Original Research Paper

A Randomized Comparative Study of Attenuation of The Pressure Response and Ease of Insertion to Awake Fibreoptic Intubation with Dexmedtomidine Infusion Alone Vs Fentanyl and Midazolam Infusion

Rekhi BK * Singh H** Kaur A*** Kaur J***
*Associate Professor ***Junior Resident, Department of Anesthesia, Government Medical College and Rajindra Hospital Patiala
**Associate Professor, Department of Surgery, Government Medical College and Rajindra Hospital Patiala.

Corresponding Author
Dr Balwinder Kaur Rekhi
Phone: +91 81466-03807
E-mail: balwinder.rekhi@yahoo.com

Article History
Received May 3, 2018 (Received in revised form June 24, 2018)
Accepted on June 25, 2018

Abstract: When performing awake fibreoptic intubation, anesthesiologists may find it difficult to provide enough sedation for patient to be comfortable and cooperative one at the same time avoiding airway compromise from too much sedation. The ideal sedation provides patient comfort and maintenance of spontaneous respiration smooth intubation conditions amnesia and stable hemodynamic.

Keywords: Awake, Fibreoptic, Intubation, Dexmedtomidine, Fentanyl, Midazolam.

Introduction:

The main aim of the awake intubation is to have calm and cooperative patient who can follow verbal commands while maintaining adequate oxygenation and ventilation. To blunt the pressor response various techniques have been tried eg. Lignocaine, adrenergic blockers, vasodilators, opioids like fentanyl, sufentanyl, alfentanyl, calcium channel blockers, etc.

Dexmedtomidine an Alpha-2 agonist posesses numerous properties that make it convenient drug.Grant[1] and collagenous described the use of dexmedtomidine for fibreoptic intubation in 3 patients undergoing cervical spine surgery and noticed no haemodynamic compromise or respiratory depression.Dexmedtomidine is highly selective alpha 2 receptor over alpha 1, 1620:19[(2)] and is valuable drug for use in fibreoptic intubation as it induces sedationand analgesia without respiratory depression [3][4]. In this study dexmedtomidine infusion was compared with fentanyl and midazolam infusion during elective nasotracheal intubation posted for elective surgery.

Material & Methods:

After the institutional ethics approval the study was conducted in Rajindra Hospital,Patiala in 60 patients of either sex aged 18-60 years of ASA grade I and II scheduled for the elective surgery requiring general anaesthesia. Awritten informed consent was obtained from each patient. Patients were divided into 2 groups of 30 each.

Exclusion criteria- patients refusal, drug abuser, allergic to drug involved in study, prisoner, obesity, cardiovascular and endocrine disease, bleeding disorders,history of nasal surgery or trauma, nasal polyp or on drug known to produce changes in HR ,BP like beta blockers , digitalis calcium channel blockers and contraceptives were excluded from the study.All the patients fasted for atleast 6 hrs before surgery . Multichannel physiologic monitors were applied and baseline haemodynamic variables were recorded (HR, SBP, DBP, SPO2).I/V line was established and each patient received ringer lactate infusion. All patients were premedicated with glycopyrolate with 0.2 mg 30 mins before the start of surgery. - Group I – Patients received dexmedtomidine 1 mcg /kg bolus infusion over 10 mins then an infusion of 0.1 mcg /kg /hr and titrated to 0.7 mcg/kg/hr so as to achieve Ramsay

sedation scale 3. Group II - received fentanyl 2mcg/kg as bolus followed by midazolam 0.02 - 0.1 mg /kg/hr infusion to achieve adequate level of sedation i.e. RSS 3.Prior to the start of airway manipulation nasal mucosa was sprayed with vasoconstrictor, xylometazoline 0.1% with 2 puff of 2% lignocaine. 2% lignocaine viscous gargles were done to achieve adequate topical anaesthesia. Nasopharyngeal dilator lubricated with lignocaine jelly was introduced in nostril. More patent nostril was chosen for intubation. When fibroscope reached upto vocal cords 2 ml of 2% lignocaine with some air was injected through epidural catheter inserted over the working channel of the fibroscope. Supplemental doses of lignocaine upto maximum of 9 mg /kg were administered to the airway.After successful passage of the tube through the vocal cords and identification of the carina endotracheal tube was railroded over the fibroscope and well secured, general anaesthesia induced and mechanical ventilation established.Comfort scale values were recorded by the anaesthesiologist performing the procedure during the preoxygenation at FOS and introduction of endotracheal tube . One of the independent study blinded observer assessed patients reaction to placement of the fibreoptic scope and endotracheal tube on a scale of 1 to 5

