The Haemodynamic Effects of Thiopentone/Propofol and Combined use of Low Dose Thiopentone and Propofol on Induction and Intubation - A Three Modality Comparative Study

Anne Kiran Kumar[1], Kaluvala Prasad Rao[2], Metta Rajasekhar[3], Anyapu Praveena[4], Jillella Sindhuja[5], Gopinath Ramchandran[6]

ABSTRACT

Introduction: Induction, Laryngoscopy and Intubation are the points at which haemodynamic changes occur during conduct of anaesthesia, with such changes leading to deleterious systemic effects in vulnerable patients. This study was conducted to compare the haemodynamic effects on induction, and intubation with endotracheal tube with conventional doses of thiopentone and propofol separately and with combined use of low dose of thiopentone and propofol.

Material and methods: The study was conducted on 90 patients of ASA Grade - I and II, and of Age between 20-50 years posted for Elective Surgery. The 90 patients were randomly assigned to three groups of 30 each. Thiopentone (5mg/kg), Propofol (2.5mg/kg) or A combination of low dose of both Thiopentone (2.5mg/kg) and Propofol (1.5mg/kg) was used as induction agent in Groups – I, II and III respectively. Heart Rate and Blood Pressure were measured non-invasively at various (Five) times - At Pre-induction, one minute after the last injection of induction drug i.e., before the performance of Laryngoscopy and Endotracheal tube placement, and at First, Third and Fifth minute of Endotracheal tube placement.

Results: The adjusted mean values of Systolic blood pressure, Diastolic blood pressure and Heart rate were assessed by Paired comparisons, by considering the variable of time. All changes were significantly different between Groups I and II. Moreover, changes in systolic and diastolic blood pressures were significantly different between Groups I and III. They were not significant for Heart rate. No significant difference was noted between Groups II and III; showing that in these groups the haemodynamic changes were small during drug injection, Laryngoscopy and Intubation as well as until five minutes after Endotracheal placement.

Conclusion: The Combined use of low dose of Thiopentone and Propofol (Group-III) for anaesthetic induction and Intubation caused less Haemodynamic changes than the higher individual dose of either alone.This modality of Anaesthesia induction may have clinical importance for the Elderly patients as well as those with Hypertension and Heart diseases and those belonging to ASA Grade – III and IV.

Keywords: Thiopentone, Propofol, Induction, Laryngoscopy, Intubation, Haemodynamic Effects

INTRODUCTION

Patients undergoing Laryngoscopy and Endotracheal Intubation are known to develop Haemodynamic changes such as increase in Blood pressure (BP) and Heart rate (HR).In susceptible patients, such changes may lead to myocardial ischemia or a rise in the Intracranial pressure (ICP).[1,2] Thiopentone sodium is one of the most commonly used intravenous induction agents throughout the world.[3,4] The induction dose of Thiopentone is 3-5 mg/kg, with dose-dependant hypotension as it's usual side effect due to decrease in myocardial contractility as well as peripheral vasodilation.[3,4] Heart rate may fall but there is often a reflex tachycardia probably due to a central vagolytic effect.[3-5]

Propofol is a short acting, rapidly metabolized intra venous anaesthetic agent used in recent years as an effective alternative to the time-tested thiopentone for intravenous induction of anesthesia. Induction with propofol is smoother, almost equally rapid, has rapid awakening and orientation times, better intubating conditions and upper airway integrity compared to thiopentone sodium.[6] However, the major disadvantages of rapid induction with propofol are impaired cardiovascular and respiratory function which may put patients at greater risk from hypotension, bradycardia, and apnea. At a dose of 2 - 2.5mg/kg it causes a 25 -40% decrease in arterial pressure after induction of anaesthesia, more so in elderly and higher ASA grade patients which is due to reduction of myocardial contractility (depressant effect on the myocardium), peripheral vascular resistance and sympathetic tone.[7-10] Vagotonic effects of propofol reduce the HR that may cause severe bradycardia, complete atrio-ventricular block and cardiac arrest.[5,7] It produces a decrease in systemic arterial pressure greater than that with a comparable dose of thiopentone at induction.[4,7,12,13]

Although the afore mentioned cardiovascular changes are significant, they are clinically unimportant in healthy patients.

[1]Associate Professor, [2]Associate Professor, [3]Senior Resident, [4]Junior Resident, [5]Junior Resident, [6]Professor and Head, Department of Anaesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad-500082, Telangana, India.

Corresponding author: Dr. Kaluvala Prasad Rao, Associate Professor, Department of Anaesthesiology and Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad-500082, Telangana, India.

