

A randomised prospective study on the effect of intramuscular lignocaine and bupivacaine on induction dose of thiopentone sodium

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Abstract

Introduction: The combination of regional and general anaesthesia is popular and there is growing interest in the possible interactions of the local anaesthetic agents(LA) with drugs used for general anaesthesia. The purpose of this study is to evaluate the hypnotic interaction between Thiopentone sodium with Lignocaine and Bupivacaine.

Materials and Method: 90 ASA grade I and II patients of either sexes between the age groups of 18 to 50 years, scheduled to undergo various elective surgical procedures under general anaesthesia were included in the study. The patients were randomly allocated into three groups of 30 patients each. Group C received 3 ml of normal saline intramuscularly (i.m.) 10 minutes before induction, group L received lignocaine (2%) 2mg/kg body weight i.m 10 minutes before induction and group B received bupivacaine (0.5%) 1 mg/kg body weight i.m. 30 minutes before induction. General anaesthesia was then induced with Thiopentone sodium till loss of eyelash reflex and the dose required was noted. The heart rate and blood pressure were noted for five minutes post induction.

Results: The induction dose of thiopentone sodium in the group C was 4.64 ± 0.35 mg/kg body weight (BW) it was significantly higher than the group L 3.65 ± 0.30 mg/kg BW ($p < 0.001$) and group B 3.23 ± 0.22 mg/kg BW ($p < 0.001$) The induction dose was reduced by 21% and 30% in the lignocaine and bupivacaine group respectively. Group L and B had a significantly attenuated response to intubation.

Conclusion: Intramuscular lignocaine and bupivacaine significantly reduce the induction dose of thiopentone sodium.

Keywords: Thiopentone sodium, Lignocaine, Bupivacaine, General anaesthesia, Local anaesthetic agents

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Introduction

Thiopentone sodium is one of the most commonly used and potent intravenous (i.v) hypnotic agent, which is widely used for induction of anaesthesia. The combination of regional and general anaesthesia is popular and there is growing interest in the possible interactions of the local anaesthetic (LA) agents with drugs used for general anaesthesia. LA have effects on the central nervous system, which are very similar to the effects of general anaesthetic agents.⁽¹⁾ This has led to a growing interest in studies investigating the interactions between general anaesthetics and local anaesthetics administered either by spinally, epidurally, intravenously and other routes.⁽¹⁻⁵⁾ There have been studies that have shown that systemic local anaesthetics reduced minimum alveolar concentration (MAC) of inhalational anaesthetics and analgesic requirements.^(6,7) In regional anaesthesia the effect of the drug injected is often limited to the part of the body to be operated on, but this is seldom seen and LA agents are known to have some effects like general anaesthetics on the central nervous system. The anaesthesiologist is often faced with a patient who has already received a dose of local anaesthetic into a soft tissue location and has to receive general anaesthesia. The possible effect of local anaesthetics injected into soft tissues is the modification of the requirements for general anaesthetics.⁽⁸⁾ The purpose of this study is to evaluate the hypnotic

interaction between the commonly used intravenous anaesthetic agent Thiopentone sodium with widely used local anaesthetic agents Lignocaine and Bupivacaine. Our hypothesis is if a hypnotic effect exists, it should result in a sparing effect upon the dose of i.v. thiopentone sodium administered.

Materials and Method

After institutional ethics committee approval and obtaining patients' written informed consent, ninety ASA grade I and II patients of either sexes between the age groups of 18 to 50 years, who were scheduled to undergo various elective surgical procedures under general anaesthesia were included in the study. Based on a previous the study, in which i.m bupivacaine reduced the induction dose of thiopentone to 2.29 ± 0.47 mg kg⁻¹ a sample size calculation with an $\alpha = 0.05$ and requiring the study to have a power of 99% indicated that 25 patients would be required in each group, to account for any dropouts or loss of data it was increased to 30 patients.⁽⁸⁾ The exclusion criteria were patients with known hypersensitivity to study drugs/local anaesthetic agents, porphyria patients on antihypertensive medication and patients with history of seizures.

