ORIGINAL RESEARCH PAPER

Anaesthesiology

KEY WORDS: Intubation Response, Haemodynamic Stress Response, Lornoxicam

EFFECT OF INTRAVENOUS LORNOXICAM ON THE HAEMODYNAMIC RESPONSE FOLLOWING LARYNGOSCOPY AND INTUBATION

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ABSTRACT

Aim:
To determine the hemodynamic effects of intravenous lornoxicam and its effect on stress response to laryngoscopy and endotracheal intubation.

Methods:
In this double - blind randomized placebo-controlled study, 50 patients about to undergo general anaesthesia with endotracheal intubation were randomly allocated into two groups. Group 1- Lornoxicam group, where 25 patients received intravenous lornoxicam 16 mg 30 minutes before laryngoscopy and intubation after test dose and Group 2- Control group, where 25 patients received placebo (normal saline) intravenously 30mts before laryngoscopy and intubation.
Systolic and diastolic BP, mean arterial pressure and heart rate changes were recorded before and after administration of general anaesthesia at 1, 3, 5 and 10 minutes post-intubation in both groups.
Results were analysed statistically using student's t test to determine the p value and significance of the observations.

Results:
Post laryngoscopy and intubation, there was a definite reduction in the peak values of systolic BP, diastolic BP, mean arterial pressure and heart rate in lornoxicam group and the difference was significant at 1mt and 3mt in case of systolic BP; 1mt, 3mt, 5mt, 10mt in case of diastolic BP; 3mt, 5mt and 10mt in case of mean arterial pressure and 1mt, 3mt, 5mt and 10mt in case of heart rate when compared to the control group.

Conclusion:
Pretreatment with16mg intravenous lornoxicam is effective in attenuating the cardiovascular stress response to laryngoscopy and tracheal intubation.

INTRODUCTION

Laryngoscopy and intubation are associated with a transient cardiovascular stress response characterized by hypertension, tachycardia, arrhythmias and elevated levels of the circulating catecholamines. This is the result of the activation of the sympathetic nervous system due to stimulation of the somatic and visceral nociceptive afferents of the airway. Though of little consequence to most patients, it increases mortality and morbidity in patients with coronary artery disease, systemic hypertension, pre eclampsia and cerebrovascular pathologies such as aneurysms, tumors or elevated intracranial pressure.

Various techniques have been proposed to attenuate or prevent the stress response following laryngoscopy and tracheal intubation, such as omitting anticholinergic premedication, increasing the depth of anaesthesia, pretreating with vasodilators such as NTG, using various opioids, beta-blockers, alpha-2-agonists and calcium channel blockers. Though effective in blunting stimulatory effects on the cardiovascular system, unfortunately, most of these agents are having well known side effects which necessitate other drugs being tried and studied, in order to minimise the peri-operative adverse events associated with laryngoscopy and intubation.

Recent studies aiming at attenuating or controlling the haemodynamic stress response to laryngoscopy and intubation has included the effect of lornoxicam with different dosages. Significantly, lornoxicam is a well tolerated NSAID belonging to the oxicam group and already being used in the treatment of acute postoperative pain to reduce the use of opioids. With the assumption that pre-operative lornoxicam could be a simple and practical method of stress response attenuation and realising the need for further studies on its hemodynamic effects before routinely being used for the same, this study is being undertaken to demonstrate the effect of pre operative administration of lornoxicam on hemodynamic changes during laryngoscopy and tracheal intubation.

AIM OF STUDY

- To determine hemodynamic effects of IV Lornoxicam during laryngoscopy and endotracheal intubation.
- To determine whether IV lornoxicam is effective in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation.

PATIENTS AND METHODS

STUDY DESIGN

This double - blind randomized placebo-controlled trial was conducted in a tertiary care hospital after ethical committee approval from the institution.

