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The Effect of Nebulization with 2% Lignocaine Or 0.5% Bupivacaine on Requirement of Propofol for Total Intravenous Anaesthesia with Endotracheal Tube in Situ

[1]Shah Pratibha Jain, MD, FICA, FIPM, Professor & Head of the Department, Department of Anaesthesia and Pain Management, Pt. Jawaharlal Nehru Memorial Medical College, Raipur, Chhattisgarh, India

[2]Dr. Ankita Bodhankar, PG Scholar, Department of Anaesthesia and Pain Management, Pt Jawaharlal Nehru Memorial Medical College, Raipur, Chhattisgarh, India

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Corresponding Author: Dr. Ankita Bodhankar, PG Scholar, Department of Anaesthesia and Pain Management, Pt Jawaharlal Nehru Memorial Medical College, Raipur, Chhattisgarh, India

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Abstract

Background & Aims

Total intravenous anaesthesia (TIVA) is a popular technique in modern era due to its practical feasibility and environment friendliness. But, higher requirement of propofol remains a concern. To determine the effect of nebulization with 2% lignocaine vs 0.5% bupivacaine on induction and maintenance doses of propofol and incidence of postoperative sore throat & coughing.

Settings and Design

Prospective, double blind randomized study

Methods and Material

Sixty patients between 20-50 years of age, weighing 50-65 kg and ASA grades I-II who underwent surgery of ≤ 2 h duration under TIVA with ETT in place were divided randomly into three groups (n=20) using sealed envelope technique: group L, B & S received 2% lignocaine, 0.5% bupivacaine & normal saline nebulization, 15 min prior to induction, respectively. Induction & maintenance dose of propofol; intraoperative haemo-dynamics and incidence of postoperative coughing & sore throat were recorded.

Results

Propofol requirement for induction and maintenance was significantly less in both L & B groups compared to S group [(1.62 & 1.69 vs 2.08 mg/kg; $p<0.01$) and (6.41, 6.56 & 8.13 mg/kg/h; $p<0.001$) respectively]. The incidence of postoperative

coughing was 1 (5%), 1 (5%) & 6 (30%) and of postoperative sore throat was 1 (5%), 2 (10%), & 7 (35%) in Group L, Group B & Group S; respectively.

Conclusions

Both 2% lignocaine or 0.5% bupivacaine nebulizationare equally effective in reducing propofol requirement for induction & maintenance of anaesthesia as well as incidence of postoperative cough & sore throat in patients undergoing surgery under TIVA with ETT in situ.

Keywords

Total intravenous anaesthesia, nebulization with lignocaine / bupivacaine, Effect of LA on Propofol doses for induction/maintenance.

Introduction

Total intravenous anaesthesia (TIVA) is a favored and more practical technique of GA in which anaesthetic agents are given exclusively via intravenous route due to well-known pharmacokinetics and pharmacodynamics of intravenous drugs like propofol and opioids. Newer concepts in pharmacokinetic models coupled with availability of advanced technology in infusion pumps allow precision and control over depth of anaesthesia with target-controlled infusion (TCI), thus fast, well controlled and smooth recovery from anaesthesia. [1] TIVA has various advantages over inhalational anaesthesia. General side effects of inhalational agents like postoperative nausea and vomiting, risk of malignant hyperthermia and postoperative shivering can be overcome using TIVA. Quality of recovery from anaesthesia is good. It is useful in procedures that require evoked potential monitoring. The precision and control over depth of anaesthesia has further improved with introduction of target-controlled infusions. Target controlled infusions administer intravenous drugs using target effect site concentrations, an approach that is similar to how anesthesiologists administered potent inhaled agents with a vaporizer as per the requirement.

Literature had observed reduced requirement of propofol with IM & IV injection of lidocaine and supplementation of opioids in TIVA. Opioid supplementation has limitation of postoperative emergence and delirium. [2] Yan xiang MS et al reported reduced propofol doses following epidural lidocaine. [3] Lidocaine has long been used to modulate the physiologic responses (airway-circulatory reflexes) to intubation, emergence and tracheal extubation via several routes including intramuscular, intravenous and topical application using spray & gel. Senturk M et al and Ben Shlomo et al found that IM administration of lignocaine and bupivacaine was associated with a decrease in both the induction and maintenance doses of propofol in TIVA. [4,5]

To our knowledge, no studies have been done to assess and compare effect of lidocaine or bupivacaine nebulization on propofol requirement for TIVA. Local anaesthetics is given by nebulization route for uniform distribution of drugs in the respiratory tract. Therefore, the present prospective observational study was conducted to study the effect of nebulization with 2% lignocaine or 0.5% bupivacaine or normal saline on propofol requirement under total intravenous anaesthesia (TIVA) with endotracheal tube. Primary outcome of this study was to determine the induction and maintenance doses of propofol. Secondary outcomes were to evaluate any changes in hemodynamic parameters like heart rate, systolic BP, diastolic BP and incidence of postoperative cough and sore throat.

