INTRAVENOUS LIGNOCAIN 2% (PLAIN) EFFICACY IN ATTENUATION OF STRESS RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION WITH IMPACT ON IN-HOSPITAL MORBIDITY AND MORTALITY

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ABSTRACT

Objective: To evaluate the efficacy of plain lignocain in attenuation of stress response to laryngoscopy and endotracheal intubation with impact on in-hospital mortality or morbidity.

***Study Design*:** A randomized control trial.

Place and Duration of Study: Our study was carried out from December 2013-14, at tertiary-care hospital.

Material and Methods: Patients (n=100 total) were randomized, using non-probability convenient sampling, dividing the population in two groups. Group A (n=50) as control, and in group B (n=50) Injection lignocain plain 2% @ 1.5 mg/kg was used 3 minutes prior to intubation. Both the groups were observed for changes in hemodynamic parameters i.e. heart rate (HR) systolic and diastolic blood pressure, Mean Arterial Pressure for every minute after baseline (0) and for 5 consecutive minutes (1, 2, 3, 4, and 5). Deviation of >20% from baseline was considered significant. The mortality (death within hospital, irrespective of cause) and morbidity (defined as emergence of 4 condition as hypertensive encephalopathy, Acute Coronary Syndrome, Lab proven Myocardial Infarction and negative pulmonary edema) within 10 days of hospitalization were noted.

Results: Statistically significant (*p*-value extremely significant at confidence interval of 98 degrees) results were obtained in the effect of study drug; however, 10 days of hospitalization remained inconclusive for emerging morbidity categories strictly due to the intubation reflexes. We consider few technicalities in peri-operative management resulted in such events.

Conclusion: Lignocain is effective in blunting the pressor response towards laryngoscopy and intubation. However the impact on mortality / morbidity for four conditions remained inconclusive.

Keywords: Laryngoscopy, Lignocain, Morbidity, Mortality, Stress response.

INTRODUCTION

In 1940, Reid and Brace first described hemodynamic response to laryngoscopy and intubation[1]. The hypertensive response to endotracheal intubation may be harmful in patients with cardiovascular disease, increased intracranial pressure, or anomalies of the cerebral vessels. Attenuating this pressor response is strongly recommended[1,2]. Various methods of attenuation are still being searched for including topical anesthesia of oropharynx (viscous lignocain) laryngotracheal instillation of lignocain, intravenous Lignocain, adrenergic blocking drugs, vasodilators like hydralazine, sodium nitroprusside, nitroglycerine, deep inhalational anesthesia, intravenous opioid and magnesium sulphate etc; No single agent is established as the most appropriate for this purpose[3-10].

The pressor response is transient occurring 30 seconds of intubation and lasting for less than 5-10 minutes as by Abou-Madi et al[11]. However Miller et al[12] found no benefit of intravenous lignocain (1.5 mg/kg) administered 1, 2 or 3 minutes before laryngoscopy and re-iterated' within 05 minute' doctrine, refusing the impact of reflex by "10 minutes" doctrine. We choose 03

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Received: 28 Aug 2015; revised received: 09 Nov 2015; accepted: 11 Nov 2015

minute timing in our study in light of such observations. The rational of this study was to test the impact of injection lignocain prior to intubation for attenuation of pressor response (impact being defined as less than 20% of changes from baseline in BP/ HR). To evaluate effects of such perturbations on mortality (defined as death within hospital, irrespective of cause) or morbidity (emergence of 4 categories as hypertensive encephalopathy, Acute Coronary Syndrome, Lab proven Myocardial Infarction and negative pulmonary edema) within the stipulated hospitalization time of 10 days.

MATERIAL AND METHODS

This was a randomized control trial, conducted over one year duration in a tertiary centre after institution research and ethics committee permission (no 12/ 0005/ anesthesia/ IREC). We compared the efficacy of lignocain in blunting the intubation response based upon inclusion criteria as patients having age (20-60 years), ASA status I-II, and patients due for elective surgical procedures. The patients were divided into two groups using non probability convenient sampling; Group A (n=50) as control) and Group B (n=50) given 2% injection lignocain plain (1.5mg/kg) 3 minutes before intubation. We excluded all patients having ASA status III or above, geriatric patients, or patients with BMI of >30 and difficulty in intubation or laryngoscopy.