INCLUSION CRITERIA

1. Patients who required tracheal intubation for elective surgical procedures
2. ASA Class I and Class II
3. Age between 30 & 50 years
4. Weight of patients 40 - 70 kg

EXCLUSION CRITERIA

1. Anticipated difficult intubation.
2. At risk of regurgitation or pulmonary aspiration
3. With renal or hepatic impairment
4. Taking drugs known to affect BP & HR
5. Allergy to NSAIDS
6. ASA physical status III or greater
7. Acid peptic disease, bronchial asthma, coagulation disorders
8. Pregnancy & Lactation

PLAN OF STUDY

After routine pre-anaesthetic check up and applying exclusion criteria 50 patients about to undergo general anaesthesia with endotracheal intubation were randomly allocated into two groups.

GROUP 1 -LORNOXICAM GROUP

This group of 25 patients received intravenous lornoxicam 16 mg 30 minutes before laryngoscopy and intubation after test dose.

GROUP 2-CONTROL GROUP

This group of 25 patients received placebo (normal saline) intravenously 30mts before laryngoscopy and intubation.

PREMEDICATION

Patients were not premedicated in this study.

ANAESTHETIC TECHNIQUE

50 patients aged between 30 to 50 years, ASA class I and Class II requiring tracheal intubation for elective surgical procedure were enrolled in this randomized double blind placebo controlled study. All patients included in the study were kept on overnight fasting from 10 pm. In the holding area an IV cannula was inserted and lactated ringers infusion was started with standard monitoring. They were divided into 2 groups to receive either lornoxicam iv or placebo (IV saline) half an hour before surgery after obtaining informed consent from the patient and the relatives.

Medications iv lornoxicam or normal saline was administered by a different anesthetist not involved in the study. Induction technique was standardised. On arrival in operating room and after preoxygenation using Bain's co-axial circuit, anaesthesia was induced with propofol 2 mg/kg. Succinyl Choline 2mg/kg was given to facilitate tracheal intubation. Systolic and diastolic BP, mean arterial pressure, heart rate and ECG changes were recorded before and after administration of the intra-venous anaesthetic and at 1,3,5 and 10 minutes after laryngoscopy and tracheal intubation.

Intubation time was defined as period from termination of manual ventilation using a face mask to restarting of ventilation through endo-tracheal tube. Patients requiring >20 sec to achieve successful tracheal intubation were excluded from the study.

Anaesthesia was maintained using 0_2 & N_20 Mixture and supplemented with intravenous agents as necessary and a non-depolarizing muscle relaxant was used to maintain muscle relaxation. After surgery and after meeting all criteria for reversal, patients were reversed with Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate. Patients were observed for 24 hours for any nausea, vomiting allergic reactions and urine output.

STATISTICAL ANALYSIS

Student's test was used to analyze demographic profile, heart rate changes, pressure changes. Student's 't' test was used for comparing means of two populations.

P value > 0.05 not significant
< 0.05 significant
< 0.01 highly significant

OBSERVATIONS AND RESULTS

The two groups were perfectly matched in terms of no. of patients, age, sex, weight, height, ASA physical status and duration of laryngoscopy.

DEMOGRAPHIC DATA MATCHING

Table 1

	Group 2 (Saline)	Group 1 (Lornoxicam)
No. of patients	25	25
Age	32.5+/.5.2	33.1+/-4.4
Sex M/F	10/15	12/13
Weight	68.7+/-4.2	66.9+/-5.3
Height	167.9 ±8.6	170±4.5
ASA I/II	11/14	12/13
Duration of Laryngoscopy	14.9 (1.7)	16.2 (1.2)

SYSTOLIC BLOOD PRESSURE CHANGES

Systolic blood pressure changes before and after laryngoscopy and intubation

Table 2

Systolic BP (Mean)	Lornoxicam Group	Placebo Group	P Value
Pre-laryngoscopy	112.48	113.92	0.6723
1mt	121.6	135.92	0.0001
3mt	116	127.92	0.0213
5mt	114.16	115.12	0.74
10mt	113.12	114.64	0.5715