The patients were randomly allocated into three groups of 30 patients each by computer generated random number tables. Group C received 3 ml of

normal saline i.m. 10 minutes before induction, group L received lignocaine (2%) 2mg/kg body weight i.m 10 minutes before induction and group B received bupivacaine (0.5%) 1 mg/kg body weight i.m. 30 minutes before induction. The dosage/ intervals between the i.m injection of lignocaine / bupivacaine and thiopentone were based on previous study.⁽⁸⁾ The i.m. injections were administered under strict aseptic precautions in the preoperative room equipped with all emergency drugs/equipment into the gluteus muscle of the patients by an anaesthesiologist not involved in the further anaesthetic management of the patient. The maximum volume of the drug injected was limited to 15 ml, if the calculated volume was more than 10 ml, the injectate was divided into two and given into the gluteus major bilaterally. The patients were not given any premedications and vitals were monitored in regular intervals. The patients were preoxygenated with 100% oxygen for three minutes. Anaesthesia was induced with injection Thiopentone sodium (2.5%) slowly till loss of eyelash reflex was noted by an anaesthesiologist blinded to which group the patient was allocated to and the dose for induction recorded. Inj. Succinylcholine 1.5 mg/kg body weight was administered for facilitation of intubation. Anaesthesia is maintained with oxygen, nitrous oxide and halothane

0.4%. The patient was monitored with electrocardiogram, pulsoximetry and non invasive blood pressure monitoring throughout. The heart rate and blood pressure were recorded at T₁ – baseline, T₂ – before induction, T₃ – after induction, T₄ – immediately after intubation, T₅ – 2 minutes after intubation and T₆ – 5 minutes after intubation. Fentanyl 2mcg/kg and atracurium 0.5mg/kg was administered i.v after 5 minutes of intubation. Postoperative follow up of the patient was done immediately after surgery, first postoperative day for any complications like pain or discomfort at injection site.

Statistical methods: The demographic data like age and weight were compared using one way analysis of the variance (ANOVA). The sex distributions in the different groups were compared using Chi square test. The mean values of dose of thiopentone given, the heart rate and blood pressure recordings were analyzed using the one way analysis of variance (ANOVA). When this test leads to the rejection of hypothesis of equality of means, then the Tukey's test was carried out for pairwise comparison. The tests were carried out at 5% level of significance, i.e. p value < 0.05 was taken as significant. Data analysis was carried out using Statistical Package for Social Science (SPSS) version 10.0. (SPSS Inc., Chicago, IL, USA).

Results

Table 1: Demographic data (mean±SD)

	Group C	Group L	Group B	P value
Age in years	35.73±11.0	32.43±8.93	33.27±11.11	0.445
Weight in kg	58.20±8.43	56.00±8.17	58.30±9.26	p=0.509
Sex (Male/Female)	14/16	16/14	16/14	p=0.556

The demographic profile was similar between the three groups (Table 1).

Table 2: Induction dose of thiopentone sodium (mean±SD)

	Group C	Group L	Group B
Dose of thiopentone sodium mg/kg body weight	4.64±0.35	3.65±0.30	3.23±0.13
S = Significant	ANOVA P=0.00 S, Group C – Group L, P=0.000 S, Group C – Group B, P=0.000 S, Group L – Group B, P=0.000 S		

The induction dose of thiopentone sodium per kg body weight in the control group C was 4.64±0.35 mg/kg body weight(BW) it was significantly higher than the group L 3.65±0.30 mg/kg BW (p<0.001) and group B 3.23±0.22 mg/kg BW (p<0.001)(Table 2). The induction dose per kg BW is reduced by 21% and 30% in the lignocaine and bupivacaine group respectively when compared to the control group (Fig. 1). In the bupivacaine group there was a 13% lesser requirement of thiopentone sodium for induction when compared to the lignocaine group. This difference between group B and L is also statistically significant (p<0.001).

