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Comparison of Dexmedetomidine Plus Ketamine Combination with Dexmedetomidine Plus Propofol for Awake Fiberoptic Nasotracheal Intubation: A Prospective Randomised and Controlled Clinical Trial

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Abstract

Background: Awake fibre optic intubation (AFOI) is a valuable technique in securing the airway in predicted difficult intubation scenario, compromised airway, airway pathology, when neck extension is to be avoided, vertebral artery insufficiency, Arnold Chiari malformation, limited mouth opening as in temporomandibular joint disease, mandibular-maxillary fixation and severe facial burns.[1] Fiberoptic intubation is the best, easiest and most successful method for awake intubation. ***Materials and Methods:*** A prospective, comparative and randomized study was conducted on 100 patients undergoing elective surgery under general anaesthesia. Patients were randomly divided into two groups of 50 each. Group-DK and group-DP patient received IV dexmedetomidine 1µg/kg over 10 mins. Upon completion of the dexmedetomidine bolus, preoxygenation was done with 100% oxygen via face mask with Bain's circuit. Group-DK patients received ketamine 0.25 mg/kg IV and Group-DP patients received propofol 1mg/kg IV so as to achieve an adequate level of sedation i.e. Ramsay sedation scale=3. Haemodynamic parameters (heart rate, systolic and diastolic blood pressure, mean arterial pressure), SpO2, EtCO2, total comfort scale and patient's tolerance were assessed during preoxygenation, fiberscope insertion and endotracheal intubation. ***Results:*** Statistically significant difference ($p<0.05$) between two groups in terms of HR, SBP, DBP, MAP, total comfort score and patient tolerance was seen during fiberscope insertion and endotracheal intubation. ***Conclusion:*** Dexmedetomidine (1µg/kg) plus ketamine (0.25mg/kg) and dexmedetomidine (1µg/kg) plus propofol (1mg/kg) are safe and effective in patients undergoing fibre optic nasotracheal intubation offering conscious sedation. There is better tolerance and comfort while maintaining oxygen saturation without any hemodynamic alteration in dexmedetomidine (1µg/kg) plus ketamine (0.25mg/kg) group while on the other side use of dexmedetomidine (1µg/kg) and propofol(1mg/kg) during fibre optic intubation causing statistically significant decrease in heart rate, blood pressure, SpO2 and provides less tolerance and comfort.

Keywords: ***Patient's Tolerance, Ramsay Sedation Score, Haemodynamic Parameters, Total Comfort Scale.***

Introduction

Awake nasal or oral flexible fiberoptic intubation (AFOI) is the airway management technique of choice in known or anticipated difficult airway, severe cervical stenosis, Chiari malformation, unstable cervical fracture, limited mouth opening as in temporomandibular disease, mandibular-maxillary fixation, severe facial burn and vertebral artery insufficiency.[1] Tracheal intubation is the placement of a flexible plastic tube into the trachea to maintain a patent airway for ventilation. Fiberoptic intubation is the best, easiest and most successful method for awake intubation. The main aim of awake intubation is to have a calm and cooperative patient who can follow verbal commands while maintaining adequate oxygenation and ventilation.

Adequate topical anaesthesia is essential to obtund the sensory afferent stimuli of the oropharyngeal and laryngotracheal region. Establishing topical anaesthesia before intubation enable the patients to be cooperative, comfortable and have blunted airway reflexes, particularly when difficult laryngeal anatomy and/or pathology are encountered. Both optimal intubating conditions and patient comfort are necessary while preparing the patient for fiberoptic intubation. An ideal sedative is expected to provide comfort and elicit patient cooperation while maintaining haemodynamic stability and spontaneous ventilation. Drugs used for sedation during awake fiberoptic intubation include midazolam, diazepam, ketamine, propofol, sevoflurane, fentanyl, remifentanil and dexmedetomidine. etc.[2-5]

