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ORIGINAL ARTICLE

NEBULIZED VERSUS INTRAVENOUS LIGNOCAINE TO SUPPRESS THE HAEMODYNAMIC RESPONSE TO ENDOTRACHEAL SUCTION IN PATIENTS ON MECHANICAL VENTILATION

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ABSTRACT: BACKGROUND: Cardiovascular response to tracheal suction is generally obtunded by intravenous lignocaine. We proposed that nebulized lignocaine in an equivalent dose could achieve a comparable suppression. **PATIENTS & METHODS:** The study was conducted in AMCU ACSR Govt. Medical College Nellore, during the period of January 2015 to April 2015. Twenty-six patients requiring tracheal suction through an endotracheal or tracheostomy tube received 1.5 mg kg"[1] of lignocaine in the nebulized form or as an intravenous injection on two different occasions. Heart rate (HR) and mean arterial pressure (MAP) were recorded at baseline, after the administration of lignocaine, after two successive suctions and once in two minutes for the next 16 minutes. **RESULTS:** HR and MAP showed significant changes in both groups. HR increased significantly in both the groups at the end of the two suctions but returned back to the baseline by minute 4 in the IV lignocaine group ($p<0.01$) and minute 6 in the nebulization group ($p<0.05$). In the nebulized lignocaine group, MAP at the end of suction 2 was significantly higher than the MAP at the end of nebulization (p-0.03). It decreased significantly by minute 4 with values at minute 4-8 being significantly lower than at the end of suction 2 ($p<0.05$). In the intravenous lignocaine group, MAP at minute 4-16 was lower than MAP at the end of suction 2 ($p<0.05$). The MAP values at minute 6-16 were, in fact, lower than the baseline values ($p<0.02$). HR and MAP changes were not significantly different between the two routes of lignocaine administration. **CONCLUSION:** Cardiovascular response to tracheal suction is similar when lignocaine is administered either by intravenous or nebulized form.

KEYWORDS: Lignocaine, Haemodynamics, Tracheal suction, nebulization**.**

INTRODUCTION: Tracheal suction is a powerful stimulus that causes intense haemodynamic changes in patients on mechanical ventilation. Traditionally, intravenous lignocaine has been used to control the haemodynamic response to tracheobronchial stimulation. While this technique is generally considered safe, in critically ill patients on mechanical ventilation requiring tracheal suctioning, there are potential risks with intravenous lignocaine. It may cause hypotension. In patients with low cardiac output, transient high plasma concentration of lignocaine with associated systemic toxicity may occur. At the same time, there is evidence to show that intravenous lignocaine is only partially effective in suppressing the response to airway stimulation.[1]

Nebulized lignocaine has been used in clinical practice for a variety of indications. It has been tried in patients with bronchial asthma to decrease the airway reactivity.[2] Awake fibreoptic intubation has been achieved by combining nebulized lignocaine with other lignocaine supplements to suppress the airway reflexes.[3'1] The efficacy of nebulized lignocaine on cardiovascular response to

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tracheal suction has not been investigated. In the present study, we compared the effect of nebulized or intravenous lignocaine on haemodynamic response to tracheal suctioning in patients on mechanical ventilation through either an endotracheal or a tracheostomy tube.

PATIENTS & METHODS: Twenty-six patients on mechanical ventilation in the intensive care unit were included in the study after institutional approval and informed consent. All the patients were haemodynamically stable at the time of inclusion in the study. Patients receiving vasoactive drug support were excluded from the study. We used a crossover design wherein each patient was subjected to both the study interventions in a random order. The interventions consisted of nebulized lignocaine and intravenous lignocaine administration before tracheal suctioning. The study protocol was as follows: Nebulized Lignocaine: Baseline heart rate (HR), mean arterial pressure (MAP) and blood gases were recorded initially. Nebulized lignocaine (4% solution) 1.5 mg kg^{-1} body weight diluted to 4 mL was administered by using a jet nebulizer (Micro Mist,® Hudson RC1, USA) connected to the ventilator, which had a facility for nebulization. The nebulizer was connected to the inspiratory limb of ventilator circuit close to the Y-piece and the drug was delivered only during the inspiratory phase of respiration. HR and MAP were recorded at the end of nebulization following which two tracheal suctions were carried out at an interval of two minuteutes by introducing a 16 gauze polyvinyl chloride (PVC) catheter up to the carina. Each suction was carried out for 15 sec. Following the first suction, the patients was connected to the ventilator until 2 minute time has elapsed and then a second suction was done. HR and MAP were recorded at one minute Ute after each suction and at 2,4,6,8,10,12,14 and 16 minuteute intervals afterwards. A second blood gas analysis was carried out at the end of the study.