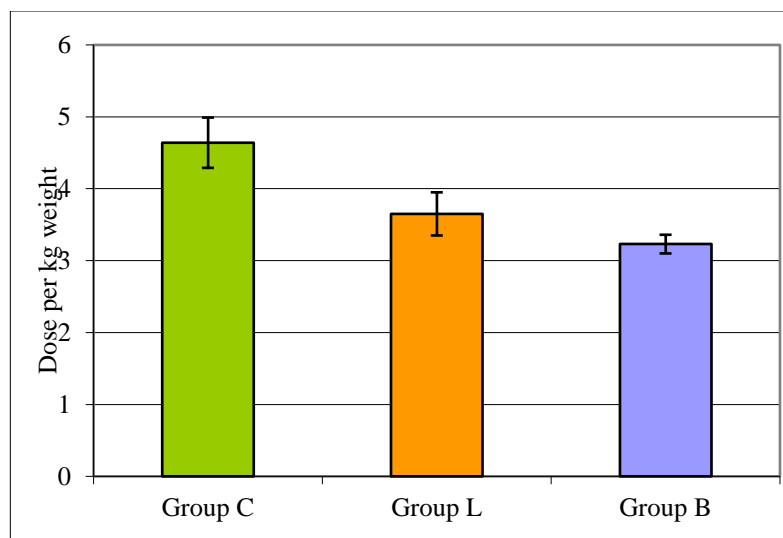


Fig. 1: Induction dose of thiopentone sodium in mg/kg body weight

Table 3: Comparison of Heart rate changes in the three groups (beats/min)

Time	Group C Mean±SD	Group L Mean±SD	Group B Mean±SD	Significance by ANOVA	Significance between groups
Basal T1	75.1±6.27	75.67±7.22	74.43±5.62	p=0.757 NS	NS
Pre-induction T2	85.17±5.96	86.83±6.83	86.03±5.64	p=0.580 NS	NS
After induction T3	91.50±5.89	90.80±6.96	88.13±5.74	p=0.093NS	B-C, p=0.09 NS
After intubation T4	111.43±6.11	106.13±7.23	104.03±4.69	p=0.000S	C-L p=0.003 S C-B p=0.000 S L-B p=0.379 NS
2 mins after intubation T5	102.70±6.03	97.20±6.02	97.33±5.22	p=0.000S	C-L p= 0.001 S C-B p=0.002 S L-B p=0.996 NS
5 mins after intubation T6	95.47±5.13	91.73±6.13	91.60±5.56	P=0.013S	C-L p=0.031 S C-B p=0.025 S L-B p=0.995 NS

S = Significant NS =Not significant

In the three groups, the basal, pre-induction and postinduction heart rates were comparable and the difference between the three groups was not statistically significant (Table 3). After intubation, the increase in heart rate from pre-induction value was more in group C, 111.43±6.11 compared to group L 106.13±7.23 and group B 104.03±4.69 (p<0.000). The differences in group L and B is not statistically significant (p=0.37). 2 minutes and 5 minutes after intubation, the heart rate was significantly more group C compared to Group L and group B (Fig. 2). The difference between group B and L was not statistically significant.

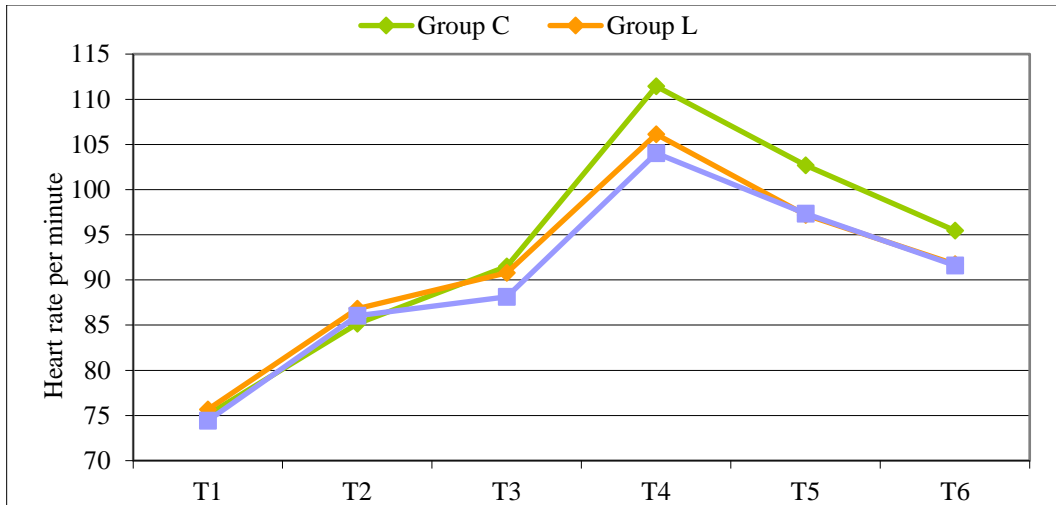


Fig. 2: Mean pattern of heart rate during the study period

Table 4: Comparison of Mean Arterial Pressure changes in the three groups (mmHg)

