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Original Article

Anaesthesia Section

Attenuation of Cardiovascular Responses to Direct Laryngoscopy and Intubation-A Comparative Study Between iv Bolus Fentanyl, Lignocaine and Placebo(NS)

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ABSTRACT

Background and objectives: Laryngoscopy and tracheal intubation is invariably associated with a reflex sympathetic pressor response resulting in elevated heart rate and blood pressures. This may prove detrimental in high risk patients. Objective of this study is to compare the effects of lignocaine and fentanyl in attenuation of this pressor response to laryngoscopy and tracheal intubation.

Methods: Seventy five ASA I and II status normotensive patients scheduled for elective surgical procedures were selected randomly and divided into three groups of 25 each. All patients received premedication with pentazocine 0.05mg/kg i.v., atropine 0.01mg/ kg intramuscularly and midazolam 0.01mg/kg i.v. half an hour prior to induction. Induction of anesthesia was standardized for all patients who received, thiopentone 5 mg/kg i.v. and and were relaxed with succinylcholine 2mg/kg i.v. The first group received fentanyl 4micrograms/kg i.v bolus, the second group received lignocaine 1.5mg i.v bolus and then third group received placebo (normal saline), 5 minutes before laryngoscopy and intubation. HR, systolic, diastolic blood pressure were recorded noninvasively one day priorly B, Before induction 0 postinduction, 1,2,3,4 and 5 minutes from the onset of laryngoscopy.

Results: After intubation incidence of tachycardia (HR>100/min) was significantly greater in placebo and lignocaine group than in fentanyl group ($p<0.05$). Rise in SBP and DBP were also statistically significant in placebo and lignocaine group than in fentanyl group ($p<0.05$).

Conclusion: Attenuation of pressor response is seen both with lignocaine and fentanyl. Of the two drugs fentanyl 4mgicrogram i.v. bolus provides a consistent, reliable and effective attenuation as compared to lignocaine 1.5mg/kg iv. bolus.

Key Words: Attenuation, Pressor response, Direct laryngoscopy, Intubation, Lignocaine

INTRODUCTION

In 1940, Reid and Brace [1] first described hemodynamic response to laryngoscopy and intubation. The hypertensive response to anesthetic induction with endotracheal intubation may be harmful in patients with cardiovascular disease, increased intracranial pressure, or anomalies of the cerebral vessels. Recommendations for attenuating the reflex hypertension and tachycardia elicited by upper airway irritation are therefore manifold. Besides minimizing the cardiovascular response, anesthesia induction for patients at risk must also satisfy the following requirements: it must be applicable regardless of patient collaboration, prevent impairment of cerebral blood flow, and avoid arousal of the patient; it should neither be time-consuming nor affect the duration or modality of the ensuing anesthesia [2].

Various methods of attenuation of response to laryngoscopy and intubation are still in search from the date of its recognition. Several studies have been made in order to attenuate these haemodynamic response to laryngoscopy and intubation. Many drugs also have been used for the same purpose [3]. The techniques include topical anaesthesia of oropharynx (viscous lignocaine) laryngotracheal instillation of lignocaine just prior to intubation, intravenous lignocaine, adrenergic blocking drugs, (either alpha or beta blockers) vasodilators like hydrallazine, sodium nitroprusside, nitroglycerine, deep inhalational anaesthesia, intravenous opioids etc., No single agent has been established as the most appropriate for this purpose. Among the recommended procedures, intravenous lidocaine or fentanyl appear to best fulfill the above mentioned criteria [2].

Lignocaine is a amide (-NHCO-) synthetic local anaesthetic. The use of lignocaine is well known in treatment of patients with ventricular dysarrthmias and as prophylaxis in treatment of ventricular tachyarrthmias especially in connection with myocardial infarction and mechanical irritation of cardia. The principal metabolic pathway of lignocaine is oxidative dealkalysation in the liver to monoethylglylcinexylidide followed by hydrolysis of this metabolite to xylidide. Monoethylglycinexylidide has approximately 80% of the activity of lignocaine for protection against cardiac dysarrythmias.

Lignocaine prevents transmission of nerve impulse (conduction blockade) by inhibiting passage of sodium ions through ion selective sodium channels in nerve membrane [4]. The sodium channel itself is a specific receptor to lignocaine molecule.