Materials and Methods

The present prospective, double-blind randomised study was conducted in Pt. J.N.M. Medical College and Dr. B.R.A.M. Hospital, Raipur (C.G) after approval from the Institutional Scientific and Ethics Committee within eighteen months study duration from January 2019 to June 2020. The study was conducted as per ethical guidelines of the Declaration of Helsinki. After thorough pre-anaesthetic check-up and written informed consent, 60 patients of age 20-50 year, weight 40-65 kg, American Society of Anaesthesiologists physical status (ASA) I–II, and ≤ 2 h duration who had undergone surgery under TIVA with ETT in place were enrolled in the study. Patients who had neurological disorders, any atopic diseases, existing sore throat & coughing, hypersensitivity to local anaesthetics, history of smoking, ingestion of cardiovascular medication, antipsychotic, antidepressant and hypnotic drugs were excluded from the study.

Sample size for the present study was calculated based on data from previous study of Sentruk et al, in which propofol requirement for induction was significantly lower in lignocaine (1.58 ± 0.39 mg/kg) & bupivacaine group (1.56 ± 0.24 mg/kg) as compared to control group (2.03±0.33 mg/kg) ($p<0.0001$).[4] With a significance level of $\alpha=0.05$ & confidence interval of 95%, calculated sample size was 20 in each group for our study (n=20).Therefore, total 60 patients (n=20) were randomly allocated into 3 groups using sealed envelope technique according to 5ml of different drugs used for nebulization. Patients in Group B were nebulized with 0.5% bupivacaine, Group L with 2% lignocaine and Group S with normal saline.

As per the institutional protocol, all patients were kept nil per oral for 6h; connected to a multipara having electrocardiograph, automatic arterial pressure cuff & pulse oximeter and had intravenous access in dorsum of hand inside the operation theatre. Baseline Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Oxygen saturation (SPO_2) were recorded. Patients were nebulized 15 minutes prior to induction as per the assigned group using Dr Morepen nebulizer. The anaesthesia resident who involved in nebulization, conduction of operation and data recording was unaware about the group allocation.

All patients were premedicated with I.V. Midazolam 0.02mg/kg and I.V. Pentazocine 0.5mg/kg; 5 minutes before induction. After preoxygenation with 100% oxygen for 3 minutes, patients were induced with I.V. propofol 10 mg slowly at the rate of 5mg every 15 sec until loss of verbal commands. Total dose required for loss of verbal command was noted. Tracheal intubation was accomplished with appropriate size ETT after administration of I.V. Succinyl choline 1.5 mg/kg. Anaesthesia was maintained with 50% oxygen: 50% air and I.V. Atracurium 0.4 mg/kg as a loading dose followed by 0.1 mg/kg IV maintenance dose. An infusion of propofol 10 mg/kg/h was started by B Braun Perfusor compact pump for maintenance of anaesthesia. The dose of propofol was titrated to keep haemodynamics stable. Inadequate anaesthesia was defined as response to surgical stimuli by hypertension (SAP> 20% above preoperative baseline value for >5 min) or tachycardia (HR >20% above preoperative baseline value). The dose of propofol was increased by 1 mg/kg/h every 20 sec, whenever HR & SBP increased by 20% above baseline value. At the end of surgery, propofol infusion was stopped and 2.5 mg of neostigmine and 0.6 mg of glycopyrrolate was given to reverse neuromuscular blockade. The total maintenance dose of propofol was calculated in mg/kg/hr. The

trachea was extubated when patient regained spontaneous breath and opened eyes on command. Immediately after tracheal extubation, oxygen was supplemented via a facemask for 5 min.

Patient's demographic data, haemodynamic parameters (HR, SBP, DBP, Sp02) at T0 (before nebulization), T1 (before induction), T2 (after induction) & every 15 min thereafter and postoperative coughing & sore throat were recorded. Total duration of surgery (in min), total induction dose (in mg/kg) and total maintenance dose of propofol (in mg/kg/min) were also calculated.