No reaction
Slight grimacing
Severe grimacing
Verbal objection
Defensive movement of head, hands and feet

The surgical procedure then proceeded as planned. Within 24 hrs of surgical procedure each patient was questioned by one of the study blinded observerto assess the experience with AFOI.

Statistical analysis – The results obtained in the study was presented in tabulated manner and analysed using IBM SPSS statistics software version 20.0. Statistical analysis was carried out using students T test. Haemodynamic variables were expressed as mean± SD. P value less than 0.05 was regarded as statistically significant. Total comfort score was computed as total of all the items of comfort scale as modified from Ambuel et al [5]. At each of the three time points preoxygention , FOS, ET.

RESULTS –Mean age, weight and M: F was statistically insignificant so both the groupswere comparable demographically.

TABLE 1: DEMOGRAPHIC DATA OF GROUP I AND GROUP II

Demographic	Group I	Group II	P value
Age (years)	43.80±12.3	40.50±12.06	0.29
Weight (kg)	62.93±6.53	63.53±4.71	0.68
Sex (F/M)	24/6	22/8	0.54

Measurement of the heart rate in 2 groups showed significant difference at RSS 3 during FOS during ET and postintubation upto 15th minute. Group I (dexmedtomidine group) showing lower mean HR compared with group II (fentanyl +midazolam).

TABLE 2: HEART RATE AT BASELINE AND RSS 3

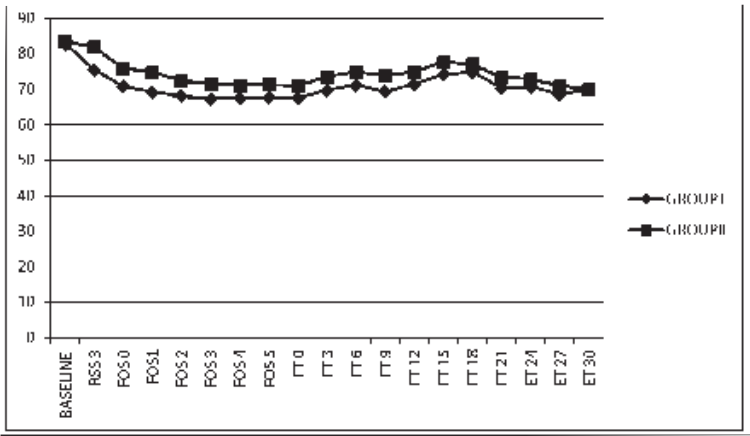
Heart rate	Group I	Group II	P value
Baseline	82.73±8.07	83.77±7.30	0.605
RSS 3	75.50±7.39	81.97±9.06	0.004

TABLE 3: HEART RATE DURING FOS

Heart rate	Group I	Group II	Pvalue
Baseline	82.73±8.07	83.77±7.30	0.605
0 min	70.90±7.10	76.13±9.03	0.016
Ist min	69.27±6.94	74.80±7.43	0.004
2nd min	68.23±5.98	72.40±6.82	0.015
3rd min	67.33±5.77	71.83±5.40	0.003
4th min	67.57±5.83	71.33±6.04	0.017
5th min	67.70±5.62	71.40±6.16	0.018

TABLE 4: HEART RATE POST INTUBATION

Heart rate	Group I	Group II	P value
Baseline	82.73±8.07	83.77±7.30	0.605
0 min	67.67±5.79	70.93±4.17	0.015
3rd min	69.73±6.36	73.57±4.73	0.010
6th min	71.27±5.41	74.87±7.19	0.033
9th min	69.43±5.43	73.97±6.96	0.007
12th min	71.47±5.36	74.80±7.26	0.048
15th min	74.20±4.95	77.77±6.77	0.023



X axis – Time in minutes (RSS – Ramsay Sedation Scale, FOS- Fibreoptic scope, E T- endotracheal intubation)
Y axis – Heart Rate

SBP, DBP showed a fall in both the groups as compared with baseline but this fall was well within the clinical range and no significant differences were noted between 2 groups.

