Efficacy of fentanyl, dexmedetomidine or lidocaine in attenuating the hemodynamic response to rigid bronchoscopy

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Abstract

Bronchoscopy entails significant manipulation of the upper and lower respiratory tracts with marked hemodynamic response and therefore represents a potentially greater hazard to safe anesthesia.There have been many attempts to attenuate these adverse effects. Dexmedetomidine is highly selective, short-acting central alpha 2 agonist. It has increasingly gained popularity among anesthesiologists as adjuvant to general and regional anesthesia techniques. This study was conducted to compare the efficacy of administratingfentanyl, dexmedetomidine or lidocaine on control of hemodynamic changes to rigid bronchoscopy in pediatric patients. Ninety ASA I-II children aged 2-12 year were randomly assigned to 3 groups: fentanyl (F), dexmedetomidine (D) and lidocaine (Z). HR, SAP, MAP, DAP and SPO2 were measured and recorded. Results revealed that patients in the D group showed minimal changes in hemodynamic parameters in response to the procedure of rigid bronchoscopy. We concluded that dexmedetomidine can be used safely and effectively to attenuate the hemodynamic responses to rigid bronchoscopy in pediatric patients.

Introduction

The hemodynamic effects of laryngoscopy and intubation have been shown to be dueto a sympatho-adrenal response to stimulation of the upper respiratory tract.Laryngoscopy produces a marked rise in heart rate and in arterial blood pressure. Bronchoscopy entails more manipulation of the upper and lower respiratory tracts, takes a significantly longer timeand would be expected to produce a longer and possibly more severe cardiovascular response.(1)(2)(3)These hemodynamic responses are of short duration and are usually well tolerated. However, unwanted effects may occur as dysrhythmias and a rise in myocardial oxygen consumption. Myocardial ischemia may result and may be especially worrying in those patients with pre-existing hypertension and ischemic heart disease, and in the elderly with accompanying lung disease.(4)(5)(6) There have been many attempts to attenuate these adverse effects. They include topical anesthesia, systemic lidocaine, Alpha and beta blockers, nitroprusside, hydralazine, midazolam, deeper inhalational techniques and different doses of fentanyl but many of these drugs have adverse and long lasting effects, and the use of some of these agents may require invasive monitoring, which is not always appropriate and some of these agents shows variable response(7)(8)(9,10)Fentanyl is a short acting synthetic opioid agonist 75-125 times more potent than morphine. It has a rapid onset but has a distinct time lag between the peak plasma fentanyl concentration and peak slowing on the EEG of around 3- 7 minutes. This reflects the lag between achievement of a drug concentration in the plasma and theclinical effect. (11)Dexmedetomidine is a relatively new, highly selective, short-acting

central alpha 2 agonist. Activation of α2-receptors leads todose dependent sedation and anxiolysis, analgesia. (12,13)Dexmedetomidine has increasingly gained popularity among anesthesiologists and intensive care physicians abroad as adjuvant to general and regional anesthetic techniquesand as a sedative. Its administration potentiates the effect of other sedative and hypnotic agents while causing minimal respiratory depression. It also reduces the sympathetic response thus minimizing changes in blood pressure and heart rate during critical moments such as laryngoscopy and intubation.(14)(15) Intravenous (IV) lidocaine which is an aminoamide local anesthetic has been popular for its role in attenuating stress response to endotracheal intubation probably because of its theoretical advantages of suppressing cough reflex (16,17), preventing increases in intracranial pressure (18), attenuating circulatory responses (19), and its antiarrhythmic properties.(20) This study was conducted to compare the efficacy of systemic administration of either Fentanyl, Dexmedetomidine or lidocaine on control of hemodynamic responses to rigid bronchoscopy in pediatric patients.