How to cite this article: Anne Kiran Kumar, Kaluvala Prasad Rao, Metta Rajasekhar, Anyapu Praveena, Jillella Sindhuja, Gopinath Ramchandran. The haemodynamic effects of thiopentone/propofol and combined use of low dose thiopentone and propofol on induction and intubation - a three modality comparative study. International Journal of Contemporary Medical Research 2018;5(7):G4-G10.

DOI: http://dx.doi.org/10.21276/ijcmr.2018.5.7.28

In elderly or high-risk patients, cardiovascular depression may have profound effects on myocardial oxygenation. Hypertension during induction of anaesthesia or in response to tracheal intubation is also undesirable in elderly, high-risk patients. An antinociceptive/analgesic effect of propofol has been proposed[13], such an effect might attenuate the pressor response to tracheal intubation. Advantage of propofol is that it is more effective in preventing the increase in arterial pressure after intubation than thiopentone.[4,7,11,12]

Barbiturates are thought to exert many of their effects via enhancement of gamma-aminobutyric acid (GABA)-mediated inhibition in the central nervous system.[14-15] Propofol probably acts by modulation of GABA neurotransmission, although the exact mechanism is unknown.[14] The interaction between thiopentone and propofol was found to be synergistic. The synergistic interaction between thiopentone and propofol may be explained on the basis of interaction at the GABA receptor complex.[16]

The concept of co-induction of anaesthesia has come forward by administering small doses of sedative or other anaesthetic agents so as to decrease the dose requirement of the induction agent to make the quality of anaesthesia better with improvement in haemodynamic stability, i.e., with fewer side-effects. The practical uses of propofol-thiopental combinations have been previously studied. Pre-treatment or co-administration of thiopental or the usage of propofol-thiopentone admixture for induction of anaesthesia produced less hypotension compared to giving propofol alone.[17-19] As lesser doses of either agent is required for induction when a combination is used, afterload and myocardial contractility is effected to a lesser extent.

Reducing the dosages of these two induction agents cannot induce or create adequate depth of Anaesthesia for Laryngoscopy and tracheal Intubation and moreover there would be Haemodynamic problems. This study was conducted to determine the effects of a combination of low dose Thiopentone and Propofol during Induction and Intubation compared with using the conventional doses of Thiopentone or Propofol alone.

MATERIAL AND METHODS

This prospective, randomized, comparative study was conducted from January to April 2018, at Nizam's Institute of Medical Sciences, Hyderabad.

Inclusion Criteria - Patients of 20-50 years of age, of either sex belonging to American society of Anaesthesiologists status -I and II (ASA-I and II), weighing between 50-80 kgs, posted for elective surgery under general anaesthesia.

Exclusion Criteria - Patients with history of alcoholism or drug addiction, allergy to egg proteins, those with difficult airway or family history of Acute intermittent porphyria and those of ASA class III and IV.

A total of 90 patients were included in this study who were randomly assigned to three groups of 30 each. Thiopentone (5mg/kg) was used as an induction agent in Group I, Propofol (2.5 mg/kg) in Group II and a Combination of Thiopentone and Propofol (2.5 mg/kg and 1.5mg/kg) in Group III.

All the patients were premedicated with Alprazolam 0.5 mg and Ranitidine 150 mg night before and on the morning of surgery. After the patient was shifted to the operating room, intravenous line was secured with 18 G IV cannula and Standard baseline monitoring was used - Pulse oximetry, Electrocardiography (ECG), Non-invasive Blood pressure. All the patients were pre-oxygenated for 2–3 min prior to induction of general anaesthesia. Anaesthesia was induced intravenously using standardized anaesthetic technique, by fentanyl 2 µg/kg followed 1min later by thiopentone 5 mg/kg, or propofol 2.5 mg/kg or a combination of a low dose of both thiopentone (2.5 mg/kg) and propofol (1.5 mg/kg). To relieve the local pain from propofol injection in patients receiving this medication, lidocaine (20 mg) was uniformly given prior to induction medication to all three groups. The designated dose of either thiopental or propofol or the combined low dose regime was given over 60 -90 s, at the completion of which loss of eyelash reflex noted. This was followed immediately by Rocuronium 0.6 mg/kg after assessment of adequate ventilation by face mask. Ventilation was controlled via face mask with 100% oxygen with frequency of 12 /min and tidal volume was adjusted to maintain end-tidal CO2 between 30 and 35 mm Hg. One minute later, Laryngoscopy and Endotracheal Intubation was performed in less than 30 seconds. Post intubation, anaesthesia was maintained with O2, air (1:1) 2l/mt and sevoflurane 1 – 2%.