TABLE 5: SBP AT BASELINE AND RSS 3

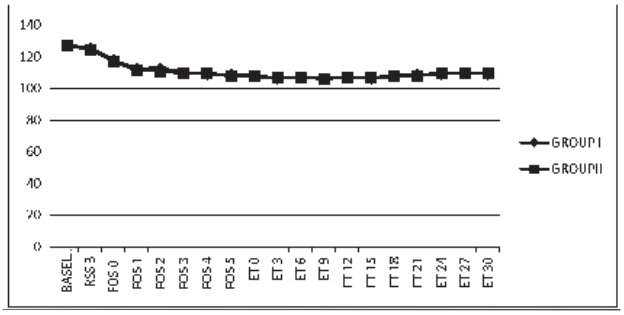
SBP	Group I	Group II	Pvalue
Baseline	127.33±2.89	127.6±4.14	0.774
RSS 3	126±3.76	124.87±3.47	0.205

TABLE 6: SBP DURING FOS

SBP	Group I	Group II	P value
baseline	127.33±2.89	127.6±4.14	0.774
0 min	118.4±3.18	117.4±5.06	0.333
Ist min	112.9±4.02	111.3±5.02	0.170
2nd min	113.2±3.38	111.1±4.77	0.058
3rd min	110.4±4.14	109.7±3.93	0.505
4th min	109.6±3.61	109.6±3.75	1.000
5th min	109.2±3.30	108.2±4.31	0.317

TABLE 7: SBP POST INTUBATION

SBP	Group I	Group II	P value
Baseline	127.33±2.89	127.6±4.14	0.774
0 min	108.6±4.46	107.8±4.67	0.501
3rd min	106.8±3.66	107.4±3.28	0.507
6th min	107.2±3.84	107.3±3.65	0.945
9th min	106.6±4.64	106.2±2.74	0.638
12th min	107.4±3.82	107.3±3.65	0.945
15th min	106.8±3.66	107.4±3.14	0.453
18th min	108.7±4.44	107.7±4.69	0.400
21st min	109.2±3.30	108.2±4.29	0.349
24th min	109.4±3.59	109.6±3.73	0.833
27th min	110.4±4.09	109.7±3.65	0.467
30th min	109.6±3.52	109.8±3.85	0.889



X axis – Time in minutes (RSS – Ramsay Sedation Scale, FOS- Fibreoptic scope, E T- endotracheal intubation)

Y axis – SBP

TABLE 8: DBP AT BASELINE AND RSS 3

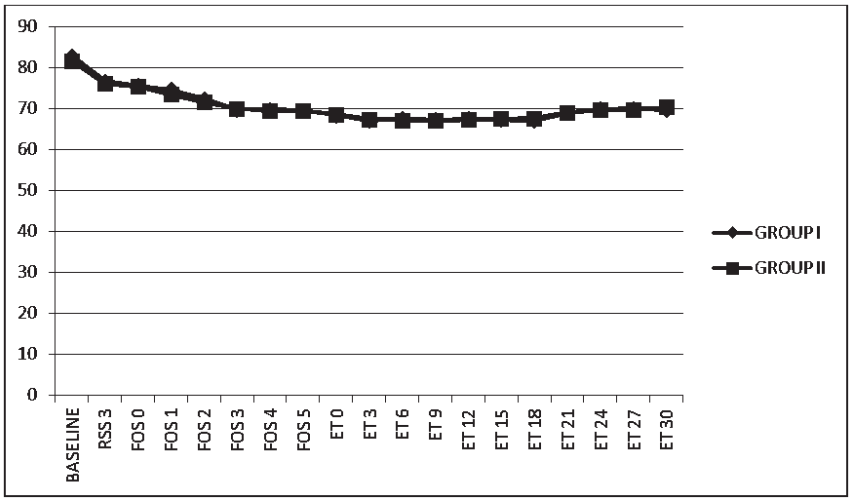
DBP	Group I	Group II	P value
Baseline	82.80±3.66	81.60±3.72	0.214
RSS 3	76.73±2.85	76.13±2.72	0.408