Patients and methods

The study was conducted after approval of the Ethical committee of Sohag university hospital and obtaining informed written consent from the parents of the patients. Ninety ASA I-II children aged 2-12 year undergoing elective rigid bronchoscopy for removal of suspected airway foreign body were enrolled in this study. Patients excluded from the study were children with congenital disease, cerebral disease, cardiovascular disease, hepatic disease, renal disease, muscular disease, predicted difficulty in laryngoscopy and intubation, those requiring prompt interventions for a life-threatening situation (acutely compromised airway with SpO2 values below 70%) and patients scheduled for additional interventions or surgery subsequent to the bronchoscopy.The fasting time before anesthesia induction was at leastsix hours for solid foods and two hours for clear liquids. On arrival in the operating theatre, patients were randomly (using sealed envelopes) assigned to 3 groups fentanyl (F),dexmedetomidine (D) and lidocaine (Z), vascular access was obtained. Anesthesiamonitor was used for monitoring ECG, heart rate (HR), peripheral oxygen saturation (SpO2), systolic (SAP), diastolic (DAP) and mean (MAP) arterial pressures at 5-minute interval.After the measurement of baseline HR, MAP, and SpO2, all patientsreceived atropine 0.01 mg/kg and dexamethasone (0.1 mg/kg) IV to decrease secretions and prevent tracheal and laryngeal edema.Before induction, all children were preoxygenated and a 10 mg/kg crystalloid bolus was given. Group F (n = 30) received 2 mcg/kg fentanyl citrate, group D (n = 30) received 1 mcg/Kgdexmedetomidine while group Z (n = 30) received 1.5 mg/kg lidocaine 2% and allthese drugs were diluted with normal saline to make 20 ml volume and administeredslowly IV over 5 minutes. Induction of anesthesia was conducted using 2 mg/kg propofol and 1.5 mg/kg succinylcholine administered intravenously. The bronchoscope was inserted 30 seconds after induction and the Patients were manually ventilated with a ‘T’ piece connected to the side arm of the rigid bronchoscope. The fresh gas flow was adjusted to 10 l/min and in case of major air leakage, an oxygen flush valve was used for adequate filling of the reservoir bag and the airway pressure limit was adjusted to `20-30 cmH_2O without desaturation of SpO_2

below 90%. All patients received 2% sevoflurane in 100% oxygen for maintenance of anesthesia. HR, SAP, MAP, DAP and SPO2 were measured and recorded before induction (t0), after induction (t1) before bronchoscopy (t2) immediately after insertion of the bronchoscope (t3) 5 minute after bronchoscopy (t4) and after extraction of the bronchoscope (t5) and 5 minutes after discontinuation of anesthesia (t6). At the end of the procedure endotracheal intubation was performed with manually controlled ventilation and anesthesia was discontinued and tracheal and oral secretions were suctioned as needed, and the patients were turned to the lateral decubitus position for recovery. When patients begin to demonstrate emergence from anesthesia by displaying a regular respiratory pattern, facial grimacing, or purposeful movement the patient was extubated. As regard to statistical analysis**;** data are presented as mean ± SD or number (%), SPSS version 16 was used for data analysis, analysis of variants (ANOVA) was utilized for comparison of continuous data between the study groups. Chi squared test was used for comparison of categorical data. Repeated measures were compared with repeated measured ANOVA. P value less than 0.05 was considered significant.

Results

Demographic data of the patients in the groups were comparable for age, weight, Hight and sex ratio with no significant statistical difference as shown in table (1)

Variable	Lidocaine (*n* = 30)	fentanyl (*n* = 30)	dexmedetomidine (*n* = 30)	P VALUE
Age (years)	6.83±3.41	6.80±3.18	7.10±3.08	0.925
Sex M	15 (50%)	16 (53.3%)	15 (50%)	0.96
Sex F	15 (50%)	14 (46.7%)	15 (50%)	
Weight (kg)	24.41±10.28	23.60±9.25	24.10±8.75	0.945
Hight (cm)	115.80±21.27	117.15±19.20	119.46±19.20	0.772

Table (1): demographic data

Patients in dexmedetomidine group showed significantly lower heart rate values (p value <0.001) at time of induction, before bronchoscope insertion, at time of bronchoscopy and five minutes after introduction of the bronchoscope, at time of bronchoscope removal and after cessation of anesthesia as shown in table (2).