Fiberoptic intubation can be performed awake under sedation with or without topical anaesthesia or with muscle relaxant (Suxamethonium, vecuronium, rocuronium, atracurium). For sedation, drugs that may be used are fentanyl/opioids, midazolam, propofol, dexmedetomidine, remifentanil. Each drug has advantages and disadvantages. Fentanyl or other narcotics reduce the discomfort and haemodynamic changes associated with airway instrumentation.[6] In order to compare the different drugs for fiberoptic laryngoscopy which produces better intubating conditions with minimal side effects or no side effects, the present study was conducted to compare the intubating condition using fentanyl plus propofol versus nalbuphine plus propofol during fiberoptic intubation.

Materials and Methods

The present prospective, comparative and randomized study was conducted in department of Anaesthesia and intensive care, Government Medical College, Rajindra Hospital, Patiala, after obtaining the approval from ethical committee and after informed consent from all the patients. The study was conducted on 100 patients of either gender aged between 18 to 60 years of age belonging to ASA-I or II and scheduled for elective surgery under general anaesthesia.

Sample size

Was estimated based on pilot study; mean difference in heart rate in two groups was 2.11 with SD of 3.20. With this our sample size n=49 per group at a power of 90% and confidence interval of 95% with z value of 1.96. For possible dropouts, it was decided to include 50 patients per group.

$n = (Z_{\alpha/2}+Z_{\beta})^{2*}2^{*}\sigma^{2}/d^{2}$, where $Z_{\alpha/2}$ is the critical value of the normal distribution at $\alpha/2$, Z_{β} is the critical value of the normal distribution at β,σ^{2} is the population variance and d is the difference between two means.

All patients were premedicated with Inj. Glycopyrrolate (0.2mg) IM 30 min before the elective surgery. During surgery, patients were placed in the supine position. Nasal mucosa was sprayed with vasoconstrictor xylometazoline 0.1%. Nasal mucosa was sprayed with 2 puffs of 10%lignocaine. 2% lignocaine viscous gargles were done to achieve adequate topical anaesthesia. For further topical anaesthesia 2 puffs of 10% lignocaine was sprayed to tonsillar pillars and back of throat. Nasopharyngeal dilator with lignocaine jelly was introduced in each nostril. The local anaesthetic dose was not exceeding 4mg/kg.[6] Transtracheal block was given through the cricothyroid membrane for blocking the sensory input of the recurrent laryngeal nerve is the transtracheal block and cricoid cartilages.[7]

Two groups of 50 each were studied. Group-DK and group-DP patient received IV dexmedetomidine 1µg/kg over 10 mins. Upon completion of the dexmedetomidine bolus, preoxygenation was done with 100% oxygen via face mask with Bain's circuit. Group-DK patients received ketamine 0.25 mg/kg IV and Group-DP patients received propofol 1mg/kg IV so as to achieve an adequate level of sedation i.e. Ramsay sedation scale=3 (patients responded to command only). Fibre optic intubation was performed by two anaesthesiologist consultants who were experienced and trained for fibre optic intubation for four years.

Under the guidance of video, fiberscope advanced. On reaching the carina, endotracheal tube was railroaded over the fiberscope. Tracheal placement confirmed by locating murphy's eye during removing the fiberscope. Fibre optic nasotracheal intubation done in both groups of patients. During the procedure, continuous oxygen was given via nasal cannula. Duration of fibre optic intubation was different in different patients ranging from 1 to 5 minutes. Once tracheal intubation was completed and the tube was secured, general anaesthesia was administered. The parameters studied were

1. Hemodynamic parameters including HR, SBP, DBP, MAP along with $EtCO_2$ and SpO_2 were recorded preoperatively, during preoxygenation, every minute during fiberscope insertion and then every minute after introduction of endotracheal tube up to five minutes.
2. Comfort scale values that will be recorded by anaesthesiologist (performing the procedure).
3. Patient's tolerance was assessed by an independent observer on the basis of 5 point FOI score:[7] No reaction(1), Slight grimacing(2), Severe grimacing (3), Verbal objection(4), Defensive movement of head, hands or feet (5).

