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Comparison of labetalol versus dexmedetomidine to assess the haemodynamic responses to laryngoscopy and intubation during induction of general anaesthesia – a prospective, randomized, controlled study

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Abstract

Background and aims: During general anaesthesia, maneuver of laryngoscopy and tracheal intubation is accompanied by varying degree of sympathetic stimulation. This may prove detrimental in patients with compromised cardiac and cerebrovascular reserve and hence many approaches have been tried to prevent the potentially adverse circulatory responses. In the present study, we compared dexmedetomidine with labetalol to assess and evaluate the haemodynamic responses to laryngoscopy and endotracheal intubation during induction of general anaesthesia and during extubation.

Material and methods: This study was carried out in ninety patients who were posted for various surgeries requiring general anaesthesia with orotracheal intubation. They were allocated into three groups. Group D patients received 0.5mcg/kg dexmedetomidine, diluted to 5ml of 0.9% normal saline, group L received 0.25mg/kg labetalol diluted to 5 ml normal saline and group C received 5ml 0.9%normal saline. All study drugs were administered over 5 minutes followed by induction with IV Propofol 2mg/kg and suxamethonium 1.5 mg/kg. Maintenance of anaesthesia was done with 100% oxygen, sevoflurane and IV Atracurium. Haemodynamic monitoring of systolic and diastolic blood pressure, heart rate(HR), mean arterial pressure(MAP) were done. Calculation of rate pressure product(RPP) were done and all parameters were compared at intubation(I_0), 1(I_1), 3(I_3), 5(I_5), 10(I_{10}) and 15(I_{15}) minutes postintubation, intraoperatively and at extubation.

Results: Group D and group L showed statistically significant fall in HR,SBP, DBP, MAP RPP at induction, at intubation(I_0), I_1, I_3, I_5, I_{10}, I_{15} than group C*($p<0.001$)*. There were decrease in HR, SBP, RPP in group D than in group L ($p<0.001$), while at I_{10} and I_{15} fall in MAP was significant in group D($p<0.001$). Group C showed incidence of tachycardia and hypertension to be 83% and 77% respectively. Group D showed bradycardia in three patients and hypotension in four out of thirty patients which were statistically insignificant when compared to group L.(*$p>0.05$).*

Conclusion: The haemodynamic responses to laryngoscopy, endotracheal intubation and extubation are better controlled with dexmedetomidine than labetalol.

Keywords: Laryngoscopy, Endotracheal intubation, Haemodynamic responses, Dexmedetomidine, Labetalol.

Introduction

Direct laryngoscopy and tracheal intubation during general anaesthesia leads to sympathetic stimulation and release of plasma catecholamines concentration which manifests clinically as tachycardia, hypertension along with raised intraocular and intracerebral pressure.[(1)]

Normally these haemodynamic responses have its peak effect within 1-2 minutes after intubation and is normalized within five minutes post intubation,[(2)] but the response may be unpredictable in duration as it also depends upon comorbid conditions of the individual patients. Sometimes the abrupt increase in systolic blood pressure may lead to untoward effects in patients of cardiovascular and cerebrovascular diseases.[(3)] An increase in heart rate, together with elevation of systolic blood pressure increases the rate pressure product, thus compromising myocardial contractility and oxygen supply.[(4)]

Variety of pretreatments ranging from topical anaesthesia of larynx to administration of several classes of drugs like nitroglycerine, B blockers and opioids have been made. Each technique has its own disadvantages, so many times multimodal therapy rather than single intervention has been in practice to attenuate this response.[(5)]

Dexmedetomidine is a selective α_2 agonist that provides multimodal features like sedation, hypnosis, analgesia and sympatholysis. It also decreases levels of catecholamines during surgery and maintains intraoperative haemodynamics.

Labetatol is a α_1 and non- selective β-adrenergic blocking drug. It is used mainly for perioperative control of blood pressure and haemodynamic stability.[(6)] So this study was conducted primarily to compare labetalol with dexmedetomidine to assess the haemodynamic responses to laryngoscopy and intubation during induction of general anaesthesia. Secondarily this study was aimed to evaluate haemodynamic responses at extubation amongst the groups.