Time	Group C Mean±SD	Group L Mean±SD	Group B Mean±SD	Significance by ANOVA	Significance between the groups
Basal T1	89.33±6.69	89.51±5.72	89.88±6.92	p=0.946 NS	NS
Pre-induction T2	89.74±6.18	89.71±5.65	90.40±7.13	p=0.893 NS	NS
After induction T3	85.09±6.52	87.43±6.11	88.15±7.12	p=0.176 NS	NS
After intubation T4	109.49±5.02	106.26±3.81	104.52±4.42	p=0.000 S	C-L p=0.016 S C-B p=0.000 S L-B p=0.281 NS
2 mins after intubation T5	102.86±4.33	98.73±4.03	98.21±5.17	p=0.000 S	C-L p=0.002 S C-B p=0.000 S L-B p=0.897 NS
5 mins after intubation T6	97.67±5.17	94.45±4.53	94.05±6.42	p=0.022 S	C-L p=0.062 NS C-B p=0.031 S L-B p=0.956 NS

S = Significant NS =Not significant

The basal T₁, preinduction T₂ and postinduction T₃ mean arterial pressure (MAP) values were similar between the three groups (Table 3). Immediately after intubation T₄ there was a rise in MAP in all three groups, but it was higher in group C (109.49±5.01) compared to group L (106.26±3.81) and group B 104.52±4.42. The difference between groups L and B was not statistically significant (p>0.05). 2 minutes after intubation the MAP was significantly higher in group C (102.86±4.33) to group L (98.73±4.30) and group B (98.21±5.17) was statistically significant (p<0.05). 5 minutes after intubation the MAP values in group B was 94.05±6.42 which was significantly lower than group C 97.67±5.17 [p<0.05]. The group L (94.45±4.53) MAP value was also lower than group C but it was near significant (p=0.061). The difference between group L and B not statistically significant (Fig. 3).

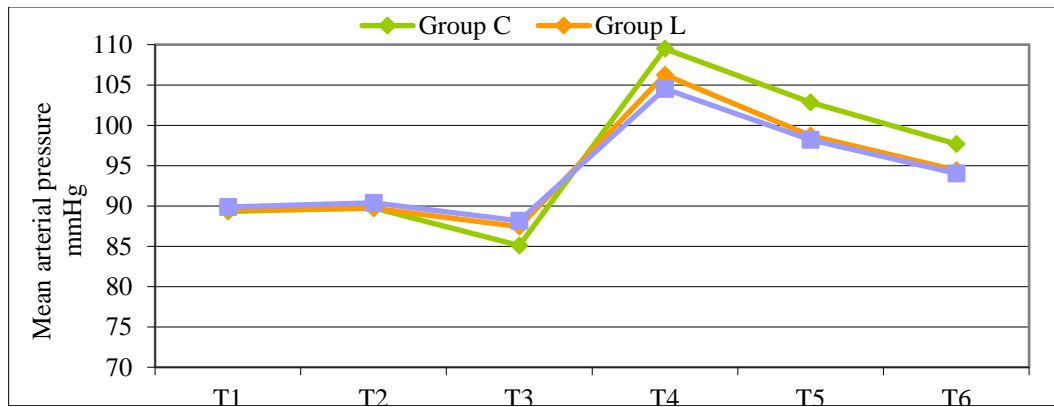


Fig. 3: Mean arterial pressure (mmHg) changes during the study period

No patient complained of local pain at the injection site. There were no adverse effects due to IM injection of local anaesthetics in the patients in the postoperative period.

Discussion

The interaction between regional anaesthetic agents and general anaesthesia gains importance today as there is growing use of regional anaesthesia with general anaesthesia. There are studies on the effect of local anaesthetic agents injected into the subarachnoid space and epidural space on the requirements of drugs used for general anaesthesia.^(4,5,9) These studies have suggested that the reduced general anaesthetic requirement is most likely due to the central effects of spinal deafferentation caused by the central neuroaxial blockade and not due to systemic effect of local anaesthetic agents.⁽¹⁾