Intravenous Lignocaine: The protocol was similar to the nebulized lignocaine protocol but for the study intervention. After recording the baseline HR and MAP and obtaining arterial blood gas sample, the patients were administered 1.5 mg kg^{-1} of 2% intravenous lignocaine. HR and MAP were noted at 2 minute after lignocaine injection. The rest of the suction procedures and data collection were similar between the two protocols.

Statistical Methods: All data are expressed as mean SD. A repeated measures analysis of variance (RMANOVA) was used to compare the within group and between-group differences in the HR and MAP. A posthoc Bonferroni's test was used to find out significant differences in the HR and MAP within the same group. Pre- and post-study blood gas parameters were compared by a paired samples t - test within the same group and by a RMANOVA between the groups. A p value < 0.05 was considered significant.

RESULTS: Twenty-six patients receiving mechanical ventilation through an endotracheal tube or a tracheostomy tube were included in the study. Six patients required mechanical ventilation for respiratory failure caused by neuromuscular paralysis (Guillain Barre syndrome 3, myasthenia gravis 1, spinal lesions 2). The rest of the patients were on mechanical ventilation for cerebral injury (traumatic 18, and nontraumatic 2). The patients with cerebrai injury had stable and well-controlled intracranial pressure (ICP) as evidenced by ICP monitor or repeated computed tomographic scans. There were 18 male and 8 female patients. Their mean age was 44 17 years and the mean body weight, 55 10 kg. At the time of study they were not on any sedative medications. Blood gas values

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before and alter the study are shown in Table 1. Though there were statistically significant but clinically inconsequential changes in pH, $PaCO_2$ and PaO, after suctioning within a given protocol, there were no significant differences between the two protocols.

Heart Rate Changes: The HR changes were not significantly different between the nebulized lignocaine and intravenous lignocaine group. There were however significant within group differences.

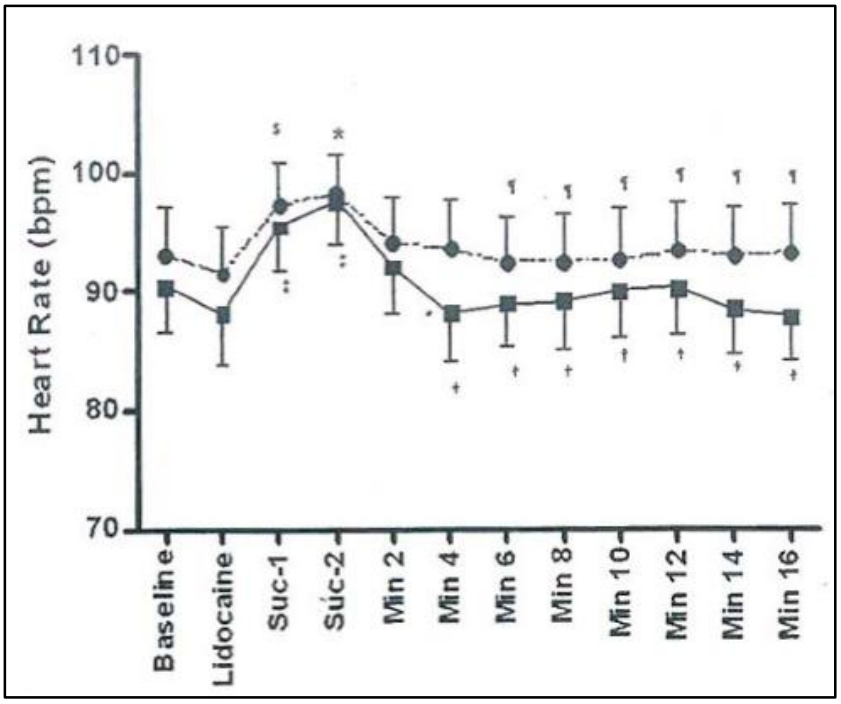

Fig. 1

Nebulized Lignocaine Group: HR changed significantly within the group (p<0.001} (Figure 1). Posthoc test showed that HR increased significantly at the end of both suction 1 and suction 2. The HR at the end of suction 1 was significantly higher than that at the end of nebulization (p=0.02). The HR at the end of suction 2 was significantly higher than that at baseline and at the end of nebulization (p=0.02). The HR returned back rapidly; HR at minute 6 to minute 16 was significantly lower than that at the end of suction 2 (p<0.05).

