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Original Research Article

Comparative Evaluation of Intravenous Dexmedetomidine with Ketamine and Intravenous Dexmedetomidine with Fentanyl in Facilitating Intubating Conditions During Awake Fiberoptic Intubation: A Prospective Randomised Double Blind Comparative Study

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Abstract:

Background and aims: Awake fiberoptic intubation (AFOI) is the gold standard for managing an anticipated difficult airway. Adequate sedation is crucial to ensure patient cooperation, suppress airway reflexes and provide haemodynamic stability. While dexmedetomidine is a preferred agent for AFOI due to its unique "cooperative sedation" profile, it can cause bradycardia and hypotension. Combining it with an opioid like fentanyl or a dissociative agent like ketamine may mitigate these side effects and improve intubating conditions. This study aimed to compare the efficacy of intravenous (IV) dexmedetomidine with ketamine versus IV dexmedetomidine with fentanyl in facilitating intubating conditions during AFOI.

Methods: In this prospective, randomized, double blind study, 64 ASA I/II patients undergoing elective surgery were allocated into two groups (n=32 each). After nebulization with 4ml of 4% lignocaine, Group DF received IV dexmedetomidine (1 mcg/kg over 15min) followed by IV fentanyl (2 mcg/kg over 5min) and Group DK received IV dexmedetomidine (1 mcg/kg over 15min) followed by IV ketamine (40 mg over 5 min). All patients then underwent AFOI. The primary objective assessed was cough score. Secondary objectives included intubating conditions, vocal cord position, haemodynamic parameters, sedation, patient satisfaction and time for intubation. Categorical and continuous data were presented as number (proportion) and mean ± standard deviation respectively. Chi-square test and t-test were applied where deemed appropriate. $P<0.05$ was considered statistically significant.

Results: The DF combination provided significantly superior intubating conditions. A greater proportion of patients in Group DF achieved optimal (Grade I) intubating conditions (69.8% v/s 15.6%, $p<0.001$) and vocal cord position (68.8% v/s 15.6%, $p<0.001$). Cough severity was significantly lower in Group DF ($p<0.001$). The mean intubation time was shorter in Group DF (211.44±27.12 sec v/s 258.88±64.02 sec, $p<0.001$). Group DF also demonstrated better hemodynamic stability with lower heart rate and blood pressure throughout the procedure ($p<0.05$) and higher postoperative patient satisfaction ($p<0.001$). The requirement of topical lignocaine was lower in Group DF ($p<0.05$). Ramsay Sedation Scores were comparable between groups.

Conclusion: The combination of IV dexmedetomidine and fentanyl provides better intubating conditions for AFOI compared to IV dexmedetomidine and ketamine. It offers superior vocal cord relaxation, fewer airway reflexes, greater haemodynamic stability, shorter procedure time, reduced local anaesthetic need, and higher patient satisfaction, making it a more effective regimen for facilitating AFOI.

Keywords: Fiberoptic, dexmedetomidine, fentanyl, ketamine.

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Introduction

The estimated incidence of patients with difficult airway in clinical anaesthesia is 1-18%. In such patients, the anatomy is frequently different from the normal and so, inadequate airway management may lead to hypoxia, hypoventilation, aspiration, brain damage and even death [1]. Up to 30% of all

deaths attributable to anaesthesia is related to difficult airway management. [2]

Awake fiberoptic intubation (AFOI) is the mainstay of anticipated difficult airway management where conventional laryngoscopy becomes difficult due to either inadequate mouth opening such as intermaxillary fixation, temporomandibular joint trauma or inability to extend the neck such as cervical spine injuries, obese patients with short neck.[3]

Further, AFOI is safe with a higher success rate because spontaneous breathing and airway muscle tone is maintained which reduces the risk of hypoxia in failed intubation scenario [3]. For performing a smooth AFOI, the patient should be cooperative with spontaneous breathing and showing minimal airway reflexes during insertion of fiberoptic scope and endotracheal tube which can be achieved with adequate sedation.[4]

Various medications such as opioids, benzodiazepines, propofol, dexmedetomidine, ketamine, midazolam, magnesium sulphate are used alone or in combination to suppress this pressor response. [4,5]

Dexmedetomidine, a highly selective α_2 adrenoreceptor agonist provides conscious sedation and analgesia with minimal respiratory depression and facilitate AFOI [6]. Fentanyl (2mcg/kg) results in attenuation of haemodynamic response and reduction of discomfort during passage of fiberoptic scope through vocal cords. It provides satisfactory intubating condition and arousable sedation without respiratory depression [7]. Ketamine, a NMDA receptor antagonist, in low dose (4mcg/kg/min) has been shown to have minimal impact on ventilatory drive and has analgesic property. When ketamine is combined with dexmedetomidine, both these drugs counteract each other's side effect on haemodynamic parameters and airway secretions and provide good intubating conditions during AFOI [8].

