Comparison of Effect of Dexmedetomidine versus Lignocaine on Haemodynamic Response and Quality of Extubation In Patients Undergoing Interventional Neuroradiological Procedures: A Randomized Double-Blind Interventional Study

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Abstract
Background and Aims: Haemodynamic and airway responses during and after extubation may be precarious in neurosurgical patients. We aimed to compare the effects of dexmedetomidine versus lignocaine on haemodynamic response and quality of extubation in patients undergoing interventional neuroradiological procedures**. Material and methods:** This prospective study was conducted in a randomized double-blind manner on a total of 80 patients of either sex aged 20-50 yrs of ASA grades I, II & III who were randomly allocated into two groups (40 in each group). In Group A inj. Dexmedetomidine 0.5mcg/kg i.v and in Group B - inj. Lignocaine 1.5mg/kg i.v was given as a single bolus in 10 ml normal saline, at the end of the procedure. Haemodynamic variables (HR, SBP, DBP, MAP) were recorded at extubation, 1, 3, 5, 10, and 15min after extubation. Quality of extubation, sedation score and side effects (bradycardia, hypotension, nausea & vomiting) were also noted. Statistical analysis was performed by using the student-t-test and Chi-square test (significant p-value $\leq$ 0.05). **Results**: The SBP, DBP and MAP were significantly higher in group B than in group A at extubation, 1min, 3min, 5min, 10min and 15min post-extubation whereas the significant difference in HR was observed only at extubation and 1min post-extubation (Group B > A). Dexmedetomidine produced a higher sedation score grade 2 (73.68%) than lignocaine (20.51%) with better quality of extubation and nonsignificant side effects. **Conclusion**: Dexmedetomidine administered 10 min before extubation effectively attenuates the haemodynamic and airway responses during extubation as compared to Lignocaine.

Keywords: Dexmedetomidine, Lignocaine, Interventional, Extubation, Haemodynamic

Introduction
Endovascular neurosurgical procedures include cerebral angiography, endovascular coiling, carotid artery angioplasty/stenting, thrombolytic therapy, and minimally invasive spine surgery.[1] Prolonged procedures improved patient safety and optimal conditions for imaging have resulted in a trend toward greater use of general anaesthesia for these procedures, especially in the aneurysm and arteriovenous malformation treatments.[2,3] The goal of anaesthesia is to ensure cardiovascular stability, avoid surges in arterial blood pressure that might cause aneurysm rupture and maintain adequate perfusion of ischaemic cerebral circulation.[4] During general anaesthesia, both intubation and extubation are stressful periods and are

associated with various cardiovascular and airway responsesleading to tachycardia, hypertension, arrhythmias, myocardial ischaemia, coughing,bronchospasm,raised intracranial and intraocular pressure. Complications at the time of extubation are three times more common than during endotracheal intubation.[5] These haemodynamics responses are transient, variable and unpredictable with little consequences in ASA Grade I and II patients but can be of major concern in patients with intracranial aneurysm and arteriovenous malformation where sudden hypertension during the extubation phase can lead to raised cerebral blood flow (CBF), intracranial pressure (ICP), brain oedema or intracranial hematoma formation which may give rise to herniation of brain tissue leading to high morbidity and mortality. So, attenuation of haemodynamic response to extubation is crucial to preserve cerebral homeostasis in these patients.

Various drugs like esmolol, labetalol, verapamil, nicardipine, diltiazem,clonidine, lignocaine, short-acting opioids (fentanyl, remifentanil), and prostaglandins E_1 have been used for attenuation of haemodynamic response to extubation but with certain limitations. Lignocaine, asynthetic amidelocal anaesthetic agent is one of the oldest economic and most easily available drug used for attenuation of haemodynamic response to laryngoscopy and intubation.[6] Dexmedetomidine is a potent highly selective alpha -2 receptor agonist having a sympatholytic effect, making it anappropriate agent for reducing airway and circulatory reflexes during emergence from anaesthesia.[7]

This study aimed to compare the effects of dexmedetomidine versus lignocaine on haemodynamic response and quality of extubation in patients undergoing interventional neuroradiological procedures. The primary outcome wasto compare the change in haemodynamic parametersbetween two groups during extubation.Quality of extubation, time of emergence and time taken for extubation, sedation score and incidence of side effects were assessed as secondary outcome measures.

