Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 3 Number 1, January - April 2016
DOI : https://dx.doi.org/10.21088/ijaa.2349.8471.3116.4

A Double Blind Comparative Study of Effect of Intravenous Magnesium Sulphate with Lignocaine and Intravenous Clonidine with Lignocaine on Heart Rate in Response to Laryngoscopy and Tracheal Intubation during General Anesthesia

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Abstract

Background and Objectives: Laryngoscopy and tracheal intubation is invariably associated with a reflexsympathetic pressor response resulting in elevated heart rate and blood pressures. Thismay prove detrimental in high risk patients. The main objectives of the present study was To study the effect of intravenous magnesium sulphate 30 mg/kg with intravenous lignocaine 1.5mg/kg, and intravenous clonidine 3mcg/kg with intravenous lignocaine 1.5mg/kg on changes in the heart rate (HR) during laryngoscopy and intubation under general anesthesia. *Methods*: 60 ASA I and II status normotensive patients scheduled for elective surgicalprocedures were selected randomly and divided into three groups of 20 each. Allpatients received premedicationwith studydrug magnesiumsulphate 30mg/kg or clonidine 3µgm / kg or normal saline (as per double blind study protocol) prepared by anaesthesia staff and glyopyrrolate 0.2mg i.v., tramadol 3mg /kg 3min before induction . Induction of anesthesia was standardized for all patients who received,thiopentone 5 mg/kg i.v. and preservative free lignoaine 1.5mg i.v and were relaxed with succinylcholine 2mg/kg i.v. and laryngoscopy and intubation is done with appropriate sized endotracheal tube. HR, systolic, diastolic blood pressure were recorded noninvasively before induction, postintubation, 1,3,5, 7 and 10 minutes from the onset of laryngoscopy. 'z' test was used for statistical analysis. *Results*: In CL group, mean heart rate at 5 min and 10 min were 96.25 and 9.83 respectively. In ML group, mean heart rate at 5 min and 10 min were 100.95 and 97.45 respectively. *Conclusion*: There was a statistically significant attenuation of heart rate response was observed after giving study drug in CL group

Keywords: Attenuation; Pressor Response; Laryngoscopy; Intubation; Lignocaine; Magnesiumsulphate; Clonidines.

Introduction

Hypertension and tachycardia during intubation under general anesthesia have been reported since1950 [1.2]. Increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased plasma norepinephrine concentration [3]. These changes may be associated with morbidity and mortality in patients with heart disease and hypertension, provoking complications like bleeding, increased intracranial and intraocular pressure.

There are various techniques by which this intubation-related stress response can be attenuated, all of which depend on reduction in input stimuli or the blockade of adrenergic responses e.g. deep anesthesia, topical anesthesia, use of ganglionic blockers, beta blockers [4], antihypertensive agents like phentolamine [5], Sodium nitroprusside, nitroglycerine [6] and calcium channel blockers [7,8].

Intravenous magnesium sulphate inhibits catecholamine release associated with tracheal intubation and produces vasodilation by directly acting on blood vessels [9].

Clonidine, α_2 adrenoreceptor agonist attenuates adrenergic hemodynamic stress response [10]. It is effective in attenuating increase in heart rate and mean arterial pressure during endotracheal intubation [11].

Intravenous preservative free lignocaine with its well established centrally depressant and anti-arrhythmic effect is a more popular method to minimize this pressor response [12,13]. This drug is used routinely for

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generalanesthesia cases in our institution.

In spite of so many studies, so far not many studies have been published for comparing the efficacy of combination of drugs. Hence the present study was undertaken to compare advantages and efficacy of combining intravenous magnesium sulphate with intravenous lignocaine, and intravenous clonidine with intravenous lignocaine on blunting heart rate response in endotracheal intubation during general anesthesia in our institution.

Methodology

A clinical doubleblind comparative study of attenuation of hemodynamic response to laryngoscopy and intubation was done in 60 patients of 15-50years of age scheduled to undergo elective surgery under general anesthesia in Medical College Hospital (MCH), VIMS, Bellary, Karnataka. The patients are included in the study by applying the following inclusion and exclusion criteria.

Inclusion Criteria

a. Patients aged between 15 to 50 years of age posted for elective surgeries under general anesthesia
b. ASA grade I and II patients
c. Patients with Mallampatti airway grade I and II

Exclusion Criteria

a. Patients refusal
b. Patients with medical comorbidities like Hypertension, ischemic heart diseases and arrythmias
c. Patients with Mallampatti III and IV
d. Expected difficult intubation
e. If patient is allergic to any of these drugs

Methods of Collection of Data

Specially designed proforma are used to collect the data which includes patient's particulars, indication for surgery, the anaesthetic details, intra-operative monitoring, observation for side effects etc. 60 patients are randomly allocated to three different groups of 20 each as using block randomization method of randomization as described below (group ML,CL, and NL)

Group ML –will receive magnesium sulphate 30mg / kg iv 3 minutes before induction

Group CL –will receive clonidine 3mcg / kg iv bolus 3 minutes before induction

Group NL –will receive normal saline 4ml iv 3 minutes before induction.