To determine the extent of Haemodynamic changes at Induction and during Laryngoscopy and Endotracheal Intubation, the Heart rate and Blood pressure (Systolic and Diastolic) were measured at various intervals (Five times) - Prior to the injection of the drugs, i.e., Pre-induction time, One minute after the last injection of induction drug, i.e., immediately before Laryngoscopy and Endotracheal Intubation, and in the First, Third and Fifth minute after Endotracheal Intubation. The data was collected by another anaesthesiologist blinded to the study. The patients who didn't have adequate relaxation for Laryngoscopy were excluded from the study.

STATISTICAL ANALYSIS

Data were analysed using SPSS Software, version 13.0 (SPSS Inc., Chicago, USA). Within group and between Group changes in Mean Blood pressure and Heart rate were compared. ANOVA and Post-hoc Tests were used as appropriate.

RESULTS

The three groups were comparable in relation to the demographic characteristics in terms of Age, Sex ratio (Male : Female) and Weight.

The baseline characteristics of patients in the three groups were not significantly different in terms of Mean systolic blood pressure, Mean diastolic blood pressure and Mean Heart rates (Table 1).

The mean values of the Systolic and Diastolic Blood pressure,

Group	Parameter	Mean Difference	Standard Error	P Value
I and II	SBP	-1.6	3.65	0.91
	DBP	-0.7	2.52	0.91
	HR	-1.5	2.31	0.76
I and III	SBP	-3.5	4.37	0.76
	DBP	+0.6	2.45	0.94
	HR	-1.2	2.34	0.90
II and III	SBP	-1.9	4.32	0.91
	DBP	+1.3	2.62	0.83
	HR	+0.3	2.55	0.96

SBP-Systolic blood pressure; DBP-Diastolic blood pressure; HR-Heart rate.

Table-1: Comparison of Baseline Mean Systolic and Diastolic Blood pressures and Heart rates between Groups.

Group	Parameter	Mean	Standard Error
I	SBP	118.32	1.67
	DBP	74.36	1.72
	HR	84.30	1.98
II	SBP	106.86	1.69
	DBP	65.02	1.89
	HR	76.68	2.21
III	SBP	111.20	1.76
	DBP	66.80	1.54
	HR	81.74	1.99

SBP-Systolic blood pressure (mmHg); DBP-diastolic blood pressure (mmHg); HR-Heart rate (bpm).

Table-2: Adjusted Mean Blood Pressures and Heart Rate in Five measurements in the groups studied.

Group	Parameter	Mean Difference	Standard Error	P Value
I and II	SBP	+11.46	1.99	0.001
	DBP	+9.34	2.66	0.003
	HR	+7.62	2.25	0.001
I and III	SBP	+7.12	2.01	0.003
	DBP	+7.56	3.13	0.045
	HR	+2.56	2.33	0.1
II and III	SBP	-4.34	2.15	1.00
	DBP	-1.78	2.93	0.79
	HR	-5.06	2.30	0.20

SBP-Systolic blood pressure; DBP-Diastolic blood pressure; HR-Heart rate.

Table-3: Comparison of Adjusted Mean Blood Pressures and Heart rate in Five measurements between the groups.