Heart rate Changes with the two Techniques of Lignocaine Administration: Dotted line represents intravenous administration and continuous line represents administration in the nebulized form, fl - p<0.05 when compared with heart rate at the end of suction 1 and 2. $ - p=0.02 compared to heart rate at the end of nebulization. *p<0.02 compared to heart rate at baseline and at the end of nebulization. f- p<0.01 when compared with HRat the end of suction 1 and 2. 'p<0.05 compared to HR at baseline and at the end of nebulization.

Intravenous Lignocaine Group: Significant within group changes were seen in the HR in this group also (p < 0.001). HR values at the end of suction 1 and 2 were significantly higher than those at baseline and at the end of administration of IV tignocaine (p < 0.05). These decreased by minute 4

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and remained significantly lower than the values at the end of suction 1 and 2 for the rest of the study period ($p < 0.01$).

MAP Changes: Significant within group differences of MAP were found. But the changes were not significantly different between the groups (Figure 2).

Nebulized Lignocaine Group: MAP at the end of suction 2 was significantly higher than MAP at the end of nebulization ($p = 0.03$). It decreased significantly by minute 4 with values at minute 4-8 being significantly lower than at the end of suction 2 ($p<0.05$).

Intravenous Lignocaine Group: This group showed prominent changes in MAP. MAP at Minute 4-16 was lower than MAP at the end of suction 2 ($p < 0.05$). The values at Minute 6-16, were, in fact, lower than at baseline ($p < 0.02$).

DISCUSSION: In this study, a short duration of hemodynamic stimulation occurred.

	Nebulized		**Lignocaine Group**			**Intravenous Lignocaine**			**Group**		**p value**
	Before Study		**End of Study**		**P**	**Before study**		**End of Study**		**P**	**between**
											groups
PH	7.41	**±**0.05	7.44 ±	0.07	0.008	7.40	**±**0.08	7.42 **±**	0.07	0.02	ns
PaCO2 (mmHg)	32.1	**±7.6**	29.8±	7.2	0.07	33.0	* 7.6	30.6 **±**	7.3	0.03	ns
PaO2 (mmHg)	117	**±**35	134±	33	0.006	118	**± 28**	132 **±**	**28**	0.02	ns
HCO3- (mmol/L)	20.2	**±**3.7	20.2±	3.5	0.96	20.1	**±**3.1	19.5 **±**	3.0	0.3	Ns

Table 1: Blood gas values before and after suction

Mean Arterial Pressure Changes with the two Techniques of Lignocaine Administration: Dotted line represents intravenous administration and continuous line represents administration in the nebulized form. TJ-p<0-05 when compared with mean arterial pressure at the end of suction 1 and 2. "p = 0.03 compared to mean arterial pressure at the end of nebulization. f-p<0.05 compared to mean arterial pressure at the end of suction 2 and Minute 2. $ - p< 0.02 compared to baseline.

In response to suction both with nebulized and intravenous lignocaine. The extent of response, however, was not significantly different between the two treatments.

Tracheal suction is a potent stimulus that causes cough and haemodynamic response in intubated intensive care patients. In addition, it may aiso cause bronchoconstriction in any patient with increased airway reactivity. Intravenous lignocaine has been used to suppress cough during tracheal intubation,[5] laryngospasm and cough during extubation,[6,7] and airway reflexes elicited by the irritation of tracheal mucosa.[8] It has also been used to suppress airway hyperreactivity and mitigate bronchoconstriction after tracheal intubation.[9]

Though use of intravenous lignocaine to suppress the airway reflexes caused by tracheal irritation has been an accepted procedure, an effective suppression may actually require a very high

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plasma lignocaine concentrations bordering on to toxic levels. In humans anaesthetized with enflurane, airway irritation elicited cough, and other respiratory reflexes such as expiration, apnoea and spasmodic panting. After administration of intravenous lignocaine, plasma concentrations of lignocaine exceeded 4.7ug tnl/m1, for abolition of all the responses except brief apnoea. The apnoeic reflex was not eliminuteated even at plasma lignocaine concentrations greater than 7.0g/ml. In a volunteer study of abolition of histamine-induced bronchospasm also, the effective lignocaine plasma concentration required to decrease bronchoconstriction, ranged at low antiarrhythmic concentrations, but caused mild central nervous system side effects in about a third of the volunteer's tested.[10] In another study comparing intravenous with inhaled lidocaine, both the techniques attenuated reflex bronchoconstriction significantly. But lignocaine plasma concentrations were significantly lower after inhalation.[11]