All three groups are coded as A, B, and C by co-ordinator. These are again randomized in all possible permutations and combinations e.g., BAC, CBA, ABC etc and a list of 20 such blocks are prepared by co-ordinator. Such blocks are selected randomly by chit method and given to the researcher ensuring adequate randomization

All the patients were visited the day before surgery and pre-anestheticcounseling was done. All patients received Diazepam 10mg orally at night on theday before surgery

Patients are explained the procedure and informed / written consent obtained.

Anestheticprocedure

- On arrival in the operating room, patient's basal parameters- B.P, heart rate and ECG are recordre using pulse oximetry, NIBP and ECG monitor.
- Intravenous access will be established and an IV infusion of Ringer lactate started
- All the patients are premedicated with Glycopyrrolate 0.2mg iv.
- Patients in each group receive respective drugs as per timing and dose mentioned earlier. The study drug will be prepared by anesthesia staff and the observer will be blind for study drug.
- After preoxygenation, Patients in each group is induced by Thiopentone sodium 5mg / kg iv. Then intravenous lignocaine 1.5mg / kg given. After this Succinyl choline 2mg / kg will be given followed by laryngoscopy and intubation with appropriate sized cuffed endotracheal tube.
- Anesthesiais maintained with Oxygen 33%. Nitrous Oxide 66% and Halothane 0.5 to 1% through Bain's circuit on controlled ventilation.
- Muscle relaxation is done with intermittent doses of Vecuronium Bromide and for analgesia iv tramadol 3mg / kg will be given.
- At the end of surgery reversal is done with Glycopyrrolate and Neostigmine 0.05mg / kg and patient will be extubated.
- The recovery time(the time between injection of reversal agent and extubation) will be noted.

- Patients recovery is monitered by aldretes score after extubation.
- All the parameters of the study will be recorded at following stages –preoperative
    - After giving the study drug
    - Immediately after intubation
    - at 1 minute, 3 minutes, 5 minutes and 10 minutes after intubation.
- All groups are decoded at the end of study by taking information from co-ordunator. Group ML and Group CL will be studied for effects of combination of drugs and Group NL will be for study of effect of single drug and all three are compared in the end.

Results obtained are analyzed statistically.

Results

Table 1: Age wise distribution of study subjects

Age group	Clonidine with lignocaine	Magnesium sulphate with lignocaine	Lignocaine only
< 25 yrs	05 (25%)	05 (25%)	02 (10%)
26-35 yrs	05 (25%)	08 (40%)	10 (50%)
36-45 yrs	05 (25%)	05 (25%)	05 (25%)
> 45 yrs	05 (25%)	02 (10%)	03 (15%)
Total	20 (100%)	20 (100%)	20 (100%)

The table1shows the age distribution in control and the two study groups. The age range was 20 – 50 years for control and study groups

Table 2: Sex wise distribution of study subjects

Sex	Clonidine with lignocaine (CL)	Magnesium sulphate with lignocaine (ML)	Lignocaine only
Male	11 (55%)	09 (45%)	12 (60%)
Female	09 (45%)	11 (55%)	08 (40%)
Total	20 (100%)	20 (100%)	20 (100%)

In CL group, 55% were males and 45% were females
In ML group, 45% were males and 55% were females
In control, 60% were males and 40% were females

Table 3: Comparison of heart rate (bpm) between three groups

Heart rate	Clonidine with lignocaine (A)	Magnesium sulphate with lignocaine (B)	Lignocaine only (C)	P value *	P value # A-B	A-C	B-C
Baseline	89.85 +/- 13.9	97.80 +/- 21.73	91.95 +/- 10.83	0.28	0.27	0.91	0.49
Pre laryngeal	85.00 +/- 16.21	99.55 +/- 16.90	93.35 +/- 11.28	0.01	0.00	0.19	0.39
One min	98.25 +/- 12.34	109.50 +/- 14.54	115.15 +/- 11.33	0.00	0.02	0.00	0.35
Three min	98.00 +/- 11.37	104.10 +/- 15.17	109.75 +/- 12.34	0.02	0.30	0.01	0.36
Five min	96.25 +/- 11.18	100.95 +/- 15.71	103.20 +/- 14.56	0.28	0.53	0.26	0.86
Ten min	94.10 +/- 9.83	97.45 +/- 16.50	97.85 +/- 15.06	0.42	0.73	0.67	0.99

* ANOVA test # Post-hoc tukey test
All values are in mean +/- sd

Statistical analysis of changes in heart rate prelaryngoscopy, post intubation at different (1 5, 10,) time intervals from onset of laryngoscopy and intubation in all the 3 study group is presented.

Group CL(A): The basal and prelaryngoscopy mean heart rate and standard deviations in this group were 89.85 +/- 13.9 and 85.00—: 6.21 respectively. After 1min of intubation 8.4bpm (9.34%) increase in the value of heart rate was observed with values of 98.25 +1- 12.3.4 and remained higher with a mean heart rate of 98.00 +/- 11.37 at 3 minutes. Subsequently a decreasing trend in the heart rate was noted starting from 5 minutes to 10 minutes after laryngoscopy. Mean heart rate at 5minutes and 10 minutes were 96.25 +/- 11.18 and 94.10 +/- 9.83 respectively.