Fentanyl is a potent, synthetic narcotic analgesic with a rapid onset and short duration of action. It is extremely lipid soluble, has a low molecular weight and is a synthetic opioid agonist which is popularly used as intravenous analgesic supplement, component of inhalation anaesthesia, balanced anaesthesia and neurolept analgesia and also as a sole anaesthetic. It is 75 to 125 times more potent than morphine as an analgesic [5]. After intravenous

administration, onset of effect is 1-2 minutes, and the duration is 1 hour. Consequently it has proved ideal for control of the short lived haemodynamic sequelae, associated with laryngoscopy and intubation.

The aim of this study is to compare Lignocaine (xylocaine), fentanyl and placebo for the attenuation of the cardiovascular response to direct laryngoscopy and intubation during general anaesthesia.

MATERIALS AND METHODS

This study was carried out in the department of Anaesthesiology at the M.R. Medical College's Basaveshwar Hospital, Govt General Hospital Gulbarga during the period of two years (October 2008 to January 2011). Seventy five Patients of either sex, aged between 20 and 60 Years, weighing between 35- 80 kgs and undergoing routine elective surgical procedures who fill the following criteria were included in the study after obtaining written informed consent in each case.

Inclusion criteria:

ASA grade I

Normotensive

Normal ECG

Exclusion Criteria: Patients with a history of regular medication, alcoholism, past history of myocardial ischemia, hypertension, cerebro-vascular accident or eclampsia.

Pre-Anaesthetic Evaluation: A careful pre-anaesthetic evaluation was done by taking history and by clinical examination. Patients pulse rate, blood pressure, respiratory rate, relevant clinical signs and symptoms were noted.

Allocation of the patients: All the selected patients were allocated into three groups consisting of 25 patients each.

Group-I Received Fentanyl 4µg /kg body weight.

Group-II Received Lignocaine(xylocaine) 1.5 mg /kg body weight

Group-III Received normal saline.

Patients were premedicated with intra-muscular atropine 0.01mg/kg, pentazocine 0.5mg/kg i.v Midazolam 0.01mg /kg half an hour prior to induction. All the patients were pre-oxygenated with 100% oxygen for 5L/ minutes using Bains Circuit with a close-fitting face-mask. Induction of anesthesia was standardized for all patients with thiopentone 5 mg/kg i.v. and were relaxed with succinylcholine 2mg/kg i.v. and intubated. Maintained with with 3L/min of oxygen and 5L/min of nitrous oxide. No additional agents were given for the first five minutes post-intubation, nor any surgical stimulus was given to these patients. Further anaesthesia in all three groups of patients was carried out as per the requirement. All patients who required a second attempt at intubation were excluded from the study.

The heart rate, blood pressure, and SPO_2 were recorded at the following time intervals.

"B" Baseline value- during the time of pre-anaesthetic check up one day priorly.

"0" Just prior to intubation.

"1" One minute after intubation

"2 Two minutes after intubation

"3" Three minutes after intubation

"4" Four minutes after intubation

"5" Five minutes after intubation

At the end of 5 minutes monitored period during which time the patient has been cleaned and draped, surgery is commenced.

ANALYSIS OF DATA

The three groups were then compared and analysed for statistical significance by using t test. P value <0.05and P value < 0.001 were considered as statistically significant, and very highly significant respectively. Heart rate changes> 20 %, and BP changes > 15% above or below the basal values were considered as clinically significant. H.R, systolic blood pressure and diastolic blood pressure at different stages of the study were calculated and the following were analyzed:

Mean arterial pressure, Pulse Pressure, Rate Pressure Product.

RESULTS AND ANALYSIS

After intubation, incidence of tachycardia (HR>100/min) was significantly greater in placebo and lignocaine group than in fentanyl group (p<0.05). Rise in systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also statistically significant in placebo and lignocaine group than in fentanyl group (p<0.05) as compared with baseline value.

Changes in Heart Rate [Table/Fig-1 & 2].

- P-values of heart rate in group I&II during the time of pre-anesthetic check-up (B), just prior to intubation (0) and at first minute(1) was statistically insignificant. While at second, third, fourth and fifth minute there was statistically high significant difference in heart rates between the group I & II (P<0.001).
- In II & III group, difference in baseline heart rate values was statistically insignificant but significant just prior to intubation. At second, third and fourth minute there was statistically high sig-

		B	0	1	2	3	4	5
Group-1 Fentanyl 4mcg/kg	Mean	80	83	80	86	85	84	82
	SD	6.7	7.54	5.62	4.14	2.13	2.21	1.65
Group-2 Lignocaine 1.5 mg/kg	Mean	78	81	82	91	90	90	89
	SD	5.5	2	1.9	2.9	2.48	2.8	2.03
Group-3 Placebo (normal saline)	Mean	76	84	86	101	95	94	90
	SD	2.28	2.6	2.31	2.92	2.5	2.3	2.03