	Z group	F group	D group	P value
Baseline	109±14.1	112±15.7	115±10.4	**0.23**
induction	101±8.3	103.75±9.9	98.4±9.9	**0.001***
before	129.5±7.8	108.25±9.4	100.2±8.2	**<0.001***
insertion	138.25±8.4	111.25±10.0	103.1±9.6	**<0.001***
5 min	144.5±13.5	122.25±15.1	105.4±8.6	**<0.001***
removing	140±13.5	120.75±15.1	104.7±11	**<0.001***
post	136.25±12.5	129±14.1	111.2±3.5	**<0.001***

Table (2): variation in heart rate (beat/min)

Changes in the systolic blood pressure were significantly lower (p value <0.001) in the dexmedetomidine group after induction of anesthesia, before bronchoscope insertion, at time of bronchoscopy and five minutes after introduction of the bronchoscope and after cessation of anesthesia but not significantly different when measured after removal of the bronchoscope as shown in table no (3).

	Z group	F group	D group	P value
Baseline	98.4±9.0	100±5.8	101.7±6.4	**0.21**
induction	92.3±9.1	95±5.9	90.1±6.5	**0.03***
before	113.7±8.6	109±5.4	90.5±6.0	**<0.001***
insertion	116.7±9.2	101.5±6.0	92.2±6.6	**<0.001***
5 min	116.7±14.3	115±11.1	103±5.7	**<0.001***
removing	115±14.3	106±11.1	104.3±6.7	**0.004**
post	113.8±13.3	105.6±10.1	96.1±7.1	**<0.001***

Table (3): variation in systolic blood pressure (mmHg)

We found that changes in the mean blood pressure were significantly lower (p value <0.001) in the dexmedetomidine group after induction of anesthesia, before bronchoscope insertion, at time of bronchoscopy and five minutes after introduction of the bronchoscope, after removal of the bronchoscope and after cessation of anesthesia as shown in table no (4).

	Z group	F group	D group	P value
Baseline	71.9±9.0	73.5±7.8	74.6±6.4	**0.41**
induction	69.1±9.1	69.3±7.9	63.4±6.5	**0.005***
before	83.4±8.6	80.3±7.4	68.1±6.0	**<0.001***
insertion	88.9±9.2	82.5±8.0	72.9±6.6	**<0.001***
5 min	86.7±9.0	81.7±7.8	76.2±6.4	**<0.001***
removing	82.8±9.1	83.17.9±	77.2±6.5	**0.005***
post	83.9±8.6	73.6±7.4	72.8±6.0	**<0.001***

Table (4): changes in mean blood pressure (mmHg)

Variations in the diastolic blood pressure measured after induction of anesthesia, before bronchoscope insertion, at time of bronchoscopy and five minutes after introduction of the bronchoscope, after removal of the bronchoscope and after cessation of anesthesiawere significantly lower (p value <0.001) in the dexmedetomidine group as shown in table no (5).

	Z group	F group	D group	P value
Baseline	62.7±5.58	60.2±4.38	61.0±4.98	**0.26**
induction	57.5±5.75	56.5±4.55	50.1±3.15	**<0.001***
before	68.3±5.24	66.0±3.04	56.9±2.64	**<0.001***
insertion	75.0±5.82	73.0±4.62	63.2±3.22	**<0.001***
5 min	71.7±5.58	65.0±5.38	62.8±2.98	**<0.001***
removing	66.7±5.75	71.7±4.55	63.6±3.15	**<0.001***
post	68.3±5.24	61.0±4.04	61.1±2.64	**<0.001***

Table (5): changes in diastolic blood pressure (mmHg)