Material and Methods

This prospective, randomized, controlled study was designed in ninety patients after approval of the institutional ethics committee and written informed consent from each patient. The inclusion criteria were patients aged 18-50 years, belonging to ASA grade I-II,

scheduled for surgery of duration less than two hours under general anaesthesia with orotracheal intubation. Patients with known hypersensitivity to study drugs, pregnant females, patients with cardiovascular, respiratory, hepatic or renal diseases, patients on β blockers, patients with anticipated difficult intubation and those patients in whom intubation was attempted for more than 30 seconds were excluded from the study.

In the operating room, an intravenous line was secured by 18 G canula and all patients were monitored for baseline vital parameters like non-invasive blood pressure, heart rate(HR), pulse oxymeter(SpO_2)and electrocardiograph(ECG). All patients were premedicated with glycopyrrolate 5mcg/kg, ondensetron 0.1mg/kg and fentanyl 1mcg/kg intravenously and were preoxygenated with 100% oxygen. Thereafter the patients were randomly allocated with the help of computer generated coded envelops based on study drugs into three groups as per protocol given below:

Group C: IV 0.9% Normal Saline 5ml
Group L: IV Labetalol 0.25mg/kg
Group D: IV Dexmedetomidine 0.5mcg/kg

The study drugs were diluted to 5ml with 0.9% normal saline and administered over 5 minutes before administering intravenous induction anaesthetic agent. The level of sedation after administering study drug was also observed. Anaesthesia was induced with propofol 2mg/kg followed by suxamethonium 1.5mg/kg. Ventilation of lungs was manually assisted till muscles were relaxed satisfactorily. Then laryngoscopy was carried out and patient's airway was secured with an endotracheal tube within 15 seconds. During surgery anaesthesia was maintained with sevoflurane in oxygen and IV atracurium as a muscle relaxant. The inspired concentration of sevoflurane was adjusted to maintain heart rate and MAP within 20% from baseline values.

Monitoring was done using SpO_2, non-invasive blood pressure(NIBP) heart rate(HR), ECG, recorded at the end of giving study drugs, at induction, at laryngoscopy and orotracheal intubation(I_0), and 1(I_1), 3(I_3), 5(I_5), 10(I_{10}), 15(I_{15}) minutes post intubation and thereafter continuously every 10 minutes till the end of surgery.

The neuromuscular block was reversed with neostigmine 0.05mg/kg and glycopyrrolate 10mcg/kg intravenously and patients were extubated. Haemodynamic responses to extubation and thereafter for 5 minutes postoperatively were again recorded. Intravenous diclofenac 75mg was supplemented in all patients for relief of postoperative pain.

Intraoperative haemodynamic stability and side effects like hypertension, hypotension, bradycardia, tachycardia and arrhythmias were recorded and managed accordingly. The haemodynamic response to extubation was also observed and compared between the three groups.

Statistical Analysis: Sample size was calculated with 80% of power analysis and 95% as confidence level and 10% as the absolute error. SPSS version19.0 was used for statistical analysis. Demographic data of the patients were expressed as mean ± standard deviation. The statistical data were analysed by paired student's t –test for intragroup variations of values and unpaired t-test for intergroup variations. Values were considered significant when $p<0.05$.

Results

There were no differences regarding demographic data($p>0.05$)(Table 1), duration of surgery and anaesthesia, baseline haemodynamic values in all three groups. Group D patients showed conscious sedative effect but it was statistically insignificant ($p>0.05$).