All collected Data were analyzed and compared statistically using Epitools software. The analysis includes frequency table, bar, association of variables based on Chi-square. All quantitative variables such as age, weight, total propofol requirement, HR, SBP & DBP were estimated using measures of central location "mean" and measures of dispersion (standard deviation). For normally distributed data, mean was compared using independent t-test (for two groups). For categorical data such as incidence of coughing and sore throat, ASA grade, Chi square test had been applied. A value of $p<0.05$ was considered statistically significant.

Results

In present study, all three groups were comparable as per demographic data and mean duration of surgery. [Table 1]

Propofol dose required for induction was significantly less in group L and group B as compared to group S [p=0.002 (Group L vs Group S); p=0.008 (Group B vs Group S). However, propofol requirement for induction was comparable between Group L & Group B (p=0.10). [Table 2] Propofol requirement for maintenance was also significantly less in Group L vs Group S (p<0.001) & Group B vs Group S (p<0.001) with comparable maintenance dose between Group L & Group B (p=0.90). [Table 2]

Baseline mean heart rate (T0) was 90.1±8.87/min, 90.75±8.06/min and 91.85±9.71/min in Group L, Group B and Group S; respectively. Then it showed significant fall after intubation (p=0.04 & p=0.02 for Group L vs Group S & Group B vs Group S; respectively) & at 15 min in group L & B (p=0.03 & p=0.04 for Group L vs Group S & Group B vs Group S; respectively). But throughout the study period, the difference in heart rate was statistically not significant (p>0.05) among the groups. (Graph 1) Similar trend was seen in mean systolic pressure and mean diastolic pressure throughout the study period. (Graph 2, 3)

The incidence of postoperative cough was 1 (5%), 1 (5%) & 6 (30%) and of postoperative sore throat was 1 (5%), 2 (10%), & 7 (35%) in Group L, Group B & Group S; respectively. That was significantly less in Group L and Group B as compared to Group S [Group L vs Group B (p=1.00), Group L vs Group S (p=0.02) & Group B vs Group S (p=0.02)]. [Graph 4] Relative risk of postoperative cough was 6 & 6 in Group L & B as compared to Group S. Relative risk of sore throat was 7 in Group L & 3.5 in Group B as compared to Group S. This signifies that the strong association of cough & sore throat in Group S as compared to Group-B & Group-L.

Discussion

In our study, propofol requirement for induction and maintenance of anaesthesia were significantly less in patients nebulized with either lignocaine or bupivacaine as compared to patients nebulized with normal saline. However, Propofol requirement for induction and maintenance in lignocaine and bupivacaine group was comparable. Incidence of postoperative coughing and sore throat

significantly low in group L and group B as compared to normal saline group.

Lidocaine has long been used to modulate the physiologic responses (airway-circulatory reflexes) to intubation, emergence and tracheal extubation via several routes including intramuscular, intravenous and topical application using spray & gel.[6] Ben Shlomo et al, Senturk M et al and Kahveci K et al found that IM administration of lignocaine and bupivacaine was associated with significant decrease in both the induction and maintenance doses of propofol in TIVA.[4,5,6] Local anasesthetics given through nebulization allows uniform distribution of drugs in the respiratory tract and peak concentrations of LA. Both volatile anaesthetics and barbiturates have been shown to block sodium channels, thus prevent generation of action potential in central neurones. General anaesthetis increase the proportion of channels in the closed inactive state. Secondly, propofol enhances GABAergic currents, which facilitate inhibitory neurotransmission in neurones. Most intravenous anaesthetics inhibit the specific GABA uptake process in vitro in striatal nerve terminals, some, such as propofol, at clinically relevant concentrations. Local anaesthetics also potentiate GABA-mediated Cl^-currents by inhibiting GABA uptake. These common mechanisms of action of local and general anaesthetics may explain synergistic hypnotic effect.[4]

