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Original Research Article

Comparative study of Dexmedetomidine, Lignocaine and their combination for the attenuation of hemodynamic response during laryngoscopy and intubation

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ABSTRACT

The procedure of laryngoscopy and intubation produces short-lived sympathoadrenal response which may be detrimental to high risk patients and sometimes may even be life-threatening. We enrolled 120 patients, ASA I&II, 20-55 year old undergoing elective surgerical procedure under general anesthesia (GA) and they were randomly assigned into 3 equal groups. Group D (Dexmedetomidine), Group L (Lignocaine) and Group DL (Dexmedetomidine plus Lignocaine). Patients were premedicated with routine drugs then Group D- received Dexmedetomidine 1 mcg/kg infusion over 10 mins and Normal saline over 3 mins, Group L- received 10 ml normal saline infusion over 10 mins and Lignocaine 1.5 mg/kg over 3 mins and Group DL- received Dexmedetomidine 0.5 mcg/kg infusion over 10 mins followed by Lignocaine 1 mg/kg over 3 mins and patients were given GA. Vital parameters such as HR, SAP, DAP and MAP were recorded, at baseline, after study drug administration, after induction, 1, 3, 5, 7, 10 and 15 mins after intubation. It was found that the mean HR and BP in group DL remained below baseline value during the entire study period of 15 mins post intubation.It was concluded that the combination of low dose of dexmedetomidine (0.5 mcg/kg) and lignocaine (1mg/kg) effectively attenuates the pressor response during laryngoscopy and intubation without any hemodynamic side effects when compared with Lignocaine (1.5 mg/kg) alone or high dose of Dexmedetomidine (1 mcg/kg) alone.

1. Introduction

The procedure of laryngoscopy and intubation is one of the most noxious stimuli and is associated with intense sympathetic activity and extreme hemodynamic stress marked by tachycardia & hypertension.[1] Although this sympathoadrenal response is short lived; it is known for decades that they may have detrimental effects in high-risk patients especially those with cardiovascular diseases, increased intracranial pressure or anomalies of cerebral vessels.[2] Various pharmacological & non – pharmacological methods have been used to attenuate the hemodynamic response to laryngoscopy & endotracheal intubation. Pharmacological methods like Inhalational agents, topical and Intravenous local anaesthetics[2] Calcium channel blockers[3] opioids[4] and vasodilators have been tried. Still, none of the above approaches or agents has proved to be ideal.

Amongst these, Lignocaine a local anaesthetic and class IB antiarrhythmic drug has been employed by intravenous route for blunting hemodynamic response to intubation very often.[2,5]

Alpha-2 adrenergic agonists have been used for attenuating the sympathetic response for more than two decades[6] and include Clonidine and Dexmedetomidine mainly. Dexmedetomidine is popular for this purpose as it is highly specific, selective and potent alpha-2 adrenoceptor compared to Clonidine.[7] But high doses of these drugs

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many at times leads hypotension and bradycardia.[8,9]

We proposed that combined use of these two agents may suppress the intubation response more effectively and also lowering the required dose of both the drugs. The present study was undertaken to compare efficacy of Lignocaine (1.5 mg/kg), Dexmedetomidine (1 mcg/kg) each alone and combination of low dose of these two [Dexmedetomidine 0.5 mcg/kg and Lignocaine 1mg/kg] in blunting the hemodynamic response to intubation.

2. Materials and Methods

Total 120 ASA grade 1 patients of age between 20 to 55 years were enrolled for this study after obtaining institutional ethical committee permission. Patients with co-morbidities like hypertension, diabetes mellitus, ischemic heart disease and emergency surgeries were excluded from study. Also, patients with anticipated difficult intubation due to any reason and patients on any cardiac drugs were also excluded. Patient who required >1 attempt of intubation or more than 1 minute duration of intubation or any assistance like Bougie, FOB, Light wand were excluded from study.

All the patients were underwent pre- anaesthesia check-up which included detail history of current and past illnesses, thorough physical examination and baseline investigations. Airway examination was done by a senior anaesthesiologist in the department. A written valid informed consent was obtained from the patient after explaining the procedure in detail. Patient were randomly divided into three groups of 40 each viz; Group L, Group D and Group DL.

Baseline vital parameters of patients' including HR, systolic arterial pressure (SAP), diastolic arterial pressure (DAP); mean arterial pressure (MAP) and oxygen saturation were recorded in the pre-operative room. An i.v. line was secured with 20-G venous cannula and Ringer's lactate infusion (6 ml/kg) was infused over half an hour to cover starvation fluid deficit. Inside operation theatre, patients were pre-medicated with i.v. inj. Glycopyrrolate 0.004 mg/kg, inj. Ondansetron 0.08 mg/kg and inj. Fentanyl 2 mcg/ kg 10 min before induction.