Table 1: Demographic Data

	Group –C	Group-L	Group -D	P-Value		
				C & L	C & D	L & D
Age (years)	32.44±11.20	42.6±7.5	40.8±6.5	>0.05	>0.05	>0.05
Gender (M/F)	22/8	21/9	23/7	>0.05	>0.05	>0.05
Weight (kg.)	54.55±8.20	55.7±7.10	53.68±7.82	>0.05	>0.05	>0.05
ASA I/II	26/4	28/2	25/5	>0.05	>0.05	>0.05

Fall in heart rate(HR) was observed in group D after giving study drug, at laryngoscopy and intubation(I_0), I_1, I_3, I_5, I_{10}, and I_{15} post intubation which was statistically significant when compared with group C and groupL ($p<0.001$). A significant fall of HR from baseline values till 15 minutes of post-intubation in group D was observed as compared to group L ($p<0.001$)while group L showed lower HR only at intubation and at I_1 and I_3 post-intubation than group C($p<0.001$)(Table 2).

Table 2: Mean Heat Rate between the three groups

	Group –C n=30	Group-L n=30	Group –D n=30	P-Value		
				C & L	C & D	L & D
Baseline	86.09±6.05	89.80 ± 8.20	85.59± 7.5	0.051	0.777	0.042
End of Pre-Med	88.10±9.60	89.60 ± 10.2	86.10 ±6.5	0.560	0.349	0.118
End of Study Drug	88.10±6.60	86.00± 7.0	79.10±6.8	0.237	<0.001	<0.001
End of Induction	90.30±8.80	90.00±10	76.30± 7.2	0.902	<0.001	<0.001
I_0	116.80±16.44	100.70±7.0	79.50±8.0	<0.001	<0.001	<0.001
I_1	112.42±14.15	98.80±7.5	70.50±10.0	<0.001	<0.001	<0.001
I_3	100.10±8.90	96.70±4.5	72.35 ±9.5	0.067	<0.001	<0.001
I_5	94.20±8.82	92.30±4.2	70.44± 10.0	0.291	<0.001	<0.001
I_{10}	94.10±9.04	92.40±5.5	72.55 ±6.5	0.383	<0.001	<0.001
I_{15}	92.20±6.24	91.50±6.5	68.00±6.5	0.672	<0.001	<0.001
Extubation	110.60±8.66	96.10±7.0	88.00± 5.5	<0.001	<0.001	<0.001
Post-op	96.56±4.23	86.20±10.0	86.00±7.5	<0.001	<0.001	0.930

Compared with group C values, there were decrease in systolic blood pressure(SBP) which were statistically significant at intubation and post-intubation till 15 minutes in group D and group L ($p<0.001$). SBP was significantly low in group D as compared to group L($p<0.001$).

Fall in diastolic blood pressure(DBP) was statistically significant after giving study drug ,at intubation and at all time stations in group D and group L as compared to group C (*$p<0.001$*), but the results were comparable in group L and group Dat intubation and till 15 minutes post-intubation($p>0.05$).

Fig. 1 shows fall in mean arterial pressure(MAP) and Fig. 2 shows rate pressure product(RPP is the product of heart rate and systolic blood pressure) after giving study drug, induction, at laryngoscopy and intubation until 15 minutes of intubation were significantly low in group L and group D as compared to group C *($p<0.001$)*. The values of MAP were not significant statistically between group L and group D($p>0.05$) at I_0, I_1, I_3, I_5 and statistically significant at I_{10}, I_{15} ($p<0.001$), while fall in RPP was more in group D as compared to group L (*$p<0.001$*).