McBurney A et al studied absorption of lignocaine (4%) and bupivacaine (0.5%) from the upper and lower respiratory tract in patients undergoing fibreoptic bronchoscopy. [7] They observed that local anaesthetics, when given by nebulization have uniform distribution of drug in the respiratory tract and found peak effect between 15 and 60 min from the start of the procedure in both the groups. Therefore, patients were nebulized with either of the local anaesthetic 15 min prior to the induction in present study. Although bupivacaine is a longer acting local anaesthetic and has a longer plasma elimination half-life ($t_{1/2}$ 2.7h) compared to 1.6h for lignocaine, they did not reveal any significant difference in the plasma elimination half-life between the two drugs in their study (mean $t_{1/2}$ lignocaine = 2.3h; mean $t_{1/2}$ bupivacaine = 2.8h). Therefore, in order to observe efficacy of studied drugs in reducing incidence of postoperative sore throat & cough, 2 hr duration of surgery was taken as inclusion criteria. (Graph 2)

Sagheer AS et al found incidence of postoperative cough to be less in lignocaine 4% group than the control group. 9 patients (18 %) experienced cough after extubation in lignocaine group as compared to 20 patients (40 %) in control group. [8]

Relative risk for the incidence of postoperative sore throat & cough was higher in Group S as compared to Group-B & Group-L. None of the previous studies had calculated the association and relative risk of postoperative sore throat & cough following nebulization.

Besides strength of our study due to randomization, blinding, comparable baseline and strong internal validity; our study had few limitations like small sample size, propofol infusion was guided by hemodynamic response not by BIS (Bispectral Index) monitoring and Target controlled infusion (TCI) was not used that delivered propofol precisely to maintain steady plasma concentration.

In future, same study could be conducted as randomized control trial considering large sample size and with use of target-controlled infusion (TCI) of propofol & BIS (Bi spectral Index) monitoring to validate our results.

Conclusion

From the observations and analysis of the present study, it is concluded that nebulization with 2% lignocaine or 0.5% bupivacaine in patients who underwent surgery under Total Intravenous Anaesthesia (TIVA) with endotracheal tube in place is equally effective in reduction of propofol doses requirement for induction and maintenance of anaesthesia. Both, 2% lignocaine or 0.5% bupivacaine are also effective in reducing incidence of postoperative cough & sore throat.

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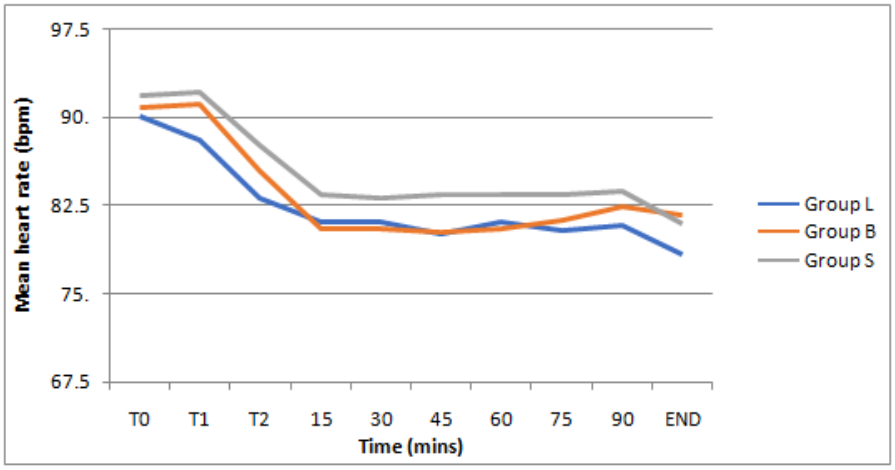
Table 1: Demographic profile and duration of surgery

	Group L	Group B	Group S
Mean age (yrs)	36.2±6.95	33.85±9.41	34.1±8.3
Male: Female	11:9	12:8	11:9
ASA I: ASA II	14:6	13:7	16:4
Mean weight (kg)	54.7±5.69	54.25±5.21	52.15±3.48
Duration of surgery (min)	80	79	81.45