Lignocaine administered intravenously has also been shown to reduce the general anaesthetic requirements and intravenous lignocaine infusion has a MAC sparing effect of 10 to 28%.^(6,7,10-13) In our study lignocaine and bupivacaine were administered via the intramuscular route to mimic a soft tissue injection. The effect on the induction requirement of thiopentone sodium was studied. In our study the induction dose of thiopentone sodium in the control group was within the recommended range for induction of anaesthesia. The induction dose of thiopentone sodium in the lignocaine group L was significantly reduced by 21% compared to the control group C. In the bupivacaine group B also the induction dose of thiopentone sodium was significantly reduced by 30%. The bupivacaine group needed 13% less thiopentone when compared to the lignocaine group. Our data indicates that intramuscularly administered local anaesthetic agents interact with subsequent bolus dose of intravenous thiopentone sodium by reducing the induction dose of the latter. In this respect the ability of bupivacaine to reduce the induction dose of thiopentone sodium was found to be greater than that of lignocaine probably due to its greater potency. The effects of IM administration of lignocaine and bupivacaine on enhancing the

induction dose of thiopentone sodium by Tverskoy et al.⁽⁸⁾ demonstrated a similar dose reduction to that observed in our study. But in their study, only female patients were studied and the slower rate of injection of thiopentone sodium probably accounts for the lesser requirements of drug compared to our study.

Ghosh BR et al.⁽¹⁴⁾ studied the effects of 1 mg/kg body weight of lignocaine and 0.5 mg/kg of bupivacaine intramuscular on the induction requirements of thiopentone sodium. They found that thiopentone sodium dose was significantly reduced in the lignocaine and bupivacaine group respectively. In our study, there was a further reduction in the thiopentone requirement due to higher dose of lignocaine and bupivacaine used in our study. There are other studies which are studied the effects of intramuscular local anaesthetic agents on the requirements of midazolam and propofol have been described.⁽¹⁵⁻¹⁷⁾ The observations of these studies and the present study are similar. However, we have increased the sample size of individual study groups (30 cases each) which is larger than in any of the above studies and secondly haemodynamic values have been monitored after induction of anaesthesia in the three groups.

According to several studies, there are two main mechanisms that may explain the interaction of local anaesthetics and general anaesthetics. Firstly, most local anaesthetic agents bind to sodium channels in the inactivated state, preventing channel activation and large transient sodium influx associated with membrane depolarization. General anaesthetics are known to have some effects on the central nervous system, which are not unlike those of local anaesthesia. Both volatile anaesthetics and barbiturates have been shown to block sodium channels (although they are more potent in blocking ligand gated ion channels in CNS) and then prevent action potential formation in central neurons.⁽¹⁸⁾ Secondly, it is well known that thiopentone sodium enhances the GABAergic currents, which facilitates inhibitory neurotransmission in neurons. Nordmark J et al. have shown that local anaesthetics potentiate GABA-mediate Cl⁻ currents by inhibiting GABA

uptake.⁽¹⁹⁾ Common mechanisms of actions of local and general anaesthetics may explain how the hypnotic effect of i.v. thiopentone sodium is enhanced by intramuscular administration of bupivacaine or lignocaine. The potency of bupivacaine is higher than that of lignocaine, which accounts for the further reduction in dose of thiopentone observed in our study.

The dose of local anaesthetic agents administered in the present series was less than half the recommended maximum doses. The changes in haemodynamic values were not the primary variables in our study. The attenuation of the cardiovascular response to intubation by i.v. lignocaine has been recognized by many studies. However, there are few studies examining the effects of intramuscular lignocaine administration on haemodynamic response to intubation.^(16,17) The intramuscular lignocaine and bupivacaine groups were associated with significantly stable haemodynamic status after both induction and intubation as compared with control group. The bupivacaine group had more stable haemodynamic status and was associated with reduced heart and blood pressure increases after intubation compared to the other two groups which is similar to previous studies.^(16,17)

The present study confirms that the requirement of inducing agents is reduced when the patient has received local anaesthetic agents at a soft tissue site. The clinical significance of this observation is in situations where general anaesthesia has to be induced in a patient in whom regional blockade has failed or is inadequate or has to be supplemented for other reasons the dose of general anaesthetics has to be carefully titrated against the patients response rather than conventional dosage regime based on patient's body weight. The use of depth of anaesthesia monitors like Bispectral index would have further confirmed our hypothesis but it was not available at the time of the study.

Conclusion

It can be concluded from the present study that when lignocaine or bupivacaine are injected into a soft tissue location the induction dose of thiopentone sodium is significantly reduced and it should be carefully titrated against the patient's response rather than the conventional regime based on the patient's body weight. Also intramuscular local anaesthetic agents were associated with an attenuated haemodynamic response to induction and intubation.

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