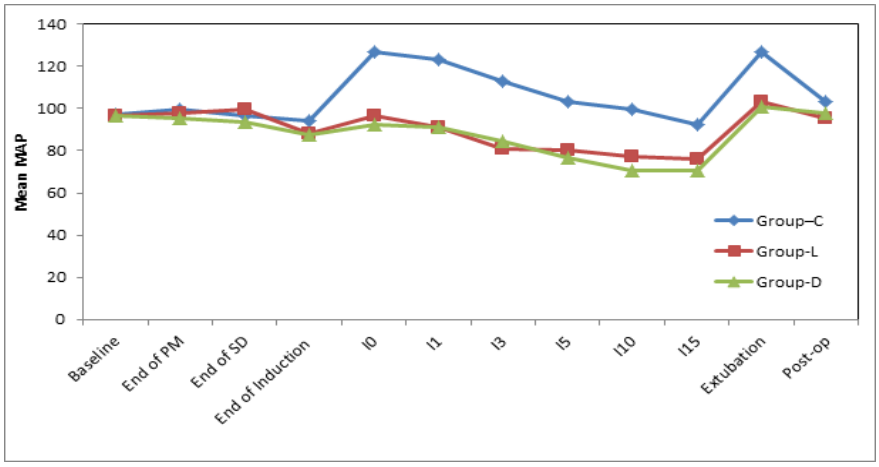

Fig. 1: Graph showing Mean arterial pressure (MAP) between three groups

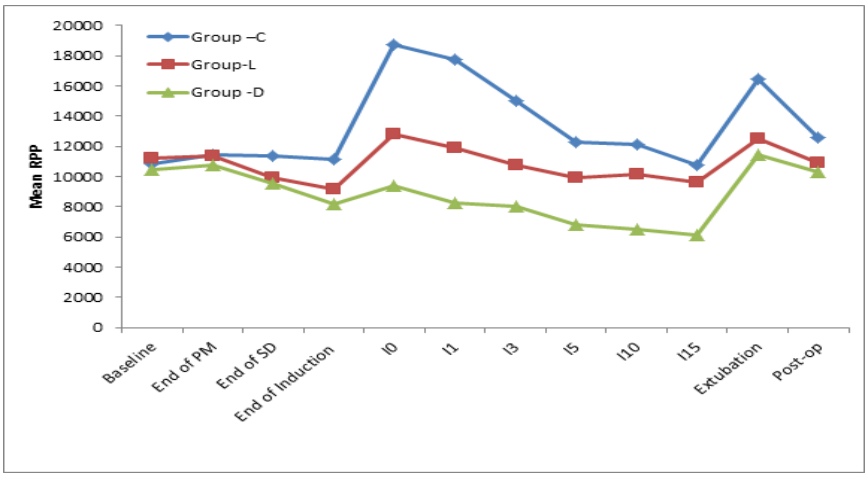

Fig. 2: Graph showing Rate Pressure Product (RPP) between three groups

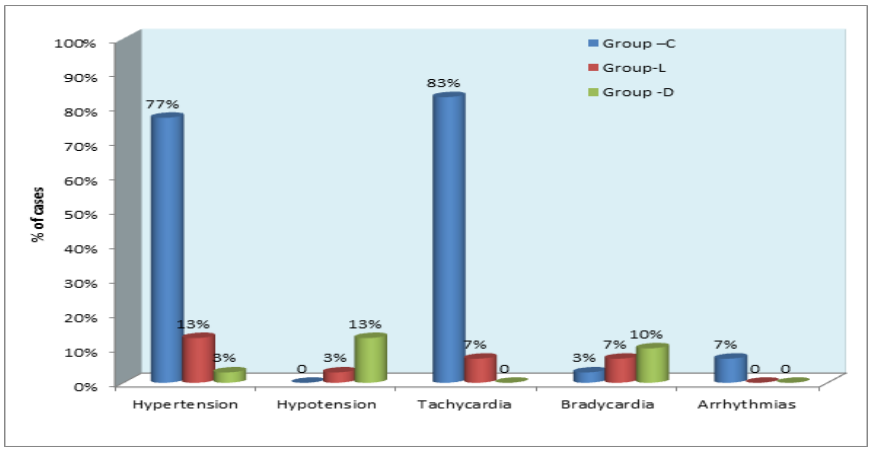

Fig. 3: Graph showing intra operative side effects between three groups

At extubation, group D and group L had significant fall in HR, SBP, DBP, MAP, RPP as compared to group C *(p<0.001)*. The values of SBP and MAP were not significant between group L and group D(p>0.05).