The study drugs were preloaded and diluted to a volume of 10 ml using normal saline and were in as coded syringes by an anaesthesiologist who was not involved in the study.

Group **D**- received Dexmedetomidine 1 mcg/kg infusion over 10 mins and Normal saline (for blinding purpose) over 3 mins.

Group **L**- received 10 ml normal saline (for blinding purpose) infusion over 10 mins and Lignocaine 1.5 mg/kg over 3 mins.

Group **DL**- received Dexmedetomidine 0.5 mcg/kg infusion over 10 mins followed by Lignocaine 1 mg/kg over 3 mins.

HR and blood pressure were recorded and pre-oxygenated for 3 min after study drug infusion. Anaesthesia induction was then performed with Inj. Propofol 2mg/kg and then Succinylcholine 2.0 mg/kg. Manual ventilation with 100% oxygen was done for 90 seconds after Succinylcholine injection after which direct laryngoscopy was done with Macintosh curved blade (no. 3 or 4 as per need). The patients were intubated with appropriate size cuffed portex endotracheal tube(ETT). Laryngoscopy and intubation were limited to 45 seconds in all patients.

Cases with failure to intubate within this period were excluded from this study. Duration of laryngoscopy and intubation were measured using stopwatch. After confirming the position and ET tube was fixed with adhesive plaster. Anaesthesia was maintained with 66% N2O and 33% oxygen in 2 L of fresh gas flow on circle absorber system. Bolus IV dose of Vecuronium 0.08 mg/kg followed by intermittent dose of 0.02 mg/kg was used for muscle relaxation. At the end of the surgery, all patients were reversed with Neostigmine 0.05 mg/kg and Glycopyrrolate0.008mg/kg IV. Patients were extubated after adequate recovery and then shifted to anaesthesia recovery room for monitoring. Vital parameters such as HR, SAP, DAP and MAP were recorded, at baseline, after study drug administration, after induction, 1, 3, 5, 7, 10 and 15 mins after intubation. No surgical intervention was allowed during this study period of 15 mins.

The hemodynamic alterations like a decrease in mean arterial pressure (MAP) greater than 20% below the baseline value was treated with primarily by pushing a bolus of IV fluid. Decrease in systemic arterial pressure (SAP)less than 90 mmHg was treated with inj. Mephenteramine 3 mg iv bolus repeated as per need. Any rise in MAP or SAP of more than 20% or SBP > 140 mmHg was taken care of by injecting a bolus dose (0.5 mg/kg) of propofol. Decrease in HR (<50 beats/min) was treated with Atropine 0.6 mg IV.

All recordings were performed by an anaesthesiologist blinded to the group allocation, thus the study was made double-blind. Data was tabulated in a Microsoft Excel spreadsheet. The statistical analysis was done by using SPSS-20. Kruskal Wallis test, Chi-square test and ANOVA were used to calculate the P value and to establish correlation between study groups. A 'p value' <0.001 was considered highly significant, a p value<0.05 was considered statistically significant, whereas a p value >0.05 was considered insignificant.

3. Observation and Results

There was no statistically difference between the groups with respect to age and gender composition. Mean age was (32.7 ± 12.80) years in group L, (33.32 ± 12) in group D and (35.87 ± 13.67) years in group DL. (p>0.05) In the group L. Mean weight in group L (58.32 ± 9.07 kg) was also comparable to group D (58.1 ± 8.25 kg) and group (58.7 ± 9.20 kg). (p >0.05).

Table 1: Comparison of mean HR between the groups

Time		Group L E MEAN ± SD	Group D MEAN ± SD	Group DL MEAN ± SD	L vs D P value	D vs DL P value	L vs DL P value
Baseline		81.65 ± 10.47	82.97 ± 11.59	86.47 ±10.90	0.85	0.33	0.12
After drug infusion		81.32 ± 9.47	58.25 ±5.76	71.02 ± 9.45	<0.0001	<0.0001	<0.0001
After induction		79.55 ± 8.93	57.97 ± 5.09	70.72 ± 9.19	<0.0001	<0.0001	<0.0001
Post Intubation	1	96.47 ± 7.29	69.82 ± 7.93	81.05 ± 9.19	<0.0001	<0.0001	<0.0001
	3	95.42 ± 7.27	67.5 ± 8.26	79.57 ± 9.01	<0.0001	<0.0001	<0.0001
	5	91.57 ± 6.63	63.45 ± 7.72	77.95 ± 8.42	<0.0001	<0.0001	<0.0001
	7	89.95 ± 6.93	60 ± 7.61	76.65 ± 8.58	<0.0001	<0.0001	<0.0001
	10	88.07 ± 7.59	60.9 ± 5.93	74.67 ± 8.91	<0.0001	<0.0001	<0.0001
	15	85.02 ± 8.35	60.37 ± 5.04	71.77 ± 8.61	<0.0001	<0.0001	<0.0001