Comfort scale values as modified from Ambuel et al8 based on parameters such as alertness, calmness, respiratory response, crying, physical movement, muscle movement, facial tone were recorded by the anaesthesiologist during pre-oxygenation, at point of introduction of fiberscope and at the introduction of ET tube.The total comfort score for each patient was calculated by summing the scores of the 7 comfort categories at each time point.

Statistical Analysis

Descriptive statistics was done for all data and reported in terms of mean and percentages. Appropriated statistical tests of comparison were applied. Continuous variables were analyzed with Mann Whitney U test and t test. Age was analyzed using t test. Categorical variables were analyzed with the help of chi square test. Statistical significance was taken as $p<0.05$. The data was analyzed using SPSS version 22 and Microsoft Excel.

Results

1. Both the groups studied were statistically similar in age, weight, gender and other baseline hemodynamic variables such as HR, MAP, sPO_2, $eTCO_2$ as shown in Table 1

Table: 1

Parameter	DK	DP	P value	
Age (years)	39.64±13.08	40.98±12.14	P=0.597	NS
Weight (kg)	63.84±10.67	64.04±8.72	P=0.919	NS
Sex	M: 13, F:37	M: 11, F:39	P=0.640	NS
HR	85.02 ±7.42442	86.3200 ±12.39230	P= 0.526	NS
MAP (mm Hg)	99.9200±6.47394	99.1800 ± 8.69832	P= 0.630	NS

SPO2	99.4400± 0.73270	99.3200± 0.71257	P= 0.317	NS
eTCo2	36.3200±1.64441	37.4600± 8.18962	P=0.697	NS

Hemodynamic parameters: Both the groups were sedated up to Ramasay scale 3 that is patient responded to commands only.

2. The change in HR during preoxygenation in both the groups was not significant. Minimum change in HR observsed in group DK as compared to group DP. The maximum percentage fall in the mean HR was 12.7% in the DP group (Table 2). However, no episodes of bradycardia that is HR<40 per minute were noted which required atropine.

Table 2: HR

HR	Time (min)	Group DK			Group DP			P value	Sig.
		Mean	%diff.	S.D	Mean	%diff.	S.D		
Base Line		85.02		7.4244	86.32		12.392	0.526	NS
During Pre-oxygenation		77.92	8.3509	7.6019	77.28	10.473	14.892	0.787	NS
During FOS	1	77.72	8.5862	7.5351	75.88	12.095	11.533	0.347	NS
	2	79.44	6.5631	7.2059	75.48	12.558	11.116	0.037	S
	3	80.78	4.9870	7.2711	76.08	11.863	10.028	0.009	HS
	4	81.814	3.7708	7.626	76.021	11.931	8.3523	<0.001	HS
	5	84.194	0.9721	6.7991	75.351	12.707	8.9852	<0.001	HS
During ET	1	84.82	0.2352	7.2159	77.66	10.032	9.3822	<0.001	HS
	2	85.64	-0.7292	7.2668	76.92	10.89	13.369	<0.001	HS
	3	86.54	-1.7878	7.7465	79.26	8.1789	8.2234	<0.001	HS
	4	87.58	-3.0110	7.8639	79.56	7.8313	7.4838	<0.001	HS
	5	88.44	-4.0225	7.8718	80.56	6.6728	6.5502	<0.001	HS

3. Similarly, the change in MAP was not significant during preoxygenation in both groups. There was highly significant decrease in MAP during fiberscope insertion and ETT insertion in group DP (P value= <0.001) as compare to group DK. The maximum decrease in MAP in group DP was 12.6% from baseline (table 3).