Patients according to assigned groups were identified by specific mark on pre-anesthetic evaluation form by a senior anesthetist who administered study drug and supervised the entire peri-operative course of patients. Rest of procedures as deemed required and intra-operative data compilation were done by other anesthetist who was kept blind of the study drug. Standard protocols for monitoring as per ASA are strictly followed. Parameters i.e. heart rate (HR), systolic blood pressure, diastolic blood pressure and mean arterial pressure (MAP) were noted as baseline (0 minute) and then every consecutive minute (1,2,3,4 and 5). For GA, intravenous Injection Thiopentone sodium (5mg/kg), followed by Injection Atracurium 0.5mg/kg for intubation are used. The anesthetic techniques were so timed that after 3 min of study drug administration, laryngoscopy was started and intubation done. Anesthesia was maintained with O2 100% and Isoflurane (MAC titrated to effect). Ventilation was controlled intermittent positive pressure through Bain circuit D co-axial modification. At the end of surgery patients were extubated as per standard departmental protocols. During post operative hospitalization, daily mandatory “post anesthetic visit” was ensured and information gathered for 4 morbidity parameters.

Statistical Analysis

The data was analyzed using online Prism Statistics and SPSS version 22.0.The qualitative parameters like the gender, ASA status are presented as frequency and percentage. Hemodynamic variables like HR, MAP, Systolic and Diastolic blood Pressure were represented by mean ± SD. Statistical significance in the means was assessed by the use of independent student t-test with p value<0.05 considered as significant.

RESULTS

Study groups were comparable in demographic profile (table-1) and baseline blood pressure and heart rate values. Immediately after intubation and at (1,2 min), comparable rise in heart rate, systolic blood pressure and MAP in both the groups was noted; p-value for HR, SBP, DBP, MAP were extremely significant (table-2). However these perturbations in study parameters started settling by 3rd -5th min, although study did not had timeline beyond 5 minutes, but clinically we assessed that these reflexes ceased by 5th minute.

Table-3 gives brief account on mortality (0% in both the groups) and morbidity (group A n=7/50 and group B n=9/50). For simplicity, the comparative analyses by complex statistical tests were not applied for morbidity variables, as we drew inference that morbidity parameters were

not caused by the effects of pressor responses of laryngoscopy but secondarily to technical aspects in anesthetic or surgical management strategies. Three cases (group A (1/50) vs B (2/50) of negative pulmonary edema were basically due to laryngospasm at extubation and clinically no relevance to intubation stress response could be found. Nevertheless the status of lignocain is proven and is re-iterated for blunting the pressor response as deem suitable for every patients.

DISCUSSION

Evidence of the hemodynamic effects at glottis intubation and mechanisms have been studied for more than 60 years[12,13]. No study in our set up has ever been conducted to observe the long term consequences of this pressor response on mortality and morbidity. It would be unethical to study the consequence of not blunting the response, invariably plans are made to avoid catastrophe in peri-operative time due to such hemodynamic perturbations by various standard

Table-1: Demographic data analysis.

Demographic variables	Group A	Group B
No of patients (n)	50	50
Age (years)	39 ± 3.71-4.01	36 ± 3.41-3.87
Gender (n)	M:F 29: 21	M:F 27 :20
Weight (kg)	M:F 72.71: 63. 8(±10.48)	M:F 79. 22: 71.03 (±7.55)
ASA status (as physical status P 1-2)	PI n=33 (66%) P2 n=17 (34%)	P1 n=39 (78%) P2 n=11 (22%)

p-value = 0.265

Table-2: Hemodynamic variables (mean±SD) in group A and group B.