There is scarcity of studies which compares effect of adding fentanyl or ketamine to dexmedetomidine in facilitating AFOI. We planned this study to compare the effect of combination of IV dexmedetomidine with ketamine and IV dexmedetomidine with fentanyl in facilitating intubating conditions during AFOI.

Material and Methods

After taking approval from institutional ethical committee (RNT/ACAD/IEC/2024/337) along with registration in Clinical Trials Registry India (CTRI/2024/09/073684), the present prospective randomized double blind comparative clinical study was carried out after informed written consent from all the patients.

Sixty four patients aged 18-60 yr of either gender, ASA physical status and II, Mallampati class I and II undergoing elective surgery under general endotracheal anaesthesia were included. Patients who had history of drug allergy, baseline heart rate <50 bpm, blood pressure <100/50mmHg, history of hypertension, cardiac disease, coagulopathy, refusal for study participation, history of long-term opioids or sedative medications and contraindication to nasal intubation were excluded from the study.

Sample size was calculated on the basis of a pilot study which showed median cough severity score was 1.8 in intravenous dexmedetomidine- ketamine group and 1 in dexmedetomidine- fentanyl group. Taking these values as reference with difference in mean severity score as 0.8 and standard deviation of 01.03 and at 95% confidence interval and 90% power, sample size was calculated as 29 in each group. To compensate for possible 10% dropouts and to remain in compliance with central limit theorem, we enrolled 32 patients in each group.

Patients were randomly allocated into two groups of 32 patients each by block randomization and random numbers thus obtained were kept in opaque sealed envelopes for allocation concealment (Fig 1). Group DK (n=32) patients received IV Dexmedetomidine 1mcg/kg diluted upto 50 ml with normal saline (NS) as an infusion over 15 min followed by infusion of IV Ketamine 40mg diluted upto 10 ml with NS over 5 min. Group DF (n=32) patients received IV Dexmedetomidine 1 mcg/kg diluted upto 50 ml with NS as an infusion over 15 min followed by infusion of IV Fentanyl 2mcg/kg diluted upto 10 ml with NS over 5 min.

For ensuring double blinding, this trial was managed by two experienced anaesthesiologists, who were skilled to perform AFOI and had performed more than 50 AFOI. One anaesthesiologist managed the drug administration while the second anaesthesiologist performed fibreoptic intubation, graded the endoscopy and intubating conditions as well as recorded the data. The intubating anaesthesiologist and patients were kept unaware of the group allocation.

Patients were subjected to routine pre-anaesthetic checkup. All patients were premedicated with alprazolam 0.5mg tablet on the night before surgery. On arrival in operating room, standard monitoring including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR) and peripheral oxygen saturation (SpO_2) were applied and recorded. An IV line with 20G IV cannula was secured and infusion of ringer lactate started. Injection glycopyrrolate at 0.005 mg/kg and injection midazolam at 0.02 mg/kg was administered to all patients. All patients received 2-

3 drops of xylometazoline 0.1% in each nostril for decongestion of the nasal mucosa. The topicalization of airway was done by nebulization with 4ml of 4% lignocaine over 20 minutes. Then, the study drugs were administered to the patients as per the group allocation.

Fibreoptic bronchoscope was inserted through one of the nostrils after assessing the patency. Lignocaine 2% was administered through the working channel of bronchoscope on visualisation of vocal cords and trachea by spray as you go technique (SAYGO) and the amount of lignocaine used was recorded. Assessment of fibreoptic intubation condition was done by a 6-point grading index (Table 1) [10].

All patients were kept undisturbed for a period of 10 min after intubation for noting the vital parameters like HR, SBP, DBP, MAP and SpO_2 at the following time points: baseline (T_B), after drug infusion (T_1), after AFOI and post-intubation at 1, 3, 5 and 10 min (T_1, T_3, T_5 and T_{10}). Time taken for AFOI was calculated as the time interval from the passage of tip of the fiberscope through the nostril to the appearance of capnography waveform. Complications such as laryngospasm, arrhythmia, regurgitation, local injury, bleeding, and cyanosis were recorded.