TABLE 9: DBP DURING FOS

DBP	Group I	Group II	P value
baseline	82.80±3.66	81.60±3.72	0.214
0 min	75.60±2.54	75.40±2.41	0.756
1st min	74.60±3.75	73.40±2.58	0.155
2nd min	72.40±3.83	71.60±2.37	0.336
3rd min	69.80±2.94	70.00±4.16	0.831
4th min	69.80±4.31	69.40±3.64	0.699
5th min	69.60±4.04	69.40±3.41	0.837

TABLE 10: DBP POST INTUBATION

DBP	Group I	Group II	GROUP III
Baseline	82.20±3.66	81.60±3.72	0.214
0 min	68.40±2.69	68.60±2.88	0.782
3rd min	67.00±3.31	67.40±2.04	0.576
6th min	67.60±2.54	67.20±1.34	0.449
9th min	67.33±1.84	67.07±1.14	0.504
12 min	67.53±2.44	67.27±1.33	0.602
15th min	67.27±1.70	67.47±1.38	o.619
18th min	67.07±3.39	67.67±2.23	0.422
21st min	68.93±2.66	69.07±2.71	0.848
24th min	69.87±4.13	69.60±3.37	0.785
27th min	70.07±4.18	69.80±3.57	0.792
30th min	69.67±3.02	70.40±4.21	0.442



X axis – Time in minutes (RSS – Ramsay Sedation Scale, FOS- Fibreoptic scope, ET- endotracheal intubation)
Y axis – DBP

SPO2 values showed statistically significant difference between two groups p value <0.05 at RSS 3. Significant differences were found in the SPO2 measurements after endotracheal intubation between 2 groups upto 18th minute.

TABLE 11: SPO2 AT BASELINE AND RSS 3

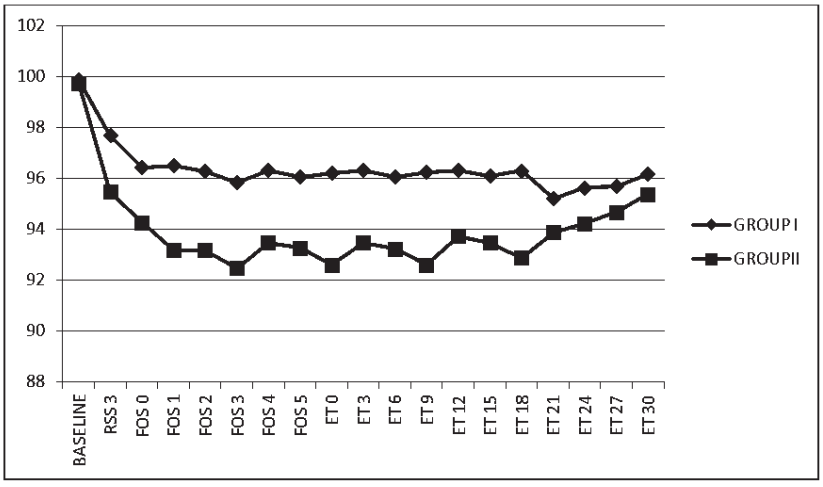
SPO2	Group I	Group II	P value
Baseline	99.87±0.34	99.73±0.58	0.286
RSS 3	97.67±2.24	95.47±2.51	0.001

TABLE 12: SPO2 DURING FOS

SPO2	Group I	Group II	P value
baseline	99.87±0.34	99.73±0.58	0.286
0 min	96.43±2.14	94.27±3.83	0.009
Ist min	96.50±1.79	93.17±2.97	<0.001
2nd min	96.27±1.70	93.17±2.79	<0.001
3rd min	95.83±2.80	92.47±2.88	<0.001
4th min	96.33±1.47	93.47±2.66	<0.001
5th min	96.07±1.79	93.27±2.53	<0.001

TABLE 13: SPO2 POST INTUBATION

SPO2	Group I	Group II	P value
baseline	99.87±0.34	99.73±0.58	0.286
1st min	96.20±2.25	92.60±2.88	<0.001
3nd min	96.33±1.47	93.47±2.66	<0.001
6th min	96.07±1.79	93.23±2.50	<0.001
9th min	96.23±2.25	92.60±2.88	<0.001
12th min	96.33±1.56	93.73±2.30	<0.001
15th min	96.10±1.66	93.47±2.30	<0.001
18th min	96.30±2.05	92.87±2.24	<0.001