Materials and method

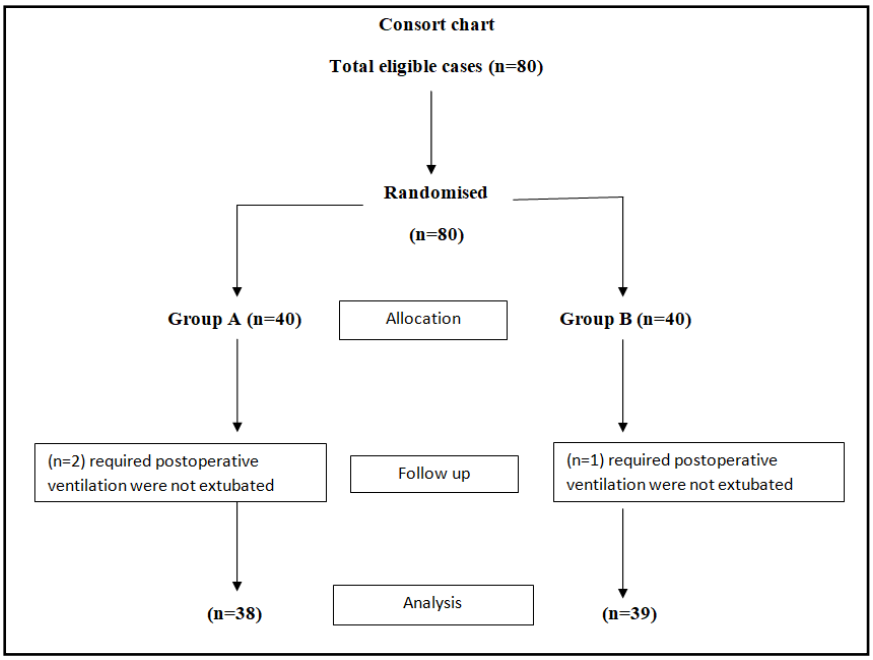
After approval from the institutional ethics committee and obtaining written informedconsentthe study was conducted in a randomized double-blind manner on 80 adult patients of either sex aged 20-50 yrs, belonging to ASA grades I, II & III scheduled for Interventional neuroradiological procedures under general Anaesthesia.Patients witha difficult airway, pregnancy, morbid obesity, history of associated cardiac, renal, hepatic and respiratory dysfunction, patients receiving-beta-blockers, digoxin, alpha - 2 agonists, or psychotropic medication, history of drug allergy, heart rate below 60 / min or arterial pressure < 100 / 60 mmHgwere excluded from the study. A sample size of 40 in each group was required at a 95% confidence level and 80% power to verify the expected difference of (6.55 ± 8.36) in heart rate variation at the time of extubation in bothgroups as per the seed article[8]. This sample size was adequate to cover other study variables too. So, for the study purpose patients were randomly allocatedinto two groups of 40 patients each using computer-generated random numbers.In Group A patients received Dexmedetomidine injection of 0.5mcg/kg i.v as a single bolus diluted in 10ml normal saline and Group B patients received Lignocaine injection of 1.5mg/kg i.v as a single bolus diluted in 10ml normal saline given at the end of the procedure.

The study drug preparation was done in two identical syringes of 10ml each by an independent Anaesthesiologist.Patients and the anaesthesia care team were blinded to this categorization.All patients underwent detailed pre-anaesthetic evaluation and were instructed to be kept NPO for 8 hours prior to surgery. Informed written consent was obtained after an explanation of the study protocol andprocedure.Inthe operationtheatre,an 18gauge peripheral venous cannula was inserted and a normal saline drip was started. All standardroutine monitors were attached including an electrocardiogram(ECG), pulse oximeter (SPO_2), non-invasiveblood pressure (NIBP), end-tidal carbon dioxide ($ETCO_2$), respiratory gas and temperature. After that, all patients were premedicated with Inj. Ranitidine (1mg/kg), Inj.Metoclopramide (0.1mg/kg), Inj.Glycopyrrolate (0.004mg/kg), Inj. Midazolam (1mg), Inj. Fentanyl (2µg/kg). Preoxygenation with 100% oxygen for 3-5minutes was followed by induction with Inj.thiopentone (5-6 mg/kg) and Inj.Rocuronium 0.6mg/kg to facilitate intubation. Anaesthesia was maintained using controlled ventilation with Sevoflurane and Inj.Atracurium intermittent doses of 0.1 mg/kg) throughout