Parameter						
Time (In minutes)	0	1	2	3	4	5
Heart Rate						
Group A (Mean)	80	82	81	78	72	70
Mean ± S.D	80 ± 1.81	82 ± 1.80	81 ± 1.80	78 ± 1.80	72 ± 2.18	70 ± 1.80
Group B (Mean)	80	83	82	76	70	78
Mean ± S.D	80 ± 0.45	83 ± 1.51	82 ± 2.22	76 ± 0.42	70 ± 0.44	78 ± 0.42
p-value	1.00	0.003	0.02	<0.001	<0.001	<0.001
Systolic BP mmHg						
Group A (Mean)	127	122	130	127	120	122
Mean ± S.D	127 ± 1.80	122 ± 1.80	130 ± 1.80	127 ± 1.80	120 ± 1.81	122 ± 1.80
Group B (Mean)	125	123	133	122	119	121
Mean ± S.D	125 ± 1.97	123 ± 2.05	133 ± 1.56	122 ± 1.56	119 ± 1.75	121 ± 1.89
p-value	<0.0001	0.012	<0.001	<0.001	0.006	0.008
Diasystolic BP mmHg						
Group A (Mean)	75	74	79	72	75	70
Mean ± S.D	75 ± 2.03	74 ± 1.85	79 ± 180	72 ± 1.80	75 ± 1.82	70 ± 1.81
Group B (Mean)	75	73	77	75	71	70
Mean ± S.D	75 ± 0.14	73 ± 1.90	77 ± 1.89	75 ± 1.87	71 ± 1.90	70 ± 1.29
p-value	1.00	0.009	0.001	<0.001	<0.001	1.00
Arterial Pressure mmHg						
Group A (Mean)	92.33	90	96	90.33	90	87.33
Mean ± S.D	92.33 ± 0.49	90 ± 0.39	96 ± 0.64	90.33 ± 0.74	90 ± 2.04	87.33 ± 1.44
Group B (Mean)	92.33	96	94	92.33	90	82.33
Mean ± S.D	92.33 ± 0.56	96 ± 0.40	94 ± 0.40	92.33 ± 0.75	90 ± 0.28	82.33 ± 0.68
p -value	1.00	<0.001	<0.001	<0.001	1.00	<0.001

methods[14,15]. We preferred lignocain for its various properties like analgesic effects, antiarrythmic effect, rapidity in onset, short duration and suppression of laryngeal reflexes (as mentioned by Badrinarayan et al)[16,17]. We choose 3 minutes time doctrine prior to intubation in line to (abou madi[11]), a review on "Prophylactic Lignocain use in pre-intubation" which recommended Lignocain 1.5 mg/kg given intravenously 3 minutes before intubation as notified by lev Rosen[16]. Hassan[17] concluded that during laryngoscopy, actual placing of endotracheal tube through the cords and inflating the cuff in infraglottic region contribute significantly to sympatho-adrenal upsurges, again supporting our findings in elderly as Ismail[18] observed exaggerated increase in Systolic blood pressure following laryngoscopy and intubation in elderly and middle aged patients as compared to young depicting the importance of age and variance in balance between sympathetic and parasympathetic outflow which is also in our selected aged population.

We observe the extreme statistical significance (at times *p*-value <0.001) in study group which might generate the argument of being a biased observation, but its similarities could be compared viz a viz the study by Miller et al, Shree et al[19] (and stoelting[5]); albeit not with lignocain as in our study.

A Cochrane review[20] included 72 randomised controls trials with 32 different drugs. Only 2 trials mentioned about mortality due to short lived reflex at intubation. These trials reported no major morbidity or mortality, consistent to our data as well. The stipulated time in our study although was 10 days, might be overwhelming and probably insignificant statistically (to determine true hospital acquired mortality), but easy for follow-up in our health care system. The observed mortality is virtually zero. The morbidity patterns are also in line of above mentioned Cochrane review, it needs to be re-emphasized as the selected parameters in morbidity might be a cause rather than an effect of hemodynamic stress response and is result of various anesthetic techniques, surgical stress; thereby as confounding variables. These results are also consistent to Wang et al[21] and Wilson[22] where carefully titrated doses of lignocain at different timelines were selected. What needs to be evaluated yet is a definitive relationship of pressor responses at bio-chemical milieu which is not possible for authors with existing resources,

Table-3: Mortality/ Morbidity pattern in study.

Hospital Outcome parameters	Group A (n=50)	Group B (n=50)
Mortality (as per study definition)	NIL	NIL
Morbidity for 4 observed Parameters		
Hypertensive encephalopathy	0	0
ACS	6	7
MI (Lab proven)	0	0
Negative Pulmonary Edema (NPPE)	1	2

similar other noteworthy limitations are;

- We conducted study on patients with anticipated normal airways. In difficult airways, longer intubation durations may lead to different results because of altered upsurges in adrenergic responses.
- We selected the population of fit soldiers or those where the underlying conditions (hypertension, diabetes, asthma, Coronary Artery disease) were well controlled without any end organ damage evidence.

CONCLUSION

There was a statistical significant between the two groups and was of practical importance in favor of the proposed method i.e. Intravenous lignocain given 3 min before intubation in attenuating hemodynamic response of laryngoscopy and intubation. The morbidity

(henceforth the mortality) parameters selected were pre-existing factors rather than to the pressor response purely in our opinion; nevertheless the principle of vigilance in the entire peri-operative period holds more logic than a tunnel vision approach surrounding the 3 minutes at intubation phase.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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