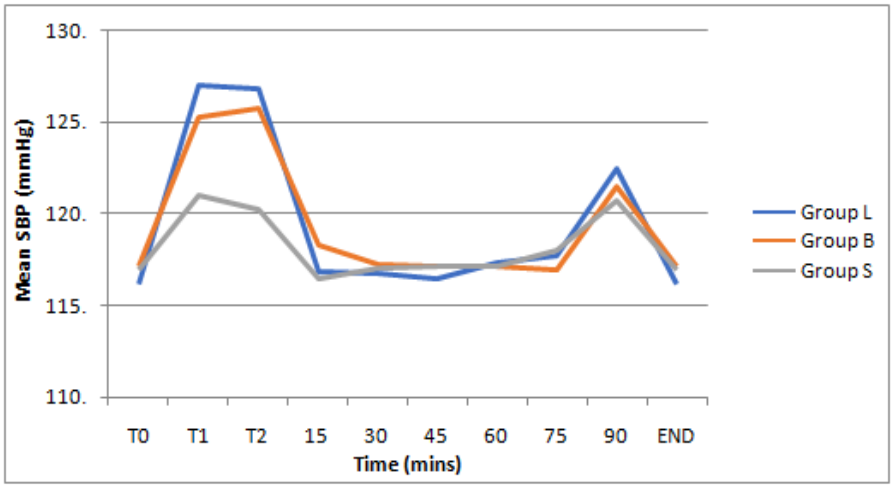
Table 2: Propofol Requirement for Induction & maintenance

Groups	Group L	Group B	Group S	p value		
				Group L vs Group B	Group L vs Group S	Group B vs Group S
Propofol requirement (mg/kg)	1.62±0.05	1.69±0.18	2.08±0.06	0.10	0.002	0.008
Propofol requirement (mg/kg/hr)	6.41±0.61	6.56±0.78	9.13±1.16	0.09	<0.001	<0.001

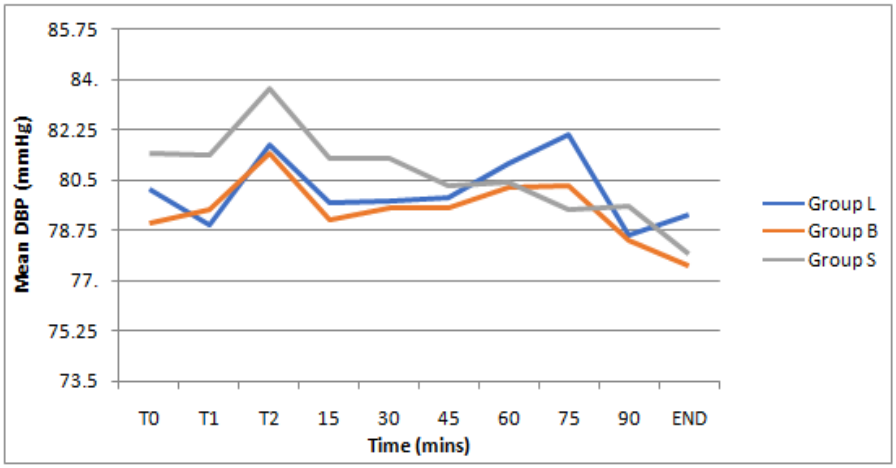
Graph 1: Mean Heart rate (bpm)



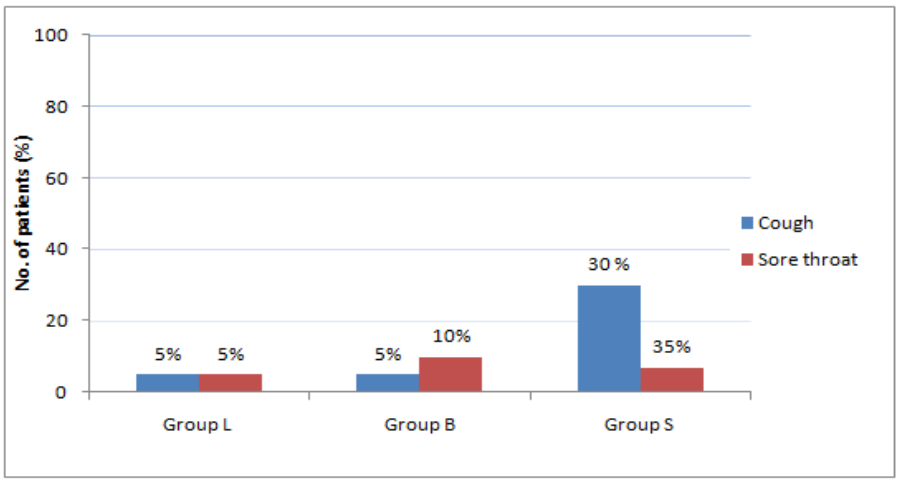
Graph 2: Mean Systolic Blood Pressure (mmHg)



Graph 3: Mean Diastolic Blood Pressure (mmHg)



Graph 4: Incidence of postoperative Coughing & Sore Throat



CONSORT Flow Diagram