After intubation, general anaesthesia was administered to all the patients by injection propofol (2 mg/kg IV), and muscle relaxation was achieved by administering injection atracurium (0.5 mg/kg IV) and surgery was allowed to proceed. All the patients also received injection paracetamol (10-15 mg/kg IV). Once the surgical procedure finished, the residual neuromuscular blockade was reversed with injection neostigmine (0.05 mg/kg IV) and injection glycopyrrolate (0.2 mg for each mg of neostigmine IV). The patients were extubated after meeting extubation criteria and were shifted to post anaesthesia care unit (PACU).

The primary outcome measured was cough score (severity of cough) whereas intubating conditions, vocal cord position, patient comfort indices, ramsay sedation score, haemodynamic parameters and postoperative patient satisfaction were evaluated as the secondary outcomes. Results obtained in the study were entered into Microsoft Excel and analysed using SPSS 25 software. Continuous variables were presented as Mean± SD and compared using Student's t test. Ordinal data were presented as Median± IQR and analysed using Mann Whitney U test. Categorical data were presented as number (proportion) and compared with Chi-square test. $p<0.05$ was regarded as statistically significant.

Results

Both the groups were statistically comparable with regard to distribution of patients according to age, gender, ASA grading, and modified mallampatti grading (Table 2).

The time taken for intubation was significantly lesser in group DF (211.44±27.12 sec) as compared to group DK (258.88±64.02 sec, p=0.00). RSS measured at the end of administration of study drugs was comparable between group DF2[2 (2-3)] and group DK [2(2-3), p=0.209].

Cough severity was significantly higher in group DF as compared to group DK (P=0.000). Significantly greater proportion (90.6%) of patients in Group DF were found in grade I, II (less severity of cough) as compared to Group DK which had majority patients in grade III (59.4%) (Table 3).

Regarding intubating condition, greater proportion (69.8%) of patients in Group DF had grade I intubating conditions as compared to Group DK (15.6%). Moreover, Group DK had 19 (59.4%) patients in Grade II as compared to 10 (31.2%) in Group DF. This difference was found statistically significant. Similar observations were noted for vocal cord position, cough score, patient comfort, post intubation assessment and patient satisfaction grading (Table 3).

HR and MAP were significantly lower in patients receiving dexmedetomidine-fentanyl combination as compared to those receiving dexmedetomidine-ketamine combination at all measured time intervals after study drug infusion (Fig 2). Lower SBP and DBP were also recorded in group DF post intubation (Fig 3). SpO_2 values although exhibited statistically significant differences, these values were still clinically within normal range.

The mean dose of lignocaine administered was statistically significantly lower in group DF as compared to group DK (197.19±9.91 mg v/s 205.31±15.1 mg, $p<0.05$). 6 patients in Group DK and 2 patients in Group DF patients experienced bleeding and local injury as side effect. None of the patients in both the groups experienced any episodes of laryngospasm, cyanosis and arrhythmias.