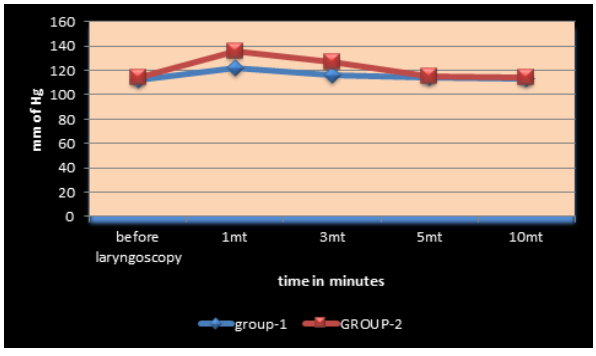
Percentage of rise in systolic BP in both groups at 1 minute

Systolic BP	Lornoxicam	Placebo
1mt	8%	19.3%

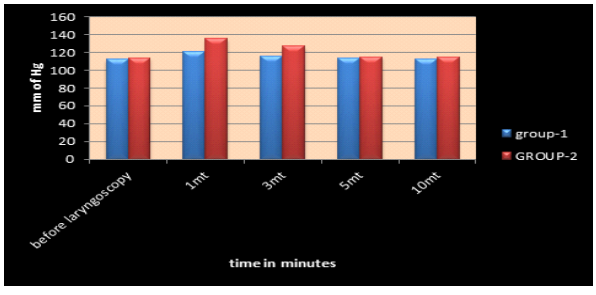
It is evident that systolic BP after induction but before laryngoscopy was comparable in both groups but there was definite reduction in stress response in lornoxicam group and difference was significant at 1 minute and 3 minute intervals.

SYSTOLIC BP CHANGES

Graph 1



Graph 2



DIASTOLIC BP CHANGES

Diastolic Blood pressure changes before and after laryngoscopy and intubation

Table 3

Diastolic BP	Lornoxicam Group	Placebo Group	P Value
Pre-laryngoscopy	68.08	69.2	0.48
1mt	72.52	81.44	0.0001
3mt	66.24	76.4	0.0001
5mt	64.44	70.64	0.0007
10mt	64.96	70.32	0.001

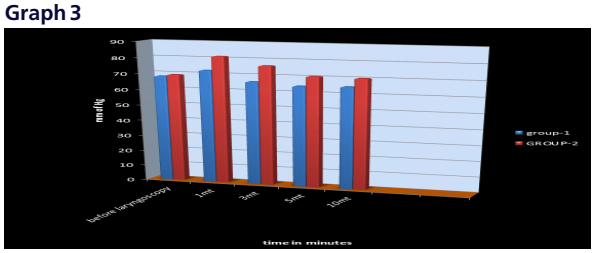
Percentage of rise in Diastolic BP in both groups at 1 minute

Diastolic BP	Lornoxicam	Placebo
3mt	6.5%	17.7%

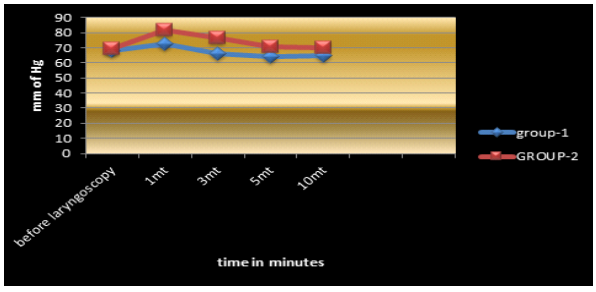
There was a significant reduction in diastolic BP in lornoxicam group when compared with placebo in response to laryngoscopy and intubation.

DIASTOLIC BP CHANGES

Graph 3



Graph 4



MEAN ARTERIAL PRESSURE

Mean arterial pressure changes for both the groups
Table 4

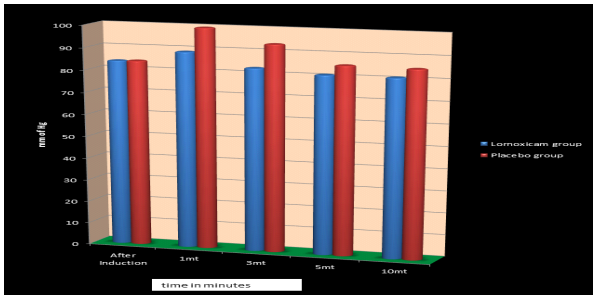
MAP (Mean)	Lornoxicam group	Placebo group	P Value
After Induction	82.88	84.1	0.46
1mt	88.88	99.75	0.13
3mt	82.82	93.57	0.0001
5mt	81.01	85.47	0.0007
10mt	81.01	85.09	0.01