Table 3: MAP

MAP	Time (min)	Group DK			Group DP			P value	Sig.
		Mean	%diff.	S.D	Mean	%diff.	S.D		
Base Line		99.92		6.4739	99.18		8.6983	0.630	NS
During Pre-oxygenation		93.58	6.3450	5.4999	91.18	8.0661	7.647	0.075	NS
During FOS	1	92.5	7.4259	5.9702	88.34	10.93	7.0728	0.002	HS
	2	94.44	5.4843	6.3605	87.32	11.958	8.2819	<0.001	HS
	3	96.02	3.9031	6.8048	86.64	12.644	8.2184	<0.001	HS
	4	97.667	2.2551	7.2706	86.979	12.302	8.3001	<0.001	HS
	5	98.387	1.5341	8.0651	86.703	12.58	7.9508	<0.001	HS
During ET	1	99.5	0.4203	7.2626	88.78	10.486	6.9084	<0.001	HS
	2	100.3	-0.3803	6.5691	89.02	10.244	6.5356	<0.001	HS
	3	101.42	-1.5012	6.5531	89.7	9.5584	6.195	<0.001	HS
	4	102.08	-2.1617	6.1705	90.58	8.6711	5.7003	<0.001	HS
	5	103.6	-3.6829	5.8624	91.62	7.6225	5.9209	<0.001	HS

4. Stasistically significant difference was found in the SpO2 measurements during fiberscope insertion and endotracheal intubation between the two groups (p<0.05). No episode of desaturation was seen in both the groups (Table 4). However, the maximum percentage fall in Spo2 observed in group DP was 9.13% from base line.

Table 4: SPo2

SPo2	Time (min)	Group DK			Group DP			P value	Sig.
		Mean	%diff.	S.D	Mean	%diff.	S.D		
Base Line		99.44		0.7329	99.32		0.7126	0.317	NS
During Pre-oxygenation		100	-0.5631	0.00000	100	-0.685	0.00000	-	-
During FOS	1	98.22	1.2268	0.6788	97.08	2.2553	2.1461	0.011	S
	2	96.94	2.5140	1.7192	95.34	4.0072	2.0265	<0.001	HS
	3	95.84	3.6202	1.1493	93.8	5.5578	1.5908	<0.001	HS
	4	95.023	4.4415	1.0348	92.319	7.0488	1.9903	<0.001	HS
	5	94.548	4.9191	1.3125	90.243	9.1389	1.3209	<0.001	HS
During ET	1	94.38	5.0884	1.3231	90.28	9.1019	1.8075	<0.001	HS
	2	95.12	4.3443	1.3037	90.74	8.6387	2.0683	<0.001	HS
	3	96.18	3.2783	1.3805	92.4	6.9674	2.665	<0.001	HS
	4	97.84	1.6090	1.1314	94.36	4.994	2.2656	<0.001	HS
	5	99.6	-0.1609	0.5714	97.04	2.2956	2.0098	<0.001	HS

5. The mean Total comfort score: There was no significant difference between the two groups (p>0.05) during preoxygenation. Duing FOS and ETT statistically significant difference was observed in mean comfort score between two groups. Patients were more comfortable in group DK as compare to group DP (Table 5).

Table 5: Mean comfort score

	DK	DP	P value
During preoxygenation	12.86±1.22	12.66±1.18	p>0.05
FOS insertion	14.00±1.90	15.06±1.13	P=0.001
ETT insertion	15.20±2.08	16.06±1.05	P=0.022

6. The mean patient tolerance: Significant differences in the patient's tolerance were found during FOS and endotracheal tube placement between the two groups (p<0.05). Better patient tolerance was observed in group DK (table 6).