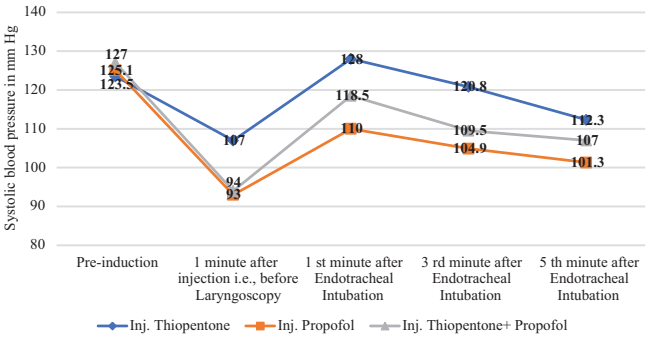

Figure-1: Mean Changes in Systolic Blood Pressure

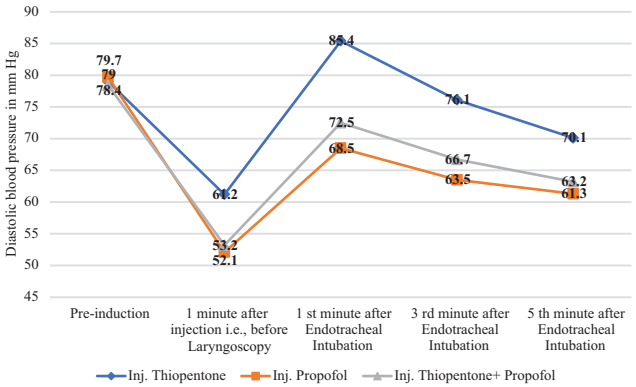

Figure-2: Mean Changes in Diastolic Blood Pressure

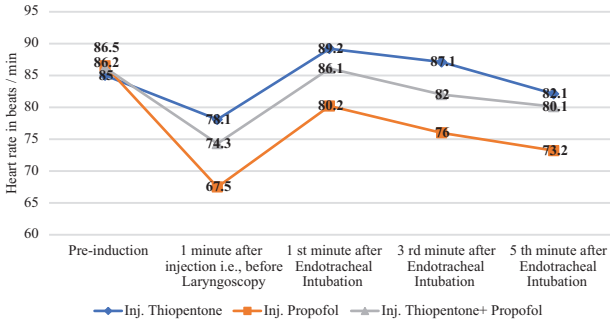

Figure-3: Mean Changes in Heart Rate

as well as Heart rate measured at various times were analysed (Table 2) and the double comparison done between Groups by the use of adjusted mean values (Table 3).

As presented in Table 3, the results of collected statistics of the tables show that the process of the changes (By cause and time) between Group I and II (paired comparision) had significant difference with reference to adjusted mean values of systolic blood pressure, diastolic blood pressure and heart rate, also mean systolic and diastolic blood pressure difference between Group I and III was significant too, but the difference for the mean Heart rate was not significant. The differences in changes in mean systolic and diastolic pressures and heart rate between Group II and III were not significant.

DISCUSSION

Laryngoscopy and Endotracheal Intubation can cause sympathetic stimulation often manifested as an increase in systolic and diastolic blood pressures and Heart rate.Thus, anaesthesiologists have been trying to use a variety of induction modalities to minimize Haemodynamic changes. Several studies have been conducted in this regard and various combinations of drugs have been proposed.

Planned simultaneous administration of multiple drugs exploits the beneficial effects of drug interactions. However, combining drugs with similar effects may result in synergistic, additive or antagonistic interactions. A synergistic interaction should bring about a decrease in adverse effects while maintaining the desired pharmacological effects. Modern day anaesthetic practice attempts to apply this principle to the induction and maintenance of anaesthesia. Midazolam has been reported to act synergistically with propofol and

thiopental. In contrast, propofol and sevoflurane interact in a simple additive manner to produce loss of consciousness. The interaction between nitrous oxide and propofol for the suppression of blood pressure elevation (non hypnotic effect) also appears to be additive.

Many studies by Mohammadi SS et al.,[18] Yeo KS et al.,[19] Sinha R et al.,[20] Rashiq S et al.,[21] and Kashtan H et al.,[22] which compared haemodynamics at induction and/or intubation, recovery characteristics (apart from other characteristics too in some of these studies) between thiopentone / propofol and/or an admixture of the two used induction doses of these medications roughly proportionate to a propofol to thiopentone (hypnotic) potency ratio of 1: 2-2.5. Different studies by Naguib M et al.,[16,23] Grounds RM et al.,[24] and Edelist G et al.,[25] comparing propofol and thiopentone with regards to their interaction / potency (and/or other characteristics) which used either failure to respond to verbal command and/or loss of eyelash reflex as end point for induction, yielded a (hypnotic) potency ratio varying from 1:1.604 to 1:2.2-2.88. Some of these studies were done on unpremedicated patients while some used premedication. Some of these studies[23], concluded that a dose-response curve reflecting one end-point of anaesthesia cannot be used to define another end-point of anaesthesia.

The endpoint of induction of anaesthesia if considered as failure to respond to verbal command, can be achieved with a smaller dose of either propofol or thiopentone than can the loss of the eyelash reflex. In the studies by Coley S et al.,[10] Rashiq S et al.,[21] and Wong W et al.,[26] comparing either the haemodynamic changes after induction and intubation, recovery characteristics or interaction between thiopentone / propofol /admixture, loss of eyelash reflex was considered as end point of induction rather than loss of response to verbal command.

Keeping in perspective all the above findings in different studies, we chose a propofol to thiopentone ratio of roughly 1 : 2, in our study, where the patient's were premedicated with fentanyl and loss of eyelash reflex was noted on completion of induction.

Consideration of giving fentanyl 2µg/kg prior to induction in our study was based upon study conducted by Harris CE et al.,[11] who concluded that use of 2µg/kg fentanyl prior to induction with thiopentone, etomidate and propofol resulted in lesser hemodynamic response (lesser rise in arterial pressure) to tracheal intubation than that after using any of these induction agents alone. The fentanyl to induction agent separation time was 60 secs in our study similar to the as in the study by Coley S et al.,[10] comparing the haemodynamic changes after induction and intubation using propofol or thiopentone in ASA I and III patients.