The mean baseline HR was almost similar in all the three groups (L=81.65 ±10.47, D=82.97 ± 11.59, DL=86.47 ± 10.90). (p >0.05). After giving study drug, mean HR remained stable in group L (81.32 ± 9.47) but had a significant decrease with plain Dexmedetomidine i.e. group D (58.25 ± 5.76) and Dexmedetomidine – Lignocaine combination i.e. group DL (71.02 ± 9.45). (p <0.0001). The fall in HR in D and DL persisted after induction too. (group L=79.55 ± 8.93, group D=57.97 ± 5.09 and group DL=70.72 ± 9.19). 1 min after laryngoscopy and intubation mean HR increased significantly (from 79.55 ± 8.93 to 96.47 ± 7.29) in group L. Although HR again dropped slowly towards baseline, it did not touch pre-induction value before incision i.e. within 15 mins. (p value <0.0001) However, it was always in clinically normal range. On the other hand, mean HR in group D, 1 min after laryngoscopy and intubation was (mean 69.82 ± 7.93), representing increase from post induction value (57.97 ± 5.09) but remained below baseline value even at (82.97 ±11.59) and by 3, 5, 7, 10, 15 minutes. 6 patients in this group had bradycardia (HR < 50). The mean HR in group DL remained below baseline value (86.47 ± 10.90) during the entire study period of 15 mins post intubation and no episode of bradycardia or tachycardia was reported in this group throughout the entire study period.

The mean baseline SBP was statistically similar in all the three groups (L= 122.07 ± 10.63, D=125.8 ± 9.22, DL= 125 ± 8.85). After giving study drug, mean SBP remained near baseline in group L (121.62 ± 10.07). SBP had a significant decrease in group DL (108.75 ± 6.76) but maximum decrease was seen in group D (95.47 ± 6.10). (p <0.0001). After induction a highly significant fall in mean SBP was seen in group L (from 121.62 ±10.07 to 103.75 ±8.74) while a moderate fall was seen in group DL, (from 108.75 ± 6.76 to 99.6 ± 4.73). Group D, however had no further decrease in SBP (from 95.47 ± 6.10 to 93.57 ± 5.12). 1 minute after laryngoscopy and intubation the mean SBP increased significantly (from 103.75 ± 8.74 to 136.2 ± 9.43) in group L remained above baseline mean SBP (122.07 ± 10.63) post laryngoscopy and intubation throughout the study period of 15 minutes.

In group D, the mean SBP, 1 min after laryngoscopy and intubation was 108.45 ± 8.12, representing increase from post induction value (93.57 ± 5.12) but, remained below baseline value (125.8 ± 9.22) even by 3, 5, 7, 10, 15 minutes 5.34. 3 patients in this group developed hypotension (SBP < 90) at 5- or 7-mins post intubation and were treated with Inj. Mephenteramine 3 to 6 mg effectively.

Group DL had trend similar to group D with the mean SBP, 1 min after laryngoscopy and intubation being (115.97 ± 5.85) representing increase from post induction value (99.6 ± 4.73). Also, SBP remained below baseline value (125 ± 8.85) and by 3, 5, 7, 10, 15 minutes like in group D but and there was no episode of bradycardia or hypotension reported in this group throughout the entire study period.

Changes in diastolic BP (DBP) and mean BP followed trends similar to SBP in all three groups. Decrease in MAP and DBP after study drug was maximum in group D. While post induction fall in mean MAP in all three groups, maximum fall in mean MAP was seen in group L (from 91.05 ± 7.49 to 72.94 ± 7.41). 1 min after laryngoscopy and intubation group D had slight increase (80.86 ± 6.42) from post induction value (67.82 ± 4.69) but, remained far below baseline value (94.78 ± 7.88). MAP increased in group DL to (85.85 ± 6.02) from post induction value (69.24 ± 4.86). In group L however, the mean MAP increased 1 min after laryngoscopy highly significantly (from 72.94 ± 7.41 to 103.44 ± 7.01) and remained above baseline mean MAP (91.50 ± 7.45) throughout the study period of 15 minutes. SPO2 remained stable throughout the study period in all three groups.