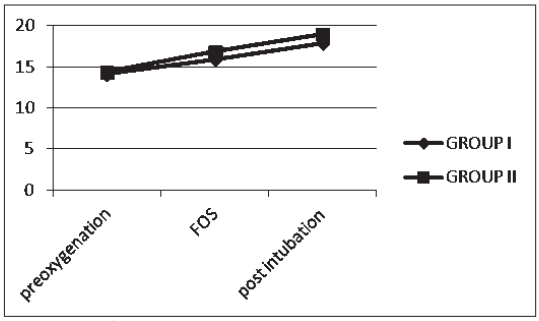
X axis – Time in minutes (RSS – Ramsay Sedation Scale, FOS- Fibreoptic scope, E T- endotracheal intubation)

Y axis – SPO_2

TOTAL COMFORT SCORE– Group I (dexmedtomidine) had lower comfort score during FOS and ET (they were more calm) as compared to group II (fentanyl and midazolam).Patients reaction to the placement of tube i.e. 5 point FOI score were higher in group II implying the better patient tolerance achieved in group I (dexmedtomidine).

TABLE 14: TOTAL COMFORT SCORE

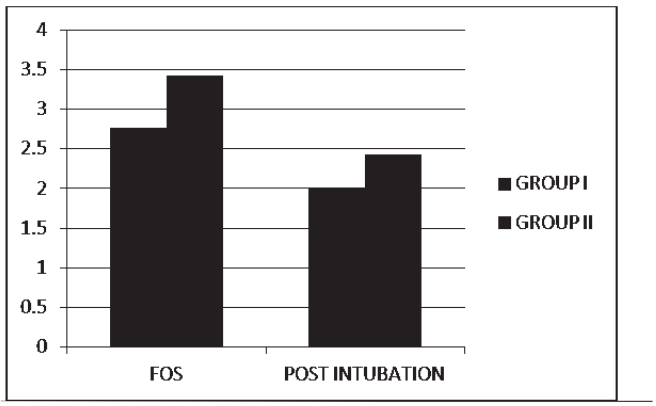
Total comfort Score	Group I	group II	pvalue
preoxygenation	14.10±1.18	14.37±0.89	0.328
FOS	15.93±1.57	16.80±1.03	0.014
Post intubation	17.87±1.50	18.97±1.75	0.011



X axis –time (FOS- Fibreoptic scope, E T- endotracheal intubation)
Y axis – total comfort score
PATIENT'S REACTION - Significant differences in the patients reaction were found during FOS and after intubation between two groups

TABLE 15: PATIENT'S REACTION TO THE PLACEMENT OF TUBE

Reaction	Group I	Group II	P value
FOS	2.77±1.00	3.43±0.81	0.007
Post intubation	2.00±0.58	2.43±0.56	0.005



X axis –time (FOS- Fibreoptic scope)
Y axis – patient's reaction
Within 24 hrs of the surgery patients judged their own AFOI experience. The group I judged their sedation more positively than group II. Group I has less pain and discomfort. Overall group I patients were more satistied with the procedure than group II (fentanyl and midazolam)

TABLE 16: QUESTIONNAIRES ASSESMENT 24 Hrs AFTER SURGERY

question	Group I	Group II	Pvalue
Q1	1.67±0.60	2.33±0.60	<0.001
Q2	1.90±0.40	2.20±0.55	0.019
Q3	1.40±0.49	1.67±0.47	0.039
Q4	1.20±0.40	1.47±0.50	0.029
Q5	1.13±0.34	1.60±0.49	0.001
Q6	1.07±0.25	2.30±0.46	0.001

Discussion:

When performing AFOI anesthesiologist may find it difficult to provide enough sedation for patient to be comfortable and cooperative while at the same time avoiding airway compromise from too much sedation. The ideal sedation provides patient comfort and maintenance of the spontaneous respiration without altering the airway function and maintaining haemodynamic stability. Many agents have been reported to achieve conscious sedation for awake intubation like midazolam, propofol, opioids, dexmedtomidine,etc. Fentanyl is a phenyl piperidine derivative of synthetic opioid which provides mild sedation analgesia alongwith haemodynamic stability but there is risk of respiratory depression, nausea , vomiting, chest wall rigidity. Benzodiazepines alone cannot substitute for inadequate analgesia with topical lignocaine and their combination with opioid provide better intubationg conditions .Dexmedtomidine is highly selective centrally acting alpha 2 agonist . It acts on the presynaptic alpha 2 receptors to provide negative feedback causing less neurotransmitter available at post synaptic alpha 1 receptor. It produces hypnosis, amnesia, analgesia, anxiolysis , sympatholysis and antisialogogue effects all of which are desirable during awake fibreoptic intubation . We compared group I – Patients received dexmedtomidine 1 mcg /kg bolus infusion over 10 mins then an infusion of 0.1 mcg /kg /hr and titrated to 0.7 mcg/kg/hr so as to achieve Ramsay sedation scale 3 with Group II - received fentanyl 2mcg/kg as bolus followed by midazolam 0.02 - 0.1 mg /kg/hr infusion to achieve adequate level of sedation i.e. RSS 3.

Heart Rate:

In our study it was observed that group I (Dexmedtomidine) completely abolished the chronotropic responsecompared with group II (fentanyl and midazolam) .There were significant differences between two groups at RSS 3 p value 0.004 during FOS and continuedupto 15 mins post intubation . These findings have been documented in other studies too[6][7][8][9][10].Various potential causes for decresed heart rate with dexmedtomidine as illucidated in literature are increased vagal tone , baroreceptor response of high vascular tone that occurs with bolus and decreased circulating levels of norepinephrine.

SBP – comparison between two groups demonstrated that there was no statiscially significant difference between mean SBP values of 2 groups upto 30 min post intubation. Similar results were observed by[13][14][15][16][17][18].

DBP -comparison between 2 groups demonstrated that there was no statistically significant difference from the time of intubation FOS upto 30 mins post intubation.

SPO2 -the mean SPO2 at RSS 3 was 96.67 +- 2.24 in dexmedtomidine group and 95.47 +- 2.5 in fentanyl +midazolam group and there was significant difference between the 2 groups. (p value <0.05). p value differences persisted upto 18 min . Thus our findings reveal that combination of fentanyl and midazolam causes more arterial desaturation than dexmedtomidine alone. Similar results were observed by[1][2][7][16][19][20][21].

Total Comfort Scope

Total comfort score when calculated and compared in total showed a significant differences between two groups during FOS and ET ($p<0.05$).thus our study shows that dexmed provided better intubating conditions as compared to group II (fentanyl and midazolam). Our study was in accordance with the studies [7][10][15][16].

Questionnaire assessment at 24 hr after surgery. Group I (dexmed) had less pain and discomfort during the procedure than group II(fentanyl and midazolam). Group I (dexmedtomidine) patients were more satisfied with the procedure than group II(fentanyl and midazolam).

Conclusion

Use of dexmedtomid at 1 mcg /kg over 10 mins with maintainenece rate 0.1 -0.7 mcg /kg/hr is safe and beneficial for patient undergoingAFOI , it appears to offer better tolerance ,preservation of the patent airway ,spontaneous ventilation while maintaining hemodynamic stability.

Conflict of Interest: None

References:

1. Grant SA, Breslin DS, Macleod DB, Gleason D, Martin G.Dexmedetomidine infusion for sedation during fiberoptic intubation: a report of three cases.J Clin Anesth. 2004 Mar;16(2):124-6.