The choice of giving the induction drugs over a period of 60 - 90 secs was based upon studies by Rashiq S et al.,[21] and Singh R et al.,[27] comparing either recovery characteristics and/or hemodynamic effects of anaesthesia induction following induction with either thiopentone / propofol / admixture of the two (or other induction agents).

When rocuronium is used, after induction with conventional doses of propofol and thiopentone, in a dose of 0.6mg/kg, satisfactory intubation conditions are usually attained in 60 secs.[28] We chose rocuronium in this dose, and the time to intubation after giving rocuronium as 60 secs, in our study for the said reasons.

In this study, before Laryngoscopy, all patients had a reduction in systolic and diastolic blood pressures as well as in heart rate after drug injection, whereas all these variables increased after Laryngoscopy and Endotracheal Intubation (Fig:1-3). The effects of this increase gradually disappeared within five minutes after Intubation.After the drug injection, the patients in Group I had lower decrease in blood pressure and Heart rate than groups II and III.The patients in Group II faced the greatest fall in blood pressure and Heart rate after induction.Moreover, compared to other groups, this group of patients had the lowest increase in blood pressure and Heart rate after Laryngoscopy and Endotracheal Intubation (Table 3).

The effect of induction agents in all the 3 groups in our study on haemodynamics at induction and laryngoscopy and intubation are similar to those observed in other studies. Harris CE et al.,[11] in their study compared the haemodynamic response to tracheal intubation was compared in 303 patients in whom anaesthesia was induced with either thiopentone 4 mg/kg, etomidate 0.3 mg/kg or propofol 2.5 mg/kg, with and without fentanyl 2 µg/kg. There was after propofol alone a significant decrease in arterial blood pressure at induction, which did not increase above control values after intubation. Significant increases in arterial pressure followed intubation in patients induced with thiopentone or etomidate alone. Increases in heart rate occurred with all agents after laryngoscopy. The use of fentanyl resulted in arterial pressures lower than those after the induction agent alone, and in an attenuation, but not abolition of the responses to laryngoscopy and intubation. The heart rate increase at intubation was equal in thiopentone, etomidate and propofol groups.

Patrick MR et al.,[12] in their study on comparision of haemodynamic effects of propofol and thiopentone in patients with coronary artery disease obseved similar findings. Twenty patients scheduled for elective coronary surgery received either propofol 1.5 mg/kg or thiopentone 2 mg/kg for induction of anaesthesia. Anaesthesia with propofol was accompanied by a reduction in arterial pressure, the decrease being severe in two patients. This was largely due to a decrease in systemic vascular resistance. Thiopentone anaesthesia resulted in a smaller decrease in arterial pressure, but a marked increase in arterial pressure followed endotracheal intubation. The doses of propofol and thiopentone used for induction in this study are much lesser than those used in our study in view of the cardiac problems of the patients considered for their study. Kashtan H et al.,[22] too in their study (induction doses of propofol 2 -2.5mg/kg vs thiopentone 4 -5 mg/kg) observed that post-intubation increases in heart rate, and systolic and diastolic blood pressures were attenuated by propofol when compared with thiopentone.

In the studies by Jones D et al.,[17], Mohammadi SS et al.,[18] and Yeo KS et al.,[19] giving an admixture of thiopentone and propofol for induction of anaesthesia produced less hypotension at induction compared to giving propofol alone. A fall in systolic blood pressure during propofol induction has been consistently reported in literature. One way of decreasing the degree of hypotension at induction with propofol is to decrease the the dose of propofol (which is usually done in combination admixture induction) and the rate of injection. A decrease in the dose of propofol in the admixture group causes a decreased effect on afterload and the myocardium.[9] A decrease in the rate of administration of propofol decreases not only the dose required for induction, but also the degree of haemodynamic change.[8]

Hypnotic effect exhibited by thiopentone and propofol when given in combination might be synergistic or additive. Naguib M et al.,[16] in their study in unpremedicated patients, on sequential co-induction found the interaction between thiopentone and propofol to exhibit hypnotic synergism which might be explained on the basis of interaction at the GABA receptor complex. However, propofol and thiopentone are found to hypnotically interact additively in other studies. Vinik HR et al.,[29] reported that propofol and thiopental given as separate bolus injections resulted in an additive interaction. Jones D et al.,[17] and Mohammadi SS et al.,[18] in their studies found the same when giving an admixture of the two drugs after a dose of fentanyl. Wong W et al.,[26] too found an additive hypnotic effect when propofol and thiopental were given simultaneously during co-induction without preoperative sedatives or narcotics.