Percentage of rise in MAP in both groups at 1 minute

MAP	Lornoxicam	Placebo
1mt	7.14%	18.6%

MAP CHANGES

Graph 5



Mean arterial pressure seen to be definitely lower in lornoxicam group and difference was significant at 3 minute, 5 minute and 10 minute intervals.

HEART RATE CHANGES Table 5

HR (Mean)	Lornoxicam group	Placebo group	P Value
Pre Laryngoscopy	88.72	87.04	0.54
1mt	95.84	114.16	0.001
3mt	89.6	112.76	0.001
5mt	83.76	101.4	0.001
10mt	84	91.96	0.003

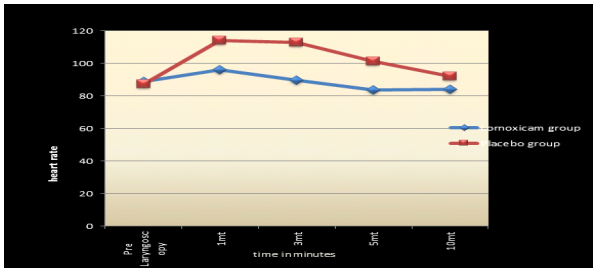
Percentage of rise in HR in both groups at 1 minute

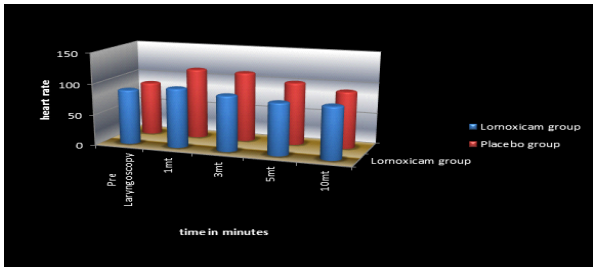
MAP	Lornoxicam	Placebo
1mt	8%	31.1%

Heart rate followed same path as diastolic BP. Rise in heart rate was significantly lower in lornoxicam group and difference was significant at I minute, 3 minute, 5 minute and 10 minute intervals.

HEART RATE CHANGES

Graph 6





STATISTICAL EVALUATION

Table 6

Significant attenuation in rise of	1mt	3mt	5mt	10mt
Systolic BP	0.0001+	0.02+	0.74X	0.57X
Diastolic BP	0.0001+	0.0001+	0.0007+	0.001+
MAP	0.13X	0.0001+	0.007+	0. 01+
Heart Rate	0.0001+	0. 001+	0. 001+	0.003+

Prelaryngoscopic blood pressure and heart rate was comparable in both lornoxicam and control group but after laryngoscopy, there was a definite reduction in the peak systolic BP, diastolic BP, mean arterial pressure and heart rate in lornoxicam group and the difference was significant at 1mt and 3mt in case of systolic BP; 1mt, 3mt, 5mt, 10mt in case of diastolic BP; 3mt, 5mt and 10mt in case of mean arterial pressure and 1mt, 3mt, 5mt and 10mt in case of heart rate when compared to the control group.

DISCUSSION

The haemodynamic stress response to laryngoscopy and intubation is supposed to be initiated by sympathetic response which starts within 5 seconds of laryngoscope pressing the base of tongue. It reaches the baseline value between 5 to 10 minutes after intubation. In the present study we have made an attempt to determine the efficacy of intra venous lornoxicam 16mg, given 30 minutes before laryngoscopy and intubation, in attenuating the haemodynamic stress response.