High plasma concentrations of lignocaine are fraught with certain potential complications, which include central nervous system symptoms such as numbness of the tongue and mouth, lightheadedness, tinnitus, visual disturbances, slurring of speech, muscular twitching, irrational conversation, unconsciousness, grand mai convulsion, coma and apnoea.[12] The incidence of such toxicity is low fn normal individuals. Critically ill patients however, have certain risk factors such as hypovoiemia and acidosis that may enhance the likelihood of increased plasma lignocaine concentration. In addition, rapid injection or inadvertent arterial injection also may be associated with systemic toxicity. In contrast, nebulized lignocaine used to provide surface anesthesia might produce the required suppression of the response to the tracheobronchial stimulation at lower plasma concentration. This has been observed in many studies where nebulized lignocaine has been used in combination with other lignocaine supplements during fibreoptic bronchoscopy. In these studies, despite the use of additional supplements of lignocaine, plasma lignocaine concentrations were less than 5mg/L, a level that is considered the toxic threshold for the drug. Most of the studies found no significant difference between the efficacy of this technique in suppressing the haemodynamic responses vis a vis that of the other regional techniques used for suppression of airway reflexes during airway interventions.[4] Thus, nebulized lignocaine seems to be clinically effective at plasma concentrations that are below toxic threshold.

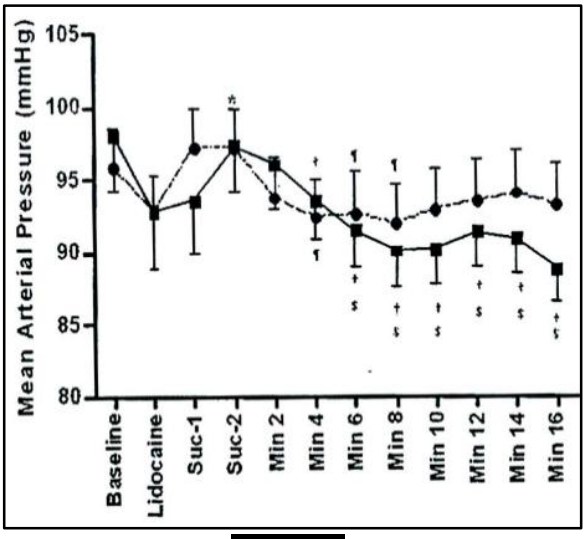

Fig. 2

The results of the present study indicate that the haemodynamic stimulation caused by tracheal suction can be effectively suppressed by both nebulized and intravenous lignocaine. While this seems to suggest that both these interventions may be used with equal efficacy, we find at least two reasons to prefer nebulization to intravenous administration. For a given dose of lignocaine, the plasma concentration will be lower with nebulization. Secondly, in the intravenous lignocaine group in our study, the MAP decreased to below the baseline level from the sixth minuteute after suction (98±20mmHg at baseline vs 89±11 mmHg at 16 minute after suction, $p < 0.01$ after Bonferroni correction for multiple comparisons). While it is essential to have a good suppression of the hypertensive response, a decrease in the blood pressure to below the baseline may be undesirable, especially in patients with cerebral injury.

We used a cross-over design in this study with each patient acting as his own control. This model decreases the influence of other confounding factors that might have affected the results if the study was carried out in two different groups of patients. The two interventions were carried out within less than 24 hours to avoid any gross changes in the clinical condition of the patients between the two studies. Also, we ensured that patients were haemodynamically stable before the study. Considering the short duration of action of lignocaine, there is little chance for the carry-over effect.

The effect of the two study interventions is similar in the present investigation. Given the earlier evidence supporting suppression of haemodynamic response to airway stimulation by lignocaine, we may infer that the response would have been more intense without these interventions. Lack of difference between the two modes of administration of lignocaine suggests that nebulization may conveniently replace the intravenous route.

In conclusion, the present study shows that the abolition of haemodynamic response to tracheal suction is similar with bothintravenous and nebulized lignocaine. But the tendency for a decrease in blood pressure after intravenous lignocaine makes nebulization a preferred alternative. With built-in nebulizer facility in the current intensive care ventilators, this technique should be easy , more effective and assure better haemodynamic stability than intravenous lignocaine during tracheal suction. Nebulization may also help to loosen the secretions and facilitate better clearance of secretions.

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