate prior to induction was 89.13±8.35bpm; which decreased by 2.34% following co-induction with Sevoflurane and Propofol. When recorded 2 min after induction, i.e., after intubation, the pulse rate had an increase of 2.3% over the pre-induction value. Throughout the period of 15min following induction, the pulse rate varied within 2% of the pre-induction value. The effect of this technique on Systolic, Diastolic & Mean arterial pressure were as follows. Post-induction of anaesthesia, the Systolic blood pressure decreased from a pre-induction mean value of 122.40±7.32mm of Hg to 114.63±6.33mm of Hg; which was a fall of 6.3%. After intubation the systolic blood pressure increased to 121.53±5.79mm of Hg. But, this was 0.7% lower than pre-induction value. Diastolic and Mean arterial pressure also showed a similar trend of 3.5% and 4.3% fall respectively following induction. Intubation did produce a surge in stress hormones and consequent rise in these blood pressure values. But this increase in diastolic and mean arterial pressure was below the pre-induction values i.e., 2% & 1.3% lower than the pre-induction values respectively.

We did not find any significant decrease in oxygen saturation values with this technique.

CONCLUSION

Combination of Propofol and Sevoflurane for induction of anaesthesia effectively blunts the haemodynamic stress response to laryngoscopy and tracheal intubation with minimal variation in haemodynamic parameters. Their additive action on

GABA-A is an option to consider for balanced anaesthesia.

Limitations

1. Intraoperative haemodynamic variations beyond 15minutes were not included.
2. Comparison with other agents and with a control study were not done.
3. Limited number of subjects were studied.

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