DISCUSSION

Regarding hemodynamic changes associated with the use of rigid bronchoscopy, our study revealed that the use of dexmedetomidine in a dose of 1 µ/kg as an adjuvant to general anesthesia was associated with less increase in heart rate, systolic, diastolic and mean blood pressures than the use of either fentanyl or lidocaine.**Sagar G et al, 2014**compared the use of dexmedetomidine and fentanyl in attenuating the pressor response during laryngoscopy and intubation in 100 adult patients and found less rise in HR, SBP , DBP and MBP in the dexmedetomidine group however he used dexmedetomidine in dose of .6 µ/kg(25). **Nermin G et al, 2013** compared the effect of dexmedetomidine versus fentanyl on preventing the hemodynamic response to intubation in 90 adult patients and found that heart rate was lower 5 and

10 min after intubation in dexmedetomidine Group.(26). **Mohamed H et al, 2015** compared the use of dexmedetomidine versus fentanyl in anesthesia of cochlear implantation in 52 pediatric patients where dexmedetomidine was given as a bolus dose of 0.4 µg/kg slowly infused over 10 min, then continuous infusion by a rate of 0.4 µg/kg/h until the end of surgery and found that dexmedetomidine group showed a decreased heart rate and mean arterial pressure compared to the baseline than fentanyl group. (27)**Suparto et al, 2010** conducted a randomized controlled trial on the effectiveness of dexmedetomidine versus fentanyl in attenuating the sympathetic response to direct laryngoscopy and endotracheal intubation in 56 patients which concluded that dexmedetomidine at 1 mcg/Kg and fentanyl at 1 mcg/Kg both produced lowering of blood pressures and cardiac rates, with significant decrease in mean heart rates and less increase in blood pressures with dexmedetomidine.**Siddareddigari V et al, 2014**compared the use of either dexmedetomidine, esmolol or placebo to attenuate the pressor response to laryngoscopy and intubation in 90 adult patients and found That the mean arterial pressure was significantly increased in patients receiving esmolol after laryngoscopy and intubation compared with those receiving dexmedetomidine.(28)**Saya R et al, 2015** compared the use of intravenous lignocaine versus intravenous dexmedetomidine for attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation in 100 adult patients and found that maximum increase in heart rate and mean arterial pressure was less in dexmedetomidine than in lignocaine group.(29)**Sreejith H et al, 2016** studied the efficacy of IV dexmedetomidine versus IV lidocaine in attenuation of stress response during intubation for laparoscopic procedures in 70 adult patients and the study revealed that the dexmedetomidine group showed significantly less heart rate, systolic & diastolic BP rise in response to intubation compared to lidocaine group.(30)**AshrafMet al, 2015**compared the use of eitherdexmedetomidine (0.1µmg/kg),lidocaine (1mg/kg) or a combination of both(0.1µmg/kg + 1mg/kg) in attenuation of cardiovascular and catecholamine responses to tracheal extubation and anesthesia emergence in 60 adult hypertensive patients and he found that heart rate, mean arterial pressure, and rate–pressure product following tracheal extubation were lower in patients receiving the dexmedetomidine–lidocaine combination than in those receiving dexmedetomidine or lidocaine as a sole drug.(31)**Ahmed A H et al,2018** studied the use of dexmedetomidine versus magnesium sulphate or lidocaine for blunting stress response to direct laryngoscopy and endotracheal intubation in 56 patients scheduled for abdominal surgery and observed that both dexmedetomidine and magnesium sulphate attenuated the rise in the mean arterial blood pressure significantly, but lidocaine failed to attenuate it. also dexmedetomidine only decreased the changes in the mean heart rate significantly.(32)**Gurulingappa et al, 2012** compared between IV bolus fentanyl (4 mcg/kg), lignocaine and placebo (normal saline) for attenuating cardiovascular responses to direct laryngoscopy and intubation in 75 adult patients and found that after intubation the incidence of tachycardia (HR>100/ min) was significantly greater in placebo and lignocaine groupthan in fentanyl group and the rise in SBP and DBP were also

statistically significant in placebo and lignocaine group than in fentanyl group.(33)

Conclusion

dexmedetomidine can be used safely and effectively to attenuate the hemodynamic responses to rigid bronchoscopy in pediatric patients.