When two drugs which act on the central nervous system are used in combination in anaesthetic practice, the primary aim is usually to take advantage of the non-hypnotic effects of one or both. However, the synergistic/additive effects described (in all these studies) could also be caused by pharmacokinetic, as opposed to pharmacodynamic factors.[36] The former must be regarded as a strong possibility, as these agents are highly protein bound, with scope for competition for binding sites, and have profound cardiovascular effects such that one might influence the volume of distribution of the other. To presume if these findings would be of any clinical value, this depends largely on whether or not the cardiorespiratory and other non-hypnotic effects also show synergism. If the interaction is pharmacokinetic, there must obviously be important synergistic effects, but if not, it is possible that there may be different types of interaction between different properties. The interaction (synergism, additiveness, antagonism) in the non hypnotic effects (cardiovascular, haemodynamic, sympathetic and parasympathetic) either pharmacokinetic or pharmacodynamic may be put to advantage for better induction characteristics (and a lesser response at laryngoscopy and intubation) when a combination of intravenous anaesthetics is used.

The physical compatibility of thiopentone and propofol mixtures was investigated. The investigations used were macroscopic and microscopic observations, zeta potential and oil droplet size measurements. There was no evidence of instability in the mixtures.[31] Admixture of thiopentone and propofol is compatible and stable due to its bactericidal properties, as it does not support the growth of micro-organisms despite the presence of nutrients in the admixture. There are presumed to be many advantages of using such an admixture or sequential or simultaneous co-induction with thiopentone and propofol.

Thiopentone reduces pain caused by propofol due to decrease in the release of kinins and change in the pH of the admixture. Jones D et al.,[17] showed that adding thiopentone to propofol could be as efficacious in preventing injection pain as mixing lignocaine 40 mg with 20 ml propofol. Mohammadi SS et al.,[18] too found that thiopentone-propofol admixture caused less pain on injection as opposed to propofol alone as induction agent. However, Lee TW et al.,[32] found thiopentone pre-treatment to be more effective than lignocaine.

Rashiq S etal.,[23] in their study on recovery characteristics following induction of anaesthesia with either thiopentone, propofol or a combination of both observed that induction with a mixture of thiopentone and propofol leads to a similar rate and quality of recovery to that of propofol alone. They noted that use of thiopentone alone leads to a slower discharge from hospital when strict discharge criteria are applied and that the induction of general anaesthesia with propofol leads to recovery that is faster than that seen after induction with thiopentone, but no faster than that seen after the use of a mixture of the two agents. They concluded that this admixture method might be advantageous in day care surgeries. The beneficial effects of admixture of thiopentone and propofol in elective surgeries in children with LMA insertion when compared to propofol alone were appreciated in the study by Sinha et al.[22]

There is earlier loss of consciousness at induction when thiopentone is used as compared to propofol.[18,22,33] The same holds good even when a combination of thiopentone and propofol is used for induction as opposed to using propofol alone.[17,21] Thiopentone and propofol might act on different loci in the brain for their sedative and nonsedative effects. Propofol has a greater amnesic effect than thiopental. An admixture of the two might prove advantageous in this regard too. In the study by Veselis RA et al.,[34] they observed that Propofol decreased rCBF in the anterior (right-sided during sedation) brain regions, whereas thiopental decreased rCBF primarily in the cerebellar and posterior brain regions at similar levels of drug effect. They concluded that these differences may help to identify the loci of action for the nonsedative effects of propofol, such as amnesia.

The advantages of using co-induction by combination regimens of induction agents would be in context of both hypnotic and non hypnotic effects. This would mean additive/synergistic hypnotic effect[16-18,26,29], earlier loss of consciousness[17,21], non sedative effect on brain such as greater amnesic effects[34], lesser haemodynamic perturbances (reduced hypotension at induction and lesser pressor response at laryngoscopy and intubation)[17-19], lesser pain on injection[17,18,32], better suppression of upper airway

reflexes (suitable conditions for LMA placement)[20], reduced incidence of convulsions[31] and better recovery characteristics in terms of rate and quality (earlier discharge and lesser vomiting in day care surgeries)[21]. These advantages might not be appreciated when using either of the induction agents alone. The advantage of this sort seen in co-induction with a combination regimen might be due to lesser doses of induction agents used as opposed to the higher doses used when they are used as sole induction agents (though these advantages might be appreciated to certain extent while using either of these agents alone they would come at the cost of other complications due to higher dosages used), thus limiting the intensity of their deleterious effects on various systems, apart from the pharmacokinetic and pharmacodynamic interactions.