4. Discussion

Dexmedetomidine, an alpha-2 adrenergic agonist and Lignocaine, a local anaesthetic, represent two different classes, both known to suppress intubation response when used in adequate doses. Intravenous lignocaine at 1.5 mg/kg given 3 mins before intubation is known to suppress intubation response effectively.[2,10] Haemodynamic effects of lignocaine involve multiple mechanisms at various levels. This includes direct cardiac depression and peripheral vasodilatation, inhibition of cough or strain associated

Table 2: Comparision of mean SBP between the groups

Time	Group L MEAN ± SD	Group D MEAN ± SD	Group DL MEAN ± SD	L vs D P value	D vs DL P value	L vs DL P value
Baseline	122.07 ± 10.63	125.8 ± 9.22	125 ± 8.85	0.19	0.92	0.36
After drug infusion	121.62 ± 10.07	95.47 ± 6.10	108.75 ± 6.76	<0.0001	<0.0001	<0.0001
After induction	103.75 ± 8.74	93.57 ± 5.12	99.6 ± 4.73	<0.0001	0.0002	0.01
1	136.2 ± 9.43	108.45 ± 8.12	115.97 ± 5.85	<0.0001	0.0001	<0.0001
3	136.4 ± 11.08	105.02 ± 9.16	117.55 ± 5.77	<0.0001	<0.0001	<0.0001
5	132.67 ± 8.01	101.12 ± 8.41	115.65 ± 5.45	<0.0001	<0.0001	<0.0001
7	130.5 ± 7.63	98.7 ± 6.48	114.22 ± 5.18	<0.0001	<0.0001	<0.0001
10	128.42 ± 8.19	98.95 ± 4.77	112 ± 4.2	<0.0001	<0.0001	<0.0001
15	125.45 ± 8.45	98.07 ± 5.34	108.67 ± 5.24	<0.0001	<0.0001	<0.0001

with tracheal manipulation,[5] attenuation of the activity in afferent C fibers from the larynx and perhaps action on central nervous system to increase the depth of anesthesia.[11] Still, there are studies showing that Lignocaine alone may not suppress the intubation response as effective as opioids like Fentanyl,[12] Remifentanil[13] and other opioids. K. Kumari and colleagues[14] (2015) found that the maximum increase in the heart rate after intubation was 19.6% less in the Dexmedetomidine 0.5 mcg/kg group than that in the placebo group and failed to completely obtund the hemodynamic response to laryngoscopy and intubation. On the other hand, Zhan. Guan, et al.[15] found that 1 mcg/kg Dexmedetomidine significantly suppressed the tracheal intubation related cardiovascular responses, however it caused significant decrease in arterial pressure subsequently 5 mins after intubation.Unlugenc et al.[9] administered1 μg/kg dose of dexmedetomidine within 10 min of induction found a marked decrease in HR within 10 min. Also, N. Solanki and colleagues[16] mentions bradycardia in 2 patients with Dexmedetomidine (1 mcg/kg) like in our study. We have noted similar findings in our study in Group D. Hence, it can be said that high doses of these agents may be associated with significant side effects while low doses may not be completely effective. This provides a rationale for combining low doses of these agents to achieve the task with minimum adverse effects. Moustafa A. et al[8] compared the efficacy of the dexmedetomidine (0.25 mg/kg)– lignocaine (1.0 mg/kg) combination with each drug alone in suppressing the hemodynamic and catecholamine responses during tracheal extubation in sixty hypertensive patients. They found that heart rate, mean arterial pressure, and rate–pressure product following tracheal extubation were significantly lower in patients receiving the dexmedetomidine–lidocaine combination than in those receiving dexmedetomidine or lidocaine. We kept the dose of lignocaine slightly higher, 0.5 mcg/ kg, as direct laryngoscopy was involved in our study. There are multiple studies which suggest that lignocaine alone may not be effective in suppressing the intubation response. Combination of Lignocaine with opioids[17] or doses higher than 1.5 mg/ kg are needed to suppress the intubation response. Similarly, dose of 0.50 mcg/kg Dexmedetomidine was found to have few cardiovascular effects but was not sufficient to prevent tracheal intubation evoked hemodynamic response in many studies[14,15] In our study also, RPP was found to be within safer range in Group DL, whereas it was found to be increased maximum in Group L and too low in Group D. This reflects the better hemodynamic stability offered by combination of low doses of Lignocaine and Dexmedetomidine.

5. Conclusion

Based on the findings of the present study and correlating these findings with the findings of studies done by different authors previously, it can be concluded that combination of low dose of dexmedetomidine (0.5 mcg/kg) and lignocaine (1mg/kg) effectively attenuates the pressor response during laryngoscopy and intubation without any hemodynamic side effects when compared with Lignocaine (1.5 mg/kg) alone or high dose of Dexmedetomidine (1 mcg/kg) alone.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

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