2. Hall JE1, Uhrich TD, Barney JA, Arain SR, Ebert TJ.Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions.Anesth Analg. 2000 Mar;90(3):699-705.
3. Kamibayashi T1, Maze M.Clinical uses of alpha2 - adrenergic agonists.Anesthesiology.2000 Nov;93(5):1345-9.
4. RM,Bradshaw CJ, Spencer R,etal . Prelimimary UK experience of dexmedtomidine , a novel agent fpr post op sedation in intensive care unit.Anaesthesia 1999:54:1136-42
5. Ambuel B, Hamlett KW, Marx CM,Blumer JL. Assessing distress in pediatric intensive care. the COMFORT scale. J Pediatr Psychol. 1992;17(1):95-109
6. Jain V, Chandak A, Ghosh A, Golhar M.Comparison of dexmedetomidine and fentanyl for attenuation of the hemodynamic response to laryngoscopy and tracheal intubation.Ain- Shams J Anaesthesiol 2015;8:236-43
7. Mondal S, Ghosh S, Bhattacharya S, Choudhury B, Mallick S, Prasad A. Comparison between dexmedetomidine and fentanyl on intubation conditions during awake fiberoptic bronchoscopy: A randomized double-blind prospective study. J Anaesthesiol Clin Pharmacol 2015;31:212-6
8. Kharwar DRK, Kumar DM, Tiwary DPK, Suwalka DU, Prakash D. A Comparison Of Intravenous Dexmedetomidine V/S Inj. Fentanyl For Attenuation Of Hemodynamic Responses During Laryngoscopy And Intubation After Propofol Induction. NJIRM. 2014; 5(3): 71-75
9. Gandhi S, Goyal V, Radhakrishnan K, Balakrishnan M. Comparison of Dexmedetomidine with fentanyl in attenuation of pressor responses during laryngoscopy and intubation. IOSR Journal of Pharmacy.2014;4(2):28-38
10. Tsai CJ, Chu KS, Chen TI, Lu DV, Wang HM, Lu IC. A comparison of the effectiveness of dexmedetomidine versus propofol target-controlled infusion for sedation during fibreoptic nasotracheal intubation. Anaesthesia 2010;65:254-9
11. Bloor BC, Ward DS, Belleville JP,Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology. 1992;77(6):1134-42.
12. Talke P, Richardson CA, Scheinin M,Fisher DM. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth Analg. 1997;85(5):1136-42.
13. Gupta K, Maggo A, Jain M, Gupta PK, Rastogi B, Singhal AB. Blood glucose estimation as an indirect assessment of modulation of neuroendocrine stress response by dexmedetomidine versus fentanyl premedication during laparoscopic cholecystectomy: A clinical study. Anesthesiol Clin Pharmacol.2015;31(2):212-216
14. Cattano D1, Lam NC, Ferrario L, Seitan C, Vahdat K, Wilcox DW, Hagberg CA.Dexmedetomidine versus Remifentanil for Sedation during Awake Fiberoptic Intubation. Anesthesiol Res Pract. 2012;2012:753107
15. Patrick BS, Sergio D, Thomas D, Soleded F,Roger D. A comparative study of dexmedetomidine with midazolam and midazolam alone for sedation during elective awake fiberoptic intubation.Journal of clinical anaesthesia. 2010;22:35-40
16. Bergese SD, Khabiri B, Roberts WD, Howie MB, McSweeney TD, Gerhardt MA. Dexmedetomidine for conscious sedation in difficult awake fiberoptic intubation cases. J Clin Anesth 2007;19:141-4.
17. Stuart AG, Dara SB,David BM,David G, Gavin M. Dexmedetomidine infusion for sedation during fibreoptic intubation:a report of three cases. J Clin Anesth.2003;16(2):124-126
18. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg 2000;90:699-705.
19. Agrawal A, Jadon A, Parida SS, Chakraborty S, Sinha N,Chandra O. Comparative evaluation of Dexmedetomidine and Fentanyl – Midazolam combination as sedative adjunct to fibreoptic intubation under topical anaesthesia. American Journal of Advances in Medical Sciences.2014;2(4):29-37.
20. 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;108:503-11.
21. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. Anesthesiology 1990; 73:826-30.
22. Chu KS, Wang FY, Hsu HT, Lu IC, Wang HM, Tsai CJ. The effectiveness of dexmedetomidine infusion for sedating oral cancer patients undergoing awake fibreoptic nasal intubation. Eur J Anaesthesiol 2010;27:36-40
23. Bergese SD, Candiotti KA, Bokesch PM, Zura A, Wisemandle W,Bekker AY. A Phase IIIb, randomized, double-blind, placebo-controlled, multicenter study evaluating the safety and efficacy of dexmedetomidine for sedation during awake fiberoptic intubation. Am J Ther. 2010; 17(6):586-95.