References

1. Tomori Z, Widdicombe JG. Muscular, bronchomotor and cardiovascular reflexes elicited by mechanical stimulation of the respiratory tract. J Physiol. 1969 Jan;200(1):25–49.
2. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth. 1970 Jul;42(7):618–24.
3. KING BD, HARRIS LCJ, GREIFENSTEIN FE, ELDER JDJ, DRIPPS RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology. 1951 Sep;12(5):556–66.
4. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anesthesiology. 1977 Dec;47(6):524–5.
5. JENKINS AV. Electrocardiographic findings during bronchoscopy. Anaesthesia [Internet]. 1966 Oct 1;21(4):449–56. Available from: https://doi.org/10.1111/j.1365-2044.1966.tb02649.x
6. Hassan G, Khan G, Yaseen M, Masood T, Qureshi W. Cardiac arrhythmias during fiberoptic bronchoscopy and relation with oxygen saturation. Lung India [Internet]. 2005 Apr 1;22(2):54–9. Available from: http://www.lungindia.com/article.asp?issn=0970-2113
7. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with sodium nitroprusside. Anesth Analg. 1979;58(2):116–9.
8. Davies MJ, Cronin KD, Cowie RW. The prevention of hypertension at intubation. A controlled study of intravenous hydrallazine on patients undergoing intracranial surgery. Anaesthesia. 1981 Feb;36(2):147–51.
9. Hosalli V, Es A, Hulkund SY, Joshi C. "Comparative efficacy of different doses of fentanyl on cardiovascular responses to laryngoscopy and tracheal intubation." J Clin Diagn Res [Internet]. 2014/09/20. 2014 Sep;8(9):GC01-GC3. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25386450
10. Boralessa H, Senior DF, Whitwam JG. Cardiovascular response to intubation. A comparative study of thiopentone and midazolam. Anaesthesia. 1983 Jul;38(7):623–7.
11. Hassani V, Movassaghi G, Goodarzi V, Safari S. Comparison of Fentanyl and Fentanyl Plus Lidocaine on Attenuation of Hemodynamic Responses to Tracheal Intubation in Controlled Hypertensive Patients Undergoing General Anesthesia. Anesthesiol Pain Med [Internet]. 2013 Jan 1;2(3):115–8. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3821130/
12. Shukry M, Miller JA. Update on dexmedetomidine: use in nonintubated patients requiring sedation for surgical procedures. Ther Clin Risk Manag. 2010 Apr;6:111–21.
13. Ryu JH, Lee SW, Lee JH, Lee EH, Do SH, Kim CS. Randomized double-blind study of remifentanil and dexmedetomidine for flexible bronchoscopy. Br J Anaesth. 2012 Mar;108(3):503–11.
14. Lee JS, Park SJ, Min KT. Dexmedetomidine for rigid bronchoscopy in an infant with tracheal web after ventricular septal defect patch repair. Yonsei Med J. 2014;55(2):539–41.
15. Mason KP, Lerman J. Review article: Dexmedetomidine in children: current knowledge and future applications. Anesth Analg. 2011 Nov;113(5):1129–42.
16. STEINHAUS JE, GASKIN L. A study of intravenous lidocaine as a suppressant of cough reflex.