the surgical procedure. After completion of the procedure at the time of check Digital Subtraction Angiography(DSA), sevoflurane was discontinued and the study drug was given as a bolus in 10ml saline dilution by slow intravenous injection over a period of 2min by an anaesthesiologist who was unaware of the group allocation. After injection of the study drug patients were reversed and extubated when attainingextubation criteria.The haemodynamic parameters (HR, SBP, DBP, MAP) were recorded just before the study drug injection(baseline), every 2 min till the extubation, at the time of extubation (E), at 1, 3, 5, 10, and 15min after extubation (E1, E3, E5, E10, E15) respectively. Any episode of bronchospasm, laryngospasm, breath-holding and desaturation was recorded. Quality of extubation was assessed by using a Four-point scale:Grade 0: No Coughing, Grade 1: Minimal Coughing [once or twice], Grade 2: Moderate coughing [3-4 times], Grade 3: Severe coughing [5 or more times]. Emergence time and extubation time were noted which are defined as: Emergence time –the time interval between discontinuation of anaesthesia and patient following verbal commands and Extubation time –the time interval between cessation of anaesthetics and tracheal extubation. Breath-holding is defined as holding breath for the 20sor more and a decrease of oxygen saturation <92 % is defined as desaturation. Ramsaysedation scale was used to assess the level of sedation.Adverse effects including bradycardia, hypotension, postoperative nausea and vomiting (PONV) werealso noted.

Statistical analysis: It was performed with SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The categorical data were presented as numbers (per cent) and were compared between groups using the Chi-square test. The quantitative data were presented as mean and standard deviation and were compared by Studentt-test. Probability (P-value)≤0.05 was considered as significant (S) and >0.05 as non-significant(NS).

Figure 1: Consort flow chart



Results

A total of 80 patients were taken up for the study and randomly allocated into two groups (n-40), two patients in Group A and one patient in Group B could not be extubated at the end of the procedure and required postoperative ventilation,those patientsexcluded from the statistical analysis, as shown in the consort flow chart (Figure1)**.**There were statistically no significant differences between the two groups in terms of the demographic profile including age,gender,weight and physical status (Table 1).

Table 1: Demographic and other characteristics of patients in both study groups

Demographic data	GroupA	Group B	P-value
Age (yrs)[a] Mean ± SD	 39.37 ±10.49	 38.85 ±9.07	 0.815(NS)
Gender(%) Male Female	 22(57.89%) 16(42.10%)	 19(48.71%) 20(51.28%)	 0.0563(NS)
ASAGrade(%) Grade I Grade II Grade III	 0% 84.21% 15.79%	 0% 87.21% 12.82%	 0.963(NS)
Weight (kg)[d] Mean ±SD	 56.55±9.62	 56.05±9.96	 0.822(NS)

a,d-student t-test used,b,c-Chi-square test used

Figure 2: Comparison of Mean SBP & DBP at different time intervals between both the groups from baseline using student t-test

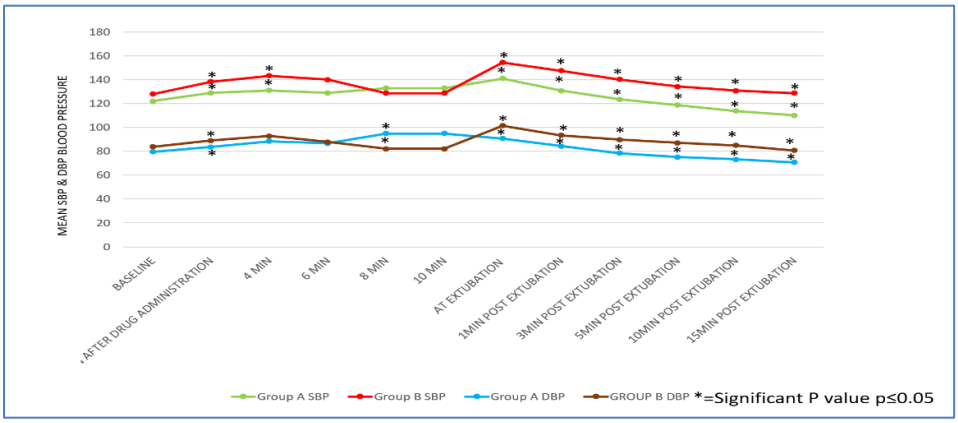


Figure 3: Comparison of Mean Arterial Pressure (mmHg) at different time intervals between both the groups from baseline using student t-test