Fig. 3 shows that incidence of intraoperative tachycardia and hypertension were observed to be 83% and 77% respectively in group C as compared to group L and group D(p<0.001). Arrhythmias in the form of atrial ectopics were recorded in ECG in two patients in group C. Group D showed bradycardia in 3 patients and hypotension in 4 patients as compared to 2 and 1 patients respectively in group L(p>0.05).

Discussion

The haemodynamic responses to laryngoscopy and endotracheal intubation results in increase in blood pressure and heart rate and hence the rate pressure product(RPP). A high RPP indicates a potential danger of myocardial ischaemia. As these adverse haemodynamic effects are controlled through sympathetic nervous system and therefore may in theory be suppressed by supplementing drugs which blocks adrenergic receptors. Many adjuvants like β-blockers, opioids, calcium channel blockers, α_2 agonist and labetalol or combinations have been tried in various studies, for blunting of haemodynamic responses, but if these adjuvants were used in higher than normal doses it had led to increased incidence of side effects.

Labetelol is unique in that it has the properties of a β adrenergic blocking drug while possessing weak α blocking potential as well. We had recorded the values of haemodynamic responses till 15 minutes after intubation in this study as it has a peak effect in 5-15 minutes after administering intravenously and is redistributed very rapidly. It decreases systemic vascular resistance and hence decrease in blood pressure and reflex tachycardia which is trigerred by vasodilatation is simultaneously blocked by β receptor-blockade. Studies have been done using labetalol in low as well as in higher doses with several anaesthetic regimes for controlling the haemodynamic responses.[3,4,7]

Nowadays, dexmedetomidine has been administered for many purposes in the practice of anaesthesia. The basic effect of α_2 agonist is related to stimulation of α_2 adrenergic receptors located in central nervous system. These receptors are involved in sympatholysis, sedo analgesic effect. Dexmedetomidine causes decrease in heart rate, systemic vascular

resistance, blood pressure and so adverse cardio vascular effects.

A number of clinical researches has been done stating that dexmedetomidine decreases the haemodynamic responses to laryngoscopy and intubation.[8,9,10] but studies are lacking comparing dexmedetomidine with labetalol for the same purpose.

Dexmedetomidine has been used in doses ranging from 1-2mcg/kg to prevent the hypertensive and tachycardia response associated with laryngoscopy and intubation, but at the cost of significant bradycardia and hypotension when it has been used at high doses.[11,12] Raval et al[2] found 1mcg/kg dexmedetomidine to be more effective than 0.5mcg/kg in attenuating haemodynamic responses with no side effects. This study is consistent with the researcher Kumari et al[13] that showed attenuation of haemodynamic responses with a single pre-induction intravenous dose of dexmedetomidine of 0.5mcg/kg.

Although labetalol had maintained the blood pressure, tachycardia was still prominent during laryngoscopy and intubation. It had partial effect to maintain the rise in heart rate. Singh et al[3] compared labetalol in the dose of 0.25mg/kg with esmolol and found labetalol to be superior in attenuation of pressor response.

Incidence of intraoperative tachycardia and hypertension was higher in placebo group as compared to when dexmedetomidine and labetalol were used prior to intubation. Dexmedetomidine causes bradycardia due to central sympatholysis and resultant unopposed vagal tone and possibly due to presynaptic mediated diminution of noradrenaline release.[14,15] Bradycardia was reported after single dose of 0.5mcg/kg to be 5% by Basar et al[10] while in our study the incidence was found to be 10%. This may due to combination with fentanyl as it also causes bradycardia and dexmedetomidine, administered along with fentanyl has synergistic effect to cause fall in heart rate.

Extubation is equally important as it can be detrimental for high risk patients. Dexmedetomidine as well as labetalol enabled a smooth change over during reversal till post-extubation phase. Due to analgesic and sympatholytic property, dexemedotomidine had led to stable haemodynamics with good control of heart rate and blood pressure when compared to labetalol at the time of extubation as well as postoperatively.

Conclusion

The haemodynamic responses to laryngoscopy, intubation and extubation are better controlled with dexmedetoidine than labetalol. Labetalol does not attenuate the tachycardia completely during laryngoscopy and intubation.

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