Anesthesiology. 1963;24:285–90.
17. POULTON AND ,THOMAS J. MD, JAMES M.D. ,FRANCIS M. III. Cough Suppression by Lidocaine. Anesthesiology [Internet]. 1979 May 1;50(5):470–2. Available from: http://dx.doi.org/
18. Donegan MF, Bedford RF. Intravenously administered lidocaine prevents intracranial hypertension during endotracheal suctioning. Anesthesiology. 1980 Jun;52(6):516–8.
19. Hamill JF, Bedford RF, Weaver DC, Colohan AR. Lidocaine before endotracheal intubation: intravenous or laryngotracheal? Anesthesiology. 1981 Nov;55(5):578–81.
20. Collinsworth KA, Kalman SM, Harrison DC. The clinical pharmacology of lidocaine as an antiarrhythymic drug. Circulation. 1974 Dec;50(6):1217–30.
21. Pinzoni F, Boniotti C, Molinaro SM, Baraldi A, Berlucchi M. Inhaled foreign bodies in pediatric patients: review of personal experience. Int J Pediatr Otorhinolaryngol. 2007 Dec;71(12):1897–903.
22. Soodan A, Pawar D, Subramanium R. Anesthesia for removal of inhaled foreign bodies in children. Pediatr Anesth [Internet]. 2004 Nov [cited 2019 Jan 19];14(11):947–52. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15500496
23. Matot I, Sichel JY, Yofe V, Gozal Y. The effect of clonidine premedication on hemodynamic responses to microlaryngoscopy and rigid bronchoscopy. Anesth Analg. 2000;91(4):828–33.
24. Abouzgheib W, Littman J, Pratter M, Bartter T. Efficacy and Safety of Dexmedetomidine During Bronchoscopy in Patients With Moderate to Severe COPD or Emphysema. J Bronchol [Internet]. 2007 Oct [cited 2019 Jan 19];14(4):233–6. Available from: https://insights.ovid.com/crossref?an=00128594-200710000-00004
25. Gandhi S, Radhakrishnan K, Balakrishnan M. Comparison of Dexmedetomidine with Fentanyl in Attenuation of Pressor Response during Laryngoscopy and Intubation. IOSR J Pharm [Internet]. 2014;4(2):2250–3013. Available from: https://pdfs.semanticscholar.org/134b/63ffad9355d57e79fc73749abab2d6a52f48.pdf
26. Gogus N, Akan B, Serger N, Baydar M. The comparison of the effects of dexmedetomidine, fentanyl and esmolol on prevention of hemodynamic response to intubation. Brazilian J Anesthesiol (English Ed [Internet]. 2014;64(5):314–9. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0104001413002303
27. El Saied MH, Mohamed NN, Mohamed HM, Amin MI. Dexmedetomidine versus fentanyl in anesthesia of cochlear implantation in pediatric patients. Egypt J Anaesth [Internet]. 2016;32(1):55–9. Available from: http://dx.doi.org/10.1016/j.egja.2015.09.016
28. Siddareddigari Velayudha Reddy, Donthu Balaji shaik NA. Dexmedetomidine versus esmolol to attenuate the hemodynamic response to laryngoscopy and tracheal intubation: A randomized double blind clinical study. Int J Appl Basic Med Res. 2014;105–12.
29. Prasad S, Matam U, Ojili G. Comparison of intravenous lignocaine and intravenous dexmedetomidine for attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation. J Dr NTR Univ Heal Sci [Internet]. 2015;4(2):86. Available from: http://www.jdrntruhs.org/text.asp?2015/4/2/86/158579
30. Sreejith Hariharan BM. and PP. Efficacy of intravenous dexmeditomidine versus lidocaine in attenuation of stress response during intubation for laproscopic procedures. Int J Biomed Res. 2016;7(3):99–107.
31. Koptan H, Moustafa A, Atalla H. Comparison of dexmedetomidine, lidocaine, and their combination in

attenuation of cardiovascular and catecholamine responses to tracheal extubation and anesthesia emergence in hypertensive patients. Res Opin Anesth Intensive Care [Internet]. 2015;1(1):1. Available from: http://www.roaic.eg.net/text.asp?2015/1/1/1/161307

32. Balata A, Abdel Latif H, Waly S, Mohamed A. Dexmedetomidine Versus Magnesium Sulphate or Lidocaine for Blunting Stress Response To Direct Laryngoscopy and Endotracheal Intubation in Abdominal Surgeries. Zagazig Univ Med J [Internet]. 2018;24(6):492–500. Available from: https://zumj.journals.ekb.eg/article_18288.html
33. Gurulingappa, Aleem MA, Awati MN, Adarsh S. Attenuation of cardiovascular responses to direct laryngoscopy and intubation-A comparative study between iv bolus fentanyl, lignocaine and placebo (NS). J Clin Diagnostic Res. 2012;6(10):1749–52.