[Table/Fig-1]: Change in Heart Rate (Beats/Min)
B= Basal, 0= Zero min, 1= 1st min, 2=2nd min, 3= 3rd min, 4= 4th min, 5= 5th min, SD= Standard deviation

	Group 1 and group 2	Group 1 and group 3	Group 2 and group 3
B	P > 0.05	P < 0.05	P > 0.05
0	P > 0.05	P > 0.05	P < 0.05
1	P > 0.05	P < 0.001	P < 0.001
2	P < 0.001	P < 0.001	P < 0.001
3	P < 0.001	P < 0.001	P < 0.001
4	P < 0.001	P < 0.001	P < 0.001
5	P < 0.001	P < 0.001	P > 0.05

[Table/Fig-2]: P Values of Heart Rate (Beats/Min)
B= Baseline, 0= Zero min, 1= 1st min, 2= 2nd min, 3= 3rd min, 4= 4th min, 5= 5th min

		B	0	1	2	3	4	5
Group-1 Fentanyl 4mcg/kg	Mean	131.6	124.08	124.8	128	130	132	130
	SD	3.83	3.42	3.10	3.65	3.29	2.35	2.88
Group-2 Lignocaine 1.5 mg/kg	Mean	132	123	128	138	144	140	132
	SD	6.48	5.6	5.06	5.35	4.39	4.08	4.39
Group-3 Placebo (normal saline)	Mean	130	128	130	166	170	156	136
	SD	5.5	5.4	5.58	4.6	5.95	5.44	3.48

[Table/Fig-3]: Change in Systolic Blood Pressure (in Mm Hg)
B= Basal,0=Zero min,1= 1st min,2= 2nd min,3= 3rd min, 4= 4th min, 5= 5th min, SD= standard deviation

		B	0	1	2	3	4	5
Group-1 Fentanyl 4mcg/kg	Mean	77	78	78	81.57	84	81.52	77.76
	SD	4.37	4.55	4.88	4.45	3.26	4.73	4.7
Group-2 Lignocaine 1.5 mg/kg	Mean	82	80	88	92	86	82	82
	SD	4.12	4.12	4	4.28	4.04	3.74	3.16
Group-3 Placebo (normal saline)	Mean	78	84	86	102	94	92	88
	SD	5.44	4.84	4	6.27	5.75	5.50	4.04

[Table/Fig-4]: Changes in Diastolic Blood Pressure (in Mm Hg)
B= Basal, 0= Zero min, 1= 1st min, 2= 2nd min, 3= 3rd min, 4= 4th min, 5= 5th min, SD= Standard deviation

nificant difference in heart rates (P<0.001) but again no significant difference was seen at fifth minute.

- In group I & III difference in heart rate values were statistically insignificant during the time of pre-anesthetic check-up (B), just prior to intubation (0). Whereas at time intervals first to fifth minute highly significant difference was seen in heart rate of both group.

CHANGES IN SYSTOLIC BLOOD PRESSURE (in mm Hg).

Changes in the systolic blood pressure are shown in [Table/Fig-3].

- Compared with baseline value, changes in systolic blood pressure in group I&II was statistically insignificant just before intubation, slight significant difference was seen at 1 minute and high significant difference at third, fourth and fifth minute. While at fifth minute statistically no significant difference was seen.

- In II & III group, statistically no difference was seen in baseline systolic blood pressure while difference was significant just before intubation. One minute after intubation, statistically no significant difference in systolic blood pressure was observed whereas at second, third and fouth minute, high significant difference was observed. Again after fifth minute difference was slight only.

- In group I &III difference in systolic blood pressure was significant as compared to baseline values. At first, second, third fourth and fifth minute statistically high significant difference in systolic blood pressures was observed.

CHANGES IN DIASTOLIC BLOOD PRESSURE [Table/Fig-4]

- There was statistically significant difference in baseline Diastolic blood pressures among group I & II (P<0.05) but no significant difference was seen just before intubation.

At first and second minutes, there was statistically high significant difference in mean diastolic blood pressure but at third minute no significant difference was observed. Again at fourth minute high significant difference was seen which decreased to slight only difference at fifth minute.

- In group II and III (P<0.05) statistically significant difference was seen in baseline Diastolic blood pressures and just before intubation but at first minute statistically no significant difference aws observed. Whereas at second, third, fourth and fifth minute high significant difference in mean diastolic blood pressure was seen.