Group ML(B): The basal and pre laryngoscopy mean heart rate and standard deviations in this group were 97.80 +/- 21.73 and 99.55 +/- 16.90 respectively. After 1 min of intubation 11.7bpm (11.93%) increase in mean heart rate was observed with mean heart rate and standard deviations of 109.50 +/- 14.54. Subsequently decreasing trend in the heart rate was noted starting from 3 minutes to 10 minutes after

laryngoscopy. Mean heart rate at 3, 5 minutes and 10 min were. 104.10 +/- 15.17, 100.95 +1- 15.71, and 97.45 +/- 16.50 respectively.

Group NL(C):The basal and pre laryngoscopy mean heart rate and standard deviations in this group were 91.95 +/- 10.83and 93.35 +/- 11.28 respectively. After l min of intubation23 bpm (25.01%) increase in heart rate was observed with mean heart rate 115.15.

No significant variations noted in all groups in heart rate basal recording. There was attenuation of heart rate response was observed after giving study drug in CL group.

Discussion

The sequence of induction anaesthesia, laryngoscopy and tracheal intubation areassociated with marked haemodynamic changes and autonomic reflex activity which may be a cause of concern in many high risk patients [14].

Laryngoscopy and intubation is associated with rise in heart rate, blood pressureand incidence of cardiac arrhythmias. These potentially dangerous changes disappearwithin 5 minutes of onset of laryngoscopy [15].

Although these responses of blood pressure and heart rate are transient and short lived they may prove to be detrimental in high risk patients especially in those with cardiovascular disease, increased intracranial pressure or anomalies of the cerebral blood vessels [16].

In group NL inj lignocaine 1.5mg / kg i.v. 3 minutes before laryngoscopy and intubation was used to blunt the pressor response, the base line value of heart rate was 91.95. bpm .One minute following laryngoscopy and intubation, the heart rate increased to 115.50 bpm, representing a rise of 23.25 bpm above the base line value.

By 3 minutes, it was 109.75 bpm, representing a rise of 18.25 bpm above the base line value. By 5 minutes it was 103.20 bpm, representing a rise of 11.5 bpm above the base line it was seen that the elevated heart rate started settling down towards base line value by 10 minutes at 97.85.

CD Miller [17] et al employed a dose of 1.5 mg lignocaine and noticed a rise in the heart 72 rate (HR) of 25 bpm and Splinter et al noticed it to be 19 bpm. Hence the results of the present study with regards to increase in the heart rate observed following laryngoscopyand intubation concurs with the observation made by Splinter et al. and CD Millller.

Group ML: where Inj. $MgSO_4$ 30mg / kg i.v. + lignocaine 1.5mg / kg i.v 3minutes before laryngoscopy and intubation was used to blunt the pressor response, the base line value of Heart rate was 97.80. bprn . One minute following laryngoscopy and intubation, the heart rate increased to 109.50 bpm, representing a rise of 11.70 bpm above the base line value.

By 3 minutes, it was 104.10 bpm, representing a rise of 6.30 bpm above the base line value. By 5 minutes it was 100.95 bpm, representing a rise of 3.15 bpm above the base line . It was seen that the elevated heart rate started settling down towards base line value by 5 minutes rached baseline value at 10 mill 97.45.

Drsanthosh kumar [18] employed study using $MGSO_4$ 60mg / kg and noticed that maximum heart rate increased after intubation is 15. Hence the results of the present study with regards to increase in the heart rate observed following laryngoscopy and intubation concurs with the observation made by Drsanthoshkumar et al and Michael FM et al

In group CL Inj. Clonidine 3µg / kg i.v.+lignocaine 1.5mg / kg i.v 3 minutes before laryngoscopy and intubation was used to blunt the pressor response, the base line value of mean heart rate was 89.85 bpm One minute following laryngoscopy and intubation, the heart rate increased to 98.25 bpm, representing a rise of 8.40 bpm above the base line value.

By 3 minutes, it was 98.10 bpm, representing a rise of 8 bpm above the base line value. By 5 minutes it was 96.25. bpm, representing a rise of 6.15 bpm above the base line. It was seen that the elevated heart rate started settling down towards base line value by 5 minutes and at 10 min HR was 94.10 a difference 4bpm compared to baseline was observed

In Marco P. Zalunardo [19] et al employed Clonidine 311g / kg i.v. 3 minutes before laryngoscopy and intubation to blunt the, pressor response and found that difference between base line and 10min post intubation heart rate was 2.4 bpm.inPeter J. Kulka et al [10] study mean heart rate after intubation was (67+/- 12) bpm.

Conclusions

In group clonidine and lignocaine, there was statistically significant attenuation of heart rate responses at one minute as compared to mgso4 and lignocaine.

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