Table 6: Mean patient tolerance during FOS and ET intubation

Patient Tolerance	Time (min)	Groups	Mean	S.D	P value	Significance
Patient Tolerance	FOS	Group DK	3.2800	0.72955	0.035	S
		Group DP	3.5600	0.61146		
	ET	Group DK	2.3800	0.53031	0.028	S

Discussion

Fibre optic nasotracheal intubation was done in both groups of patients. Demographic parameters were compared in group DP and DK. Vitals were recorded which included heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SpO2, EtCO2 and in addition total comfort score and patient tolerance score were also noted. Any complication or any drug used during procedure was noted. After intubation, routine general anaesthesia was administered.

In our study, distribution of patients according to age, weight and gender was similar in both groups and statistically no significant difference was seen between two groups (p>0.05)

There is better hemodynamic stability pertaining to HR, SBP, DBP, MAP while maintaining oxygen saturation in dexmedetomidine (1µg/kg) plus ketamine (0.25mg/kg) group while on the other side dexmedetomidine (1µg/kg) plus propofol(1mg/kg) group showed statistically significant decrease in HR, MAP and Spo2 but no case had bradycardia requiring atropine. The MAP remained near baseline or slightly increased in the DK group while in the DP group statistically significant decrease was noted with no clinically significant hypotention. The Spo2 values also decreased in DP group than DK group. Howsoever, no periods of apnea were seen

A case report by Scher CS et al[8] on the combined use of dexmedetomidine and low dose ketamine to provide sedation for awake fibre optic intubation in a 52 yr old male with difficult airway. It was observed that Ketamine prevented bradycardia and hypotension caused by dexmedetomidine. Sinha SK et al[9] compared the combination of dexmedetomidine plus ketamine with dexmedetomidine alone for AFOI. Group DK patients had better hemodynamic stability because of attenuation of bradycardia by ketamine. Present study also concluded that HR, MAP, sPo2 clinically remained stable in both groups and there was statistically significant decrease in HR and MAP from baseline in group DP.

Dexmedetomidine provides appropriate sedation in which the patient is calm and easily arousable from sleep to wakefulness to allow cooperation, excellent communication and task performance while being ventilated and intubated and then quickly back to sleep when not stimulated.[10] The primary site of action of alpha2 agonists is the locus ceruleous and not the cerebral cortex, unlike gamma-amino butyric acidmimetic drugs.[11] Locus ceruleous (nucleus in the pons) that is involved in physiological response to stress and anxiety is the principal site in the brain for norepinephrine synthesis. The opposing action of ketamine and dexmedetomidine on cardiac and sympathetic system probably resulted in a more stable hemodynamic response.[8] Dexmedetomidine has been reported to prevent the hemodynamic response to tracheal intubation more effectively than esmolol.[12] The use of dexmedetomidine was associated with a decrease in MAP and HR, which might result from decrease in noradrenaline release, a decrease in centrally mediated sympathetic tone and an increase in vagal activity.[13,14] Dexmedetomidine is reported to produce severe bradycardia, hypotension, hypertension and arrhythmias as side-effects. We never encountered severe bradycardia, hyotension or arrhythmias in our study.

Tsai CJ et al[15] compared the effectiveness of dexmedetomidine versus propofol target control infusion for sedation during fibre optic nasotracheal intubation. They concluded that dexmedetomidine allows better tolerance. Patients in propofol group were agitated. The results match to our study.

In group DP there was statistically significant decrease in heart rate, blood pressure, SpO2 and provides less tolerance and comfort during fibre optic intubation. The mean ramsay sedation scale in the two groups did not depict any significant difference. Mean 5 point intubation score during fiberoscope insertion and endotracheal tube placement showed significant differences in the two groups (p<0.05) as shown in the table 6. The patient tolerance was better in DK group with no incidence of agitation.

Conclusion

The use of dexmedetomidine (1µg/kg) plus ketamine (0.25mg/kg) and dexmedetomidine (1µg/kg) plus propofol (1mg/kg) were safe and effective in patients undergoing fibre optic nasotracheal intubation offering conscious sedation. There was better tolerance and comfort while maintaining oxygen saturation without any hemodynamic alteration in dexmedetomidine (1µg/kg) plus ketamine (0.25mg/kg) group while on the other side use of dexmedetomidine (1µg/kg) and propofol(1mg/kg) during fibre optic intubation causing statistically significant decrease in heart rate, blood pressure, SpO2 and provides less tolerance and comfort.