- No significant difference among groups I and III (P>0.05) was seen in baseline DSP but it became highly significant just before and at 1 to 5 minutes after intubation.

DISCUSSION

Endotracheal intubation and laryngoscopy is associated with rise in blood pressure, heart rate and cardiac dysarrythmias [6]. These above mentioned effects may be short lived but they may have adverse effects in high risk patients like, those with cardiovascular diseases, increased intracranial pressure or anomalies of cerebral vessels [7].

FENTANYL

Fentanyl acts at opioid receptors and predominantly acts on μ receptors [9]. Fentanyl brings haemodynamic stability during perioperative period by its action on cardiovascular and autonomic regulatory areas. It decreases sympathetic tone and increases parasympathetic tone.

Fentanyl inhibits pituitary adrenal response directly or indirectly via hypothalamus. It attenuates the response at 2μg/kg IV given before laryngoscopy and intubation. Optimal time of administration is 5 minutes before laryngoscopy and intubation [10]. In our study 4μg / kg were used and the efficacy was compared with placebo and lignocaine group.

Yushi et al., in his study concluded that 2 μg/kg fentanyl suppresses the hemodynamic response to endotracheal intubation more than the response to laryngoscopy [11].

It was shown that supplementation of anesthetic induction with fentanyl 2 μg/kg significantly attenuated the increase in heart rate, arterial pressure and rate pressure product after laryngoscopy and intubation, and fentanyl 6 μg/kg completely abolished pressure responses [12].

Gupta and Tank [3] showed that fentanyl in bolus dose of 2 μg/kg before induction of anesthesia are effective in attenuating the hemodynamic responses to laryngoscopy and endotracheal intubation like heart rate and rate pressure product.

Low doses of fentanyl were employed because a large dose was lead to muscular rigidity, bradycardia, nausea and vomiting. Large doses may also cause postoperative respiratory depression; especially in surgery with short duration of less than 1 hour [12,13]. McClain et al., reported apnoeic episodes in four out of seven patients who received 3.2-6.5 μg/kg fentanyl [14].

LIGNOCAINE

Lignocaine blocks the sodium channels in the cell membranes of the heart and reduces the rate of the rise of the action potential and hence the conduction velocity above all the His Purkinje system and in the atrial and ventricular musculature.

Some studies note a response of intravenous lignocaine in blunt-

ing rises in pulse, blood pressure, intracranial and intraocular pressure. Studies have discussed the possible mechanisms to account for these observations with IV lignocaine. These include a direct myocardial depressant effect, a peripheral vasodilating effect and finally an effect on synaptic transmission [8]. A review on "Prophylactic lidocaine use preintubation". They said that a dose of prophylactic lidocaine of 1.5 mg/kg given intravenously 3 minutes before intubation is optimal. No studies document any harmful effects of prophylactic lidocaine given preintubation [15].

Wang et al., [16] reported most optimal time of administration of intravenous lidocaine to attenuate the increase of intraocular pressure seemed to be the space between 1-3 minutes before laryngoscopy and tracheal intubation.

Wilson et al., [17] showed that irrespective of the timing of administration of injection of lignocaine 2, 3 or 4 minutes before tracheal intubation, there was a significant increase in heart rate of 21-26% in all groups.

There was no significant increase in mean artrial pressure (MAP) in response to intubation in any group of patients given lignocaine before intubation, but in the placebo group, MAP increased by 19% compared to baseline values.

Mollick et al., [18] observed that intravenous lignocaine with pethidine did attenuate the sympathetic responses to laryngoscopy and endotracheal intubation which came down to base line before 5 minute after intubation. But the group of patients which was treated only with lignocaine, their sympathetic responses did not come down to base line at 5 minute after laryngoscopy and endotracheal intubation.

Similar to our observation Bachofen M [2] too reported that fentanyl showed a significant pressure-lowering action persisting over the whole observation period in all patients while no significant effect of lidocaine on the pressure response could be observed.

Malde and Sarode [19] concluded that " given 5 minutes prior to intubation, lignocaine (1.5 mg/kg) and fentanyl (2 µg/kg) both attenuated the rise in pulse rate, though fentanyl was better". Kobayashi also reported Intubation conditions were better in the fentanyl group than in the lignocaine group.

CONCLUSIONS

In the present study, Attenuation of pressor response was seen both with lignocaine and fentanyl. Of the 2 drugs fentanyl 4µg/kg bolus provides a consistent, reliable and effective attenuation of haemodynamic response to laryngoscopy and endotracheal intubation as compared to lignocaine 1.5mg/kg iv. bolus.

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