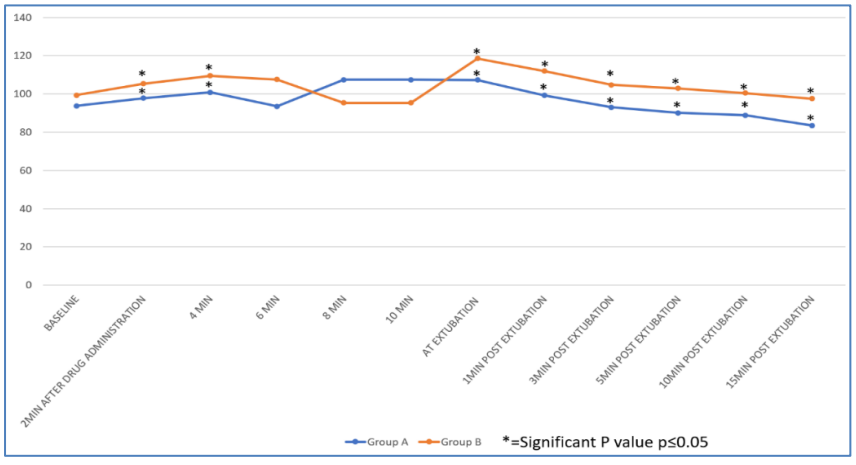
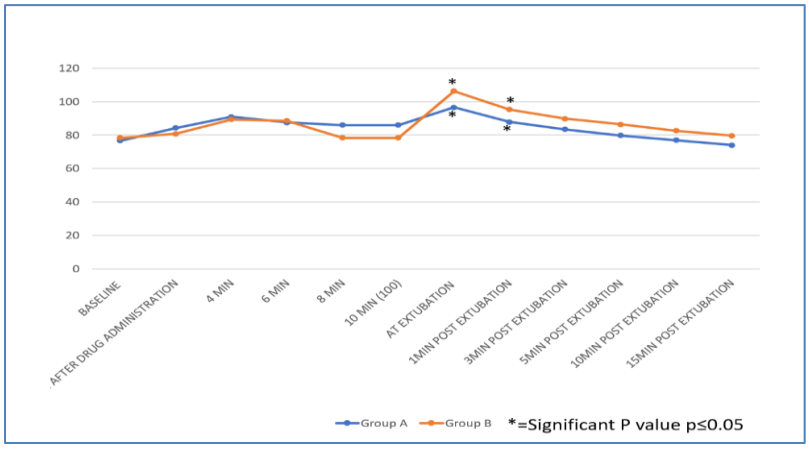


Figure 4: Comparison of Mean Heart Rate (bpm) at different time intervals between both the groups from baseline using student t-test



Figures 2, 3 and 4 depict the comparison and change in mean SBP,DBP, MAP and HR. *P-value ≤ 0.05 was considered as statistically significant.

Baseline haemodynamic parameters (HR,SBP,DBP,MAP) were comparable in both groups withstatistically nonsignificant differences(p-value>0.05).The mean of SBP,DBP and MAP was significantly higher in Group B as compared to Group A after 2min of drug administration. At the time of 4 min after drug administration difference in mean SBP and MAP was statistically significantandhigher in group B than group A, whereas at 8 minafter drug administrationmean DBP was statistically significantly lower in group B than group A.On intergroup comparison between the groups, it was observed that changes in SBP, DBP and MAP were statistically significant and higherin Group B as compared to Group A (P-value< 0.05) at the time of extubation and post-extubation 1min, 3min, 5min, 10min and 15min.Intergroup comparisonof mean HR showed a significant rise in Group B than Group A at the time of extubation and 1min post-extubation thereafter the difference between the groups was statistically nonsignificant till 15 min of post-extubation.