Apart from further studies which are needed to arrive at correct potency ratios and dosage requirements in terms of hypnotic synergism / additiveness for a combined sequential / admixture regime of thiopentone and propofol for co-induction in the presence or absence of premedication, need for the same with regards to non hypnotic effects (haemodynamic changes at induction and intubation and many other effects on varied systems) of the combined regime should be recognised.

In our study, after drug injection, decrease in blood pressure and Heart rate in patients of group III was lower than group II and higher than group I. Further more, after Laryngoscopy and Endotracheal Intubation, the increase in the above mentioned variables was lower in this group than in Group I and higher than in Group II (Fig : 1-3, Table 3). In other words, the patients of this group did not have substantial decrease in blood pressure and Heart rate as much as the changes induced by Propofol. Likewise the increase in blood pressure and Heart rate was not as high as the changes caused by Thiopentone after Laryngoscopy and Endotracheal Intubation. In general, the whole trend of changes in Group III was closer to group II.

None of the 90 patients in our study faced severe stress-induced symptoms such as coughing or straining etc., during Laryngoscopy and Endotracheal Intubation. We did not observe any drastic drop in Blood Pressure and Heart rate after Induction and any deleterious surge in these variables after Laryngoscopy and Endotracheal Intubation in any of the three groups in our study.

CONCLUSION

In this study, simultaneous use of low dose Thiopentone and Propofol for anaesthetic induction reduced the dose and Haemodynamic effects of each drug used alone.The Combined use of low dose of these drugs, caused less Haemodynamic changes than the higher dose of either alone. Although, all statistically significant differences documented in this study are not necessarily clinically significant in the age group of 20-50 years and patients in ASA Grade-I and II, this modality of anaesthesia induction may have clinical importance for the elderly patients as well as those with hypertension and heart diseases, and those belonging to ASA Grade – III and IV, needing lesser dose of medications.

Further research in this field is needed to determine the appropriate doses / potency ratios for additive/synergistic hypnotic and non hypnotic effects of the induction drugs.

REFERENCES

1. Edwards ND, Alford AM, Dobson PM, Peacock JE, Reilly CS. Myocardial ischaemia during tracheal Intubation and extubation. Br J Anaesth 1994; 73:537-9.
2. Prys-Roberts C, Greene LT, Meloche R, Foex P. Studies of Anaesthesia in relation to hypertension II: Haemodynamic consequences of induction and Endotracheal Intubation. Br J Anaesth 1971; 43:531-47.
3. Aitkenhead AR. Thiopentone sodium as induction agent. In: Aitkenhead AR, Rowbotham DJ, Smith G eds.Intravenous anesthetic agents Edinburgh: Churchill Livingstone, 2001; 171-2.
4. Morgan GE. Cardiovascular effects of barbiturates. In: Morgan GE, Mikhail MS, Murray MJ eds. Non volatile anesthetic agents. Chicago: McGraw-Hill companies, 2006; 186.
5. Riznyk L, Fijalkowska M, Przesmycki K. Effects of Thiopentone and Propofol on heart rate variability during fentanyl-based induction of general anaesthesia. Pharmacol Rep 2005; 57:128-34.
6. McKeating K, Bali IM, Dundee JW. The effects of thiopentone and propofol on upper airway integrity. Anaesthesia 1988; 43:638-40.
7. Stoelting RK.Cardiovascular effects of propofol. In: Stoetling RK eds. Non-barbiturate induction drugs. New York: Lippincott-Raven, 1999; 143.
8. Peacock JE, Lewis RP, Reilly CS, Nimmo WS. Effect of different rates of infusion of propofol for induction of anesthesia in elderly patients. Br J Anaesth 1990; 65:346-52.
9. Gauss A, Heinrich H, Wilder-Smith OH. Echocardioghaphic assessment of the haemodynamic effects of propofol: a comparison with etomidate and thiopentone. Anaesthesia 1991; 46:99-105.
10. Coley S, Mobley KA, Bone ME, Fell D. Haemodynamic changes after induction of anaesthesia and tracheal intubation following propofol or thiopentone in patients of ASA grade I and III. Br J Anaesth 1989; 63:423-8.
11. Harris CE, Murray AM, Anderson JM, Grounds RM, Morgan M. Effects of Thiopentone, Etomidate and Propofol on the hemodynamic response to tracheal Intubation. Anaesthesia 1988; 43:32-6.
12. Patrick MR, Blair IJ, Feneck RO, Sebel PS. A comparison of the haemodynamic effects of propofol ('Diprivan') and thiopentone in patients with coronary artery disease. Postgraduate Medical Journal 1985; 61:23-7.
13. Briggs LP, Dundee JW, Bahar M, Clarke RSJ. Comparison of the effect of diisopropyl phenol (ICI 35868) and thiopentone on response to somatic pain. Br J Anaesth 1982; 54:307-11.
14. Enna SJ. GABA receptors. Trends Pharmacol Sci 1981; 2:62-4.
15. Snyder SH. Drug and neurotransmitter receptors. New perspectives with clinical relevance. JAMA 1989; 261:3126-9.
16. Naguib M, Sari-Kouzel A. Thiopentone-Propofol