There are a few studies available on use of ketamine in AFOI till now. So further evaluation is required in this area.

References

[1] Artime C. Flexible fiberoptic intubation. In: Hagberg CA, Daily WH, eds. The difficult airway: a practical guide. Oxford University Press 2013.

[2] Lallo A, Billard V, Bourgain JL. A comparison of propofol and remifentanil target-controlled infusions to facilitate fiberoptic nasotracheal intubation. Anaesthesia and Analgesia 2009; 108(3):852-7.

[3] Stamenkovic DM, Hassid M. Dexmedetomidine for fiberoptic intubation of a patient with severe mental retardation and atlantoaxial instability. Acta Anaethesiologica Scandinavica 2006; 50(10):1314-5.

[4] Knolle E, Oehmke MJ, Gustorff B, et al. Target-controlled infusion of propofol for fibreoptic intubation. European Journal of Anaesthesiology 2003; 20(7):565-9.

[5] Machata AM, Gonano C, Holzer A, et al. Awake nasotracheal fibreoptic intubation: patient comfort, intubating condition and haemodynamic stability during conscious sedation with remifentanil. Anesth Analg 2003; 97(3):904-8. Sutherland AD, Williams RT. Cardiovascular responses and lidocaine absorption in fiberoptic-assisted awake intubation. Anesth Analg. 1986;65:389–391.

[6] Furlan JC. Anatomical study applied to anesthetic block technique of the superior laryngeal nerve. Acta Anaesthesiol Scand 2002; 46(2); 199-202.

[7] Ambuel B, Hamlett KW, Marx CM, Blumer JL. Assessing distress in Pediatric Intensive Care Env: The Comfort Scale. J Pediatr. Psychol 1992;17(1):95-109

[8] Scher CS, Gitlin MC. Dexmedetomidine and low-dose ketamine provide adequate sedation for awake fibreoptic intubation. Can J Anesth 2003; 50: 607-10.

[9] Sinha SK, Joshiraj B, Chaudhary L, et al. A comparison of dexmedetomidine plus ketamine combination with dexmedetomidine alone for awake fibreoptic nasotracheal intubation: A randomized controlled study. J ClinAnaesth. 2014; 30:514-519.

[10] Dere K, Sucullu I, Budak ET, Yeyen S, Filiz AI, Ozkan S, et al. A comparison of dexmedetomidine versus midazolam for sedation, pain and hemodynamic control, during colonoscopy under conscious sedation. Eur J Anaesthesiol 2010; 27:648-52.

[11] Kaygusuz K, Gokce G, Gursoy S, Ayan S, Mimaroglu C, Gultekin Y. A comparison of sedation with dexmedetomidine or propofol during shockwave lithotripsy: A randomized controlled trial. Anesth Analg 2008; 106:114-9.

[12] Yavascaoglu B, Kaya FN, Baykara M, Bozkurt M, Korkmaz S. A comparison of esmolol and dexmedetomidine for attenuation of intraocular pressure and haemodynamic responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol 2008; 25:517-9.

[13] Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology 1992; 77:1134-42.

[14] Aantaa R, Jalonen J. Perioperative use of alpha2-adrenoceptor agonists and the cardiac patient. Eur J Anaesthesiol 2006; 23:361-72.

[15] Tsai, C.-J., Chu, K.-S., Chen, T.-I., Lu, D. V., Wang, H.-M., & Lu, I.-C. (2010). A comparison of the effectiveness of dexmedetomidine versus propofol target-controlled infusion for sedation during fibreoptic nasotracheal intubation. Anaesthesia, 65(3), 254–259. doi:10.1111/j.1365-2044.2009.06226.x