Figure 5: Comparison of change in HR, SBP, DBP at extubation (E) and 1 minute after extubation(E1) from the baseline in both the groups

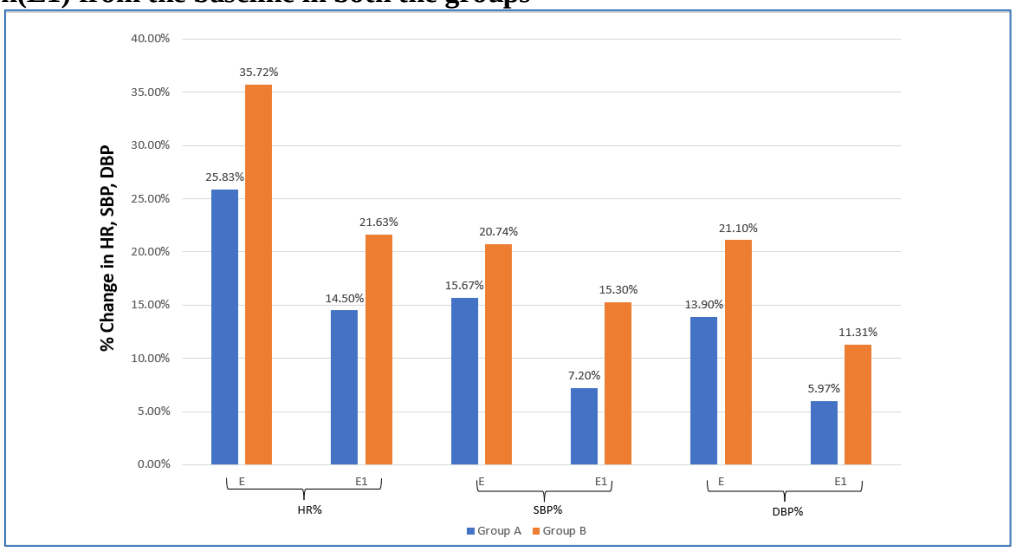


Figure (5) depicts haemodynamic parameters (HR,SBP,DBP) changes and comparisons from the baselineat the time of extubation (E) and 1min after extubation (E_1).Patients in both the study group showed a statistically significant increase in mean HR,SBP and DBP (group A< B) from baseline values (p value< 0.05). The difference in the quality of extubation grading was statistically significant (p-value 0.003), in group A none of the patients had coughing (grade 0; 100%) whereas 29 patients (74.35%) were found to be grade 0 and 10 patients (25.64%)to grade 1 in Group B. Sedation scoresweresignificantly (p-value 0.001) higherin group A (Grade I, grade II; 26.32%,73.68%) as compared to group B (Grade I, grade II; 79.49%, 20.51%). There was no statistically significant difference in extubation time in min (Group A- 4.49±2.10, Group B-4.89±2.12 and emergence time (Group A 6.82±2.96,Group B 7.61±3.20) between the groups. No statistically significant difference in terms of side effects or postoperative complications (breath-holding, laryngospasm, bronchospasm, desaturation episodes, hypotension, bradycardia higher) were found in the study groups. Only two patients had bradycardia in Group A postoperatively.

Discussion

Haemodynamicchanges duringextubationare multifactorial and may be attributed to the increased level of catecholamines,[9] airway irritation due to suction, intense pain from surgical wounds and emergence.[10] These responses are transient, variable and unpredictable and are more marked in hypertensive patients than in normotensive individuals. In neurosurgery patients,these haemodynamic responses may be catastrophic since the sudden increase in cerebral blood flow due to disturbed autoregulation can increase intracranial pressure and decrease cerebral perfusion pressure which may lead to herniation of the brain and cerebral ischemia. Leech et alobserved a rise of up to 55mm of Hg in intracranial pressure during the removal of endotracheal tube.[11]

Various attempts have been made to counteract the stress response by the use of drugs such as narcoticanalgesics, increasing depth of anaesthesia by inhalational agents,local anaesthetics, adrenoreceptor blockers and vasodilator agents.[12] When extubating neurosurgical patients, it is best to avoid using medications that relax the vascular smooth muscle since the resulting cerebral vasodilatation may raise cerebral blood volume and consequently intracranial pressure. Dexmedetomidine is a highly specific and selective α_2-adrenergic agonist that has sedative, anxiolytic and analgesic effects without significant respiratory depression.[13-16] It also has a sympatholytic effect through decreases in the concentration of norepinephrine.This in turn decreases blood pressure and heart rate.[17-19] Lignocaine a sodium channel blocker attenuates the haemodynamicsresponse and airway reflex to tracheal extubation by inhibiting sodium channels in the neuronal cell membrane. It also has analgesic, antiarrhythmic,direct cardiac depressant, and peripheral vasodilator properties.[20]

We designed this study to compare the attenuating effects of single-dose dexmedetomidine and lignocaine on haemodynamic and airway responses during extubation in patients undergoing interventional neuroradiological procedures. Demographic data (age,gender, weight, height) between the study groups were comparable and the difference observed was statistically non-significant in both groups.Haemodynamic variables (HR, SBP, DBP, and MAP) were significantly higher in group B (lignocaine) as compared to group A (dexmedetomidine) at different time intervals at the time of extubation and after thatup to 15 min. Our study demonstrates that dexmedetomidine(0.5µg/kg) given at the end of the procedure provided significant attenuation of haemodynamic response during extubation as compared to lignocaine (1.5mg/kg).