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The mechanism of stress response attenuation by lornoxicam can be attributed to a decrease in the serum catecholamine levels thus obtunding cardiovascular sympathetic response during laryngoscopy and tracheal intubation. It also increases endogenous opioids dynorphine and beta endorphine. Lornoxicam also causes prostaglandin inhibition and thus cut-off visceral and somatic nociceptive afferents contributing to stress response during laryngoscopy.

In our study, the lornoxicam group and control group were comparable in various parameters like age, weight, height, sex, ASA grading and duration of laryngoscopy. The study was designed as a double-blind randomized controlled trial to investigate the effect of lornoxicam on the changes in blood pressure and heart rate (HR) observed during laryngoscopy and tracheal intubation in 50 ASA I & II patients. They were divided into two groups of 25 each, one being the study group receiving 16 mg iv lornoxicam and the other the control group receiving iv placebo. Heart rate and blood pressure were recorded at various intervals during laryngoscopy and endotracheal intubation.

In our study, the baseline values of both groups showed no significant difference. Lornoxicam group had a significantly lower mean heart rate of 95.84 compared to control group at 1 minute after intubation which showed a heart rate of 114.16. Likewise lornoxicam group also had a significantly lower heart rate at 3 minutes, 5 minutes and 10 minutes after intubation.

In comparison with control group, the lornoxicam group did not show a significant rise of systolic blood pressure at 1 minute and 3 minute intervals. Control group showed a peak in blood pressure at 1 minute after intubation with a systolic BP of 135.92 at 1 minute. The values of systolic blood pressure were near the baseline values at 10 minutes in both the groups.

Likewise, diastolic blood pressure and mean arterial pressure of both groups were showing an increase from basic values but the diastolic BP and MAP recorded from the lornoxicam group showed a significantly lower value.

From the observations, it is evident that the peak values reached by lornoxicam group are significantly lower compared to control group.

Comparing with other international studies, Riad and Moussa in 2008 conducted a study on the effects of preoperative iv lornoxicam on elderly patients. In this study 50 patients aged between 65 and 75 were selected. They were divided into two groups to receive iv lornoxicam 8mg or placebo 30 min before surgery. Heart rate and blood pressure changes were recorded before tracheal intubation and one ,three, five and ten minutes after intubation. The results showed a significant increase in all the parameters that were monitored in the control group. In agreement with the above study, our results also showed a significant increase in systolic, diastolic, mean arterial pressures and heart rate in the control group compared to lornoxicam group though a higher dose of lornoxicam was used. Again, in comparison with the above study by Riad and Moussa we used lornoxicam alone while lornoxicam and fentanyl was used by them. This can be considered as an advantage of our study because we can attribute the reduction in cardiovascular parameters in lornoxicam group to lornoxicam alone.

M.Dabiss et.al in 2010 conducted a study to demonstrate the effect of 16mg iv lornoxicam on cardiovascular stress response and level of serum catecholamine following laryngoscopy and intubation.50 patients were chosen for the study. They were randomly divided into two groups to receive intravenous injection (i.v) of either Lornoxicam 16 mg diluted in 4ml saline or 4ml normal saline half an hour before induction of anaesthesia. No premedication was given to the patients. Baseline values for systolic and diastolic blood pressure, mean arterial pressure, heart rate and SpO_2 were recorded and blood was drawn for measuring the serum catecholamine level before induction. All these parameters were recorded immediately after intubation and every minute that followed, for ten minutes. Their results showed a significant increase in the haemodynamic parameters and serum catecholamine in the control group. They concluded that 16mg iv lornoxicam is effective in blunting the cardiovascular stress response following laryngoscopy and intubation. The results of our study was also in agreement with the above study. In our study there was a significant reduction in all the haemodynamic parameters following intubation in the lornoxicam group. In comparison with the above study we could not measure the serum catecholamine levels as the facility was not available in our centre.

CONCLUSION

Pretreatment with16mg intravenous lornoxicam is effective in attenuating the cardiovascular stress response to laryngoscopy and tracheal intubation. As the peri-operative use of lornoxicam is becoming more frequent, more studies which focus on its effects on old age, ASA III & IV patients and its effect on stress mediators are needed.

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