hypnotic synergism in patients. Br J Anaesth 1991;67:4-6.

17. Jones D, Prankerd R, Lang C, Chilvers M, Bignell S, Short T. Propofol-thiopentone admixture-hypnotic dose, pain on injection and effect on central compartment pressure. Anaesth Intensive Care 1999; 27:346-56.
18. Mohammadi SS, Nasiri AK, Shoeibi G. Effects of Propofol-Thiopental Sodium Admixture on Hypnotic Dose, Pain on Injection and Hemodynamic Responses During Induction of Anesthesia. Intl J Pharmacol 2006; 2:443-6.
19. Yeo KS, Kua SW, Teoh GS, Onsiong MK. The use of thiopentone/propofol admixture for laryngeal mask airway insertion. Anaesth Intensive Care 2001; 29:38-42.
20. Sinha R, Shende D, Garg R. Comparision of propofol (1%) with admixture (1:1) of thiopentone (1.25%) and propofol (0.5%) for laryngeal mask airway insertion in children undergoing elective eye surgery: Double-masked randomized clinical trial. Indian J Anaesth 2010; 54:104-8.
21. Rashiq S, Gallant B, Grace M, Jolly DT. Recovery characteristics following induction of anaesthesia with a combination of thiopentone and propofol. Can J Anaesth 1994; 41:1166–71.
22. Kashtan H, Edelist G, Mallon J, Kapala D. Comparative evaluation of propofol and thiopentone for total intravenous anaesthesia. Can J Anaesth 1990; 37:170-6.
23. Naguib M, Sari-Kouzel A, Seraj M, el-Gammal M, Gomma M. Induction dose-responses studies with propofol and thiopentone. Br J Anaesth 1992; 68:308-10.
24. Grounds RM, Moore M, Morgan M. The relative potencies of thiopentone and propofol. Eur J Anaesthesiol 1986; 3:11-7.
25. Edelist G. A comparison of propofol and thiopentone as induction agents in outpatient surgery. Can J Anaesth 1987; 34:110-6.
26. Wong W, Lim T, Lim K. Interaction between propofol and thiopental: Isobolographic analysis using dose, central compartment and effect compartment concentrations. IJA 2007; 17(1).
27. Singh R, Choudhury M, Kapoor PM, Kiran U. A randomized trial of anaesthetic induction agents in patients with coronary artery disease and left ventricular dysfunction. Ann Card Anaesth 2010; 13:217-23.
28. Dobson AP, McCluskey A, Meakin G, Baker RD. Effective time to satisfactory intubation conditions after administration of rocuronium in adults. Comparison of propofol and thiopentone for rapid sequence induction of anaesthesia. Anaesthesia 1999; 54:172-6.
29. Vinik HR, Bradley EL, Kissin I. Isobolographic Analysis of Propofol-Thiopental Hypnotic Interaction in Surgical Patients. Anesth Analg 1999 ; 88:667-70.
30. McKay AC. Synergism among IV anesthetics (editorial). Br J Anaesth 1991; 67:1-3.
31. Paw HG, Garrood M, Fillery-Travis AJ, Rich GT. Thiopentone and propofol: a compatible mixture? Eur J Anaesth 1998; 15:409-13.
32. Lee TW, Loewenthal AE, Strachan JA, Todd BD. Pain during injection of propofol, the effect of prior administration of thiopentone. Anaesthesia 1994; 49:817-8.
33. Sorensen MK, Dolven TL, Rasmussen LS. Onset time and haemodynamic response after thiopentone vs. Propofol in the elderly: a randomized trial. Acta Anaesthesiol Scand 2011; 55:429-34.
34. Veselis RA, Feshchenko VA, Reinsel RA, Dnistrian AM, Beattie B, Akhurst TJ. Thiopentone and Propofol affect different regions of the brain at similar pharmacological effects. Anaesth Analg 2004; 99:399-408.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 26-06-2018; **Accepted:** 02-08-2018; **Published:** 13-08-2018