Our results are in accordance with Kothari D et al, whocompared the dexmedetomidine versus lignocaine for attenuation of circulatory and airway reflexes in patients undergoing craniotomies for intracerebral space-occupying lesion.[8] They observed that there was a lesser rise in haemodynamic parameters during extubation and post-extubation in the dexmedetomidine group as compared to the lignocaine group.

Kothari D et al[8] and Muzzi et al[21]concluded that a possible cause of the rise of haemodynamic parameters at the time of extubation and immediate post-extubation could be the light plane of anaesthaesiafollowing discontinuation of volatile anaesthetic agents before extubation. Turan et al[22] also found that

dexmedetomidine administered 5 min before the end of surgery provided stable haemodynamics, and comfortable recovery,our results coincidedwith their study. Other researchers also confirmed that a single dose of dexmedetomidine (0.5 mcg/kg) facilitated extubation with stable hemodynamics and easy recovery in patients after intracranial and intraocular interventions.[22-24]

Antony D et al assessed the effectiveness of two different doses of dexmedetomidine 0.5µg/kg and 1µ/kggivenbefore completion of surgery to attenuate the cardiovascular responses to tracheal extubation and observed that0.5µg/kg of dexmedetomidine wasas effective as 1µ/kg and also providedlower sedation scoresand early extubationwithout respiratory depression.[25] The dose-dependent reduction of HR with dexmedetomidine is primarily mediated by the decrease in sympathetic tone, partly by baroreceptor reflex and enhanced vagal activity.[26-28]

In contrast to our study, Luthra A et al observed a significant reduction in HR and MAP atextubation and post-extubation in both the group's dexmedetomidine (0.2µg /kg/h and 0.4µg/kg/h).[7] In our study,we observed a rise in all haemodynamic parameters at extubation and 1min post-extubation in both dexmedetomidine and lignocaine groups but less in the dexmedetomidine group.This could be due to the difference in the dosage, in their study all patients in both the groups received a loading dose of dexmedetomidine (0.5µg/kg) over 10min followed by an infusion of dexmedetomidine (0.2µg /kg/h or 0.4µg/kg/h) and we used single bolus dose in our study.

In our study, in dexmedetomidine group none of the patients had cough,whereas in the lignocaine group 25% had Grade I cough during extubation. Our results coincide with the studies of Kothari D et al,[8] Luthra A et al,[7] and Hu Set al.[29] The better quality of extubation with dexmedetomidine than with lignocaine may be due to the sedative action of dexmedetomidine and also because it relaxes the bronchial muscles and prevents airway irritation. It may be beneficial as it decreases postoperative hoarseness due to the tracheal tube. We observed that sedation scores were significantly higher in the dexmedetomidine group,this could be due to its action on α adrenoreceptor, reduced sympathetic activity and level of arousal,similar results were also found by Kothari D et al.[8]

The study of emergence time is of utmost importance as faster recovery is required to facilitate early neurological assessment. There was no statistically significant difference in emergence and extubation time between both the groups which is similar to Luthra A et al.[7] None of the patients had breath-holding, laryngospasm, bronchospasm, or episodes of desaturation.In a systematic review, Dexmedetomidine 0.4 to 0.5 ug/kg was associated with smooth extubation, minimal coughing, no laryngospasm/ bronchospasm, and stable hemodynamics, without causing respiratory depression, PONV, and desaturation.[30]

Limitations

This study was single-centre and the sample size was smaller so the conclusion still required to be supported by large sample size and multi-centre study.

Conclusion

Single bolus of intravenous Dexmedetomidine (0.5µg/kg)administered 10 minbefore tracheal extubation effectively attenuates the haemodynamic response to tracheal extubation as compared to Lignocaine.Dexmedetomidine provideda better quality of extubation and higher sedation scorewithout causing hypotension, bradycardia and respiratory depression.

Conflict of interest: Nil

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