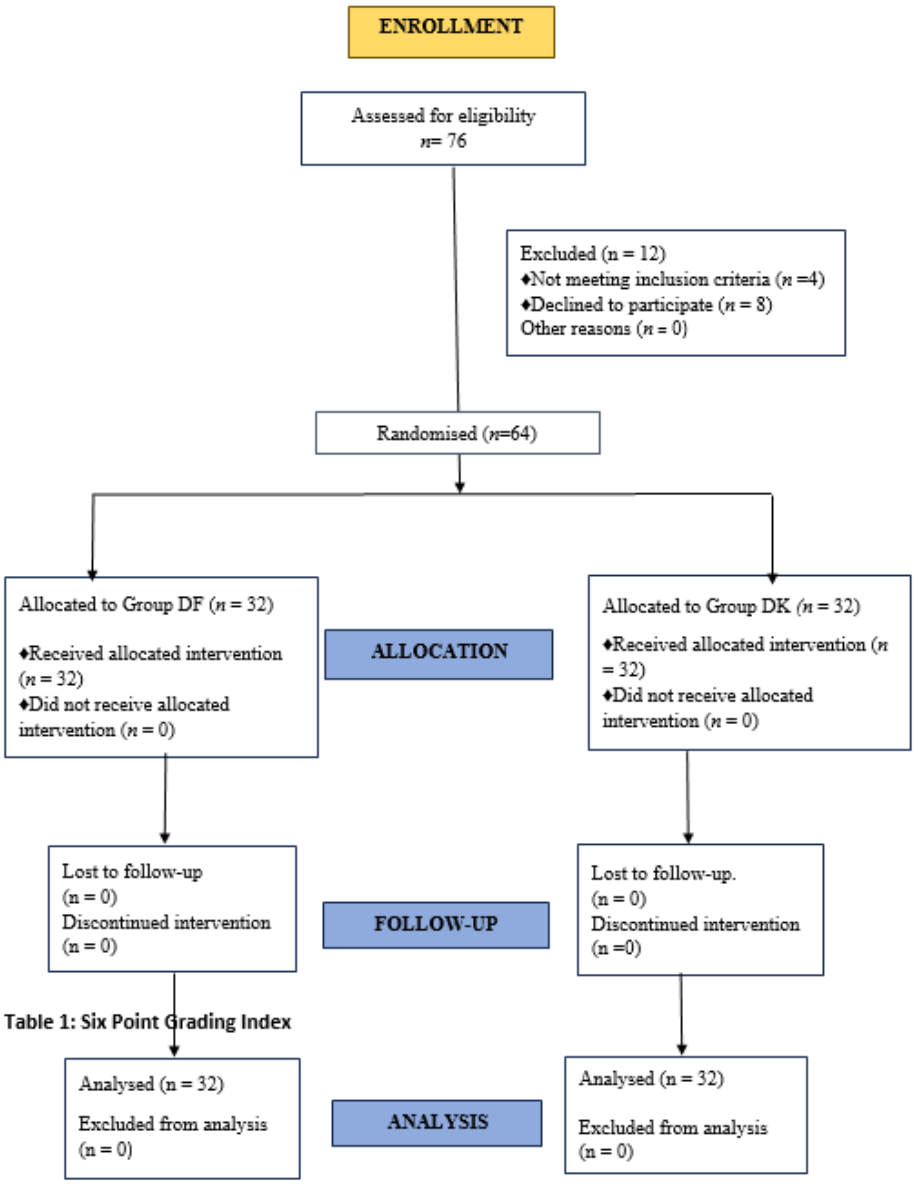

Figure 1: Consort chart

Table 1: Six Point Grading Index

Grade	Intubating Conditions	Vocal Cord Position	Patient Comfort Indices			Postoperative Patient Satisfaction
			Cough Severity During Intubation	Comfort During Intubation	Post-Intubation Assessment	
Grade 1	**Optimal**: No hold-up or collision of tracheal tube with vocal cords	Relaxed / glottis open	No cough	No reaction	Cooperative	Excellent
Grade 2	**Suboptimal**: Hold-up relieved by one rotation of the tube	Moving / glottis partially open	Slight: <2 coughs	Grimacing / minimal resistance	Restless	Good
Grade 3	**Difficult**: Hold-up requiring more than one rotation of the tube	Adducted / glottis closed	Moderate: 3–5 coughs	Verbal objection	Severe resistance / requirement of immediate general anaesthesia	Fair
Grade 4	**Failure**: Failed attempt at awake intubation	—	Severe: >5 coughs	Defensive movements	—	Poor

Table 2: Demographic parameters and Intubation time

	Group DF(n=32)	Group DK(n=32)	P value
Age (years)	39.28±10.87	39.62±11.60	0.903
Gender (M/F)	16(50.00%)/16(50.00%)	19(49.40%)/13(40.60%)	0.451
ASA grading (I/II)	22(68.8%)/10(31.2%)	22(68.8%)/10(31.2%)	1.0
MPG (I/II)	3(9.4%)/29(90.6%)	8(25%)/24(75%)	0.098
Time taken for intubation (sec)	211.44±27.12	258.88±64.02	**0.000**

Table 3: Comparative assessment of intubating conditions between groups

Parameter	Grade	Group DF	Group DK	P value
Cough severity	I	10(31.2%)	1(3.1%)	**0.000**
	II	19(59.4%)	7(21.9%)	
	III	3(9.4%)	19(59.4%)	
	IV	0(0%)	5(15.6%)	
Intubating Conditions	I	22(69.8%)	5(15.6%)	**0.000**
	II	10(31.2%)	19(59.4%)	
	III	0(0%)	8(25.0%)	
	IV	0(0%)	0(0%)	
Vocal cord position	I	22(68.8%)	5(15.6%)	**0.000**
	II	10(31.2%)	19(59.4%)	
	III	0(0%)	8(25.0%)	
Comfort during intubation	I	14(43.8%)	6(18.7%)	**0.055**
	II	18(56.2%)	22(68.8%)	
	III	0(0%)	3(9.4%)	
	IV	0(0%)	1(3.1%)	
Post intubation assessment	I	22(68.8.%)	10(31.2%)	**0.003**
	II	10(31.2%)	17(53.2%)	
	III	0(0%)	5(15.6%)	
Postoperative satisfaction	I	13(40.6%)	3(9.4%)	**0.000**
	II	17(53.1%)	9(28.1%)	
	III	2(6.3%)	14(43.7%)	
	IV	0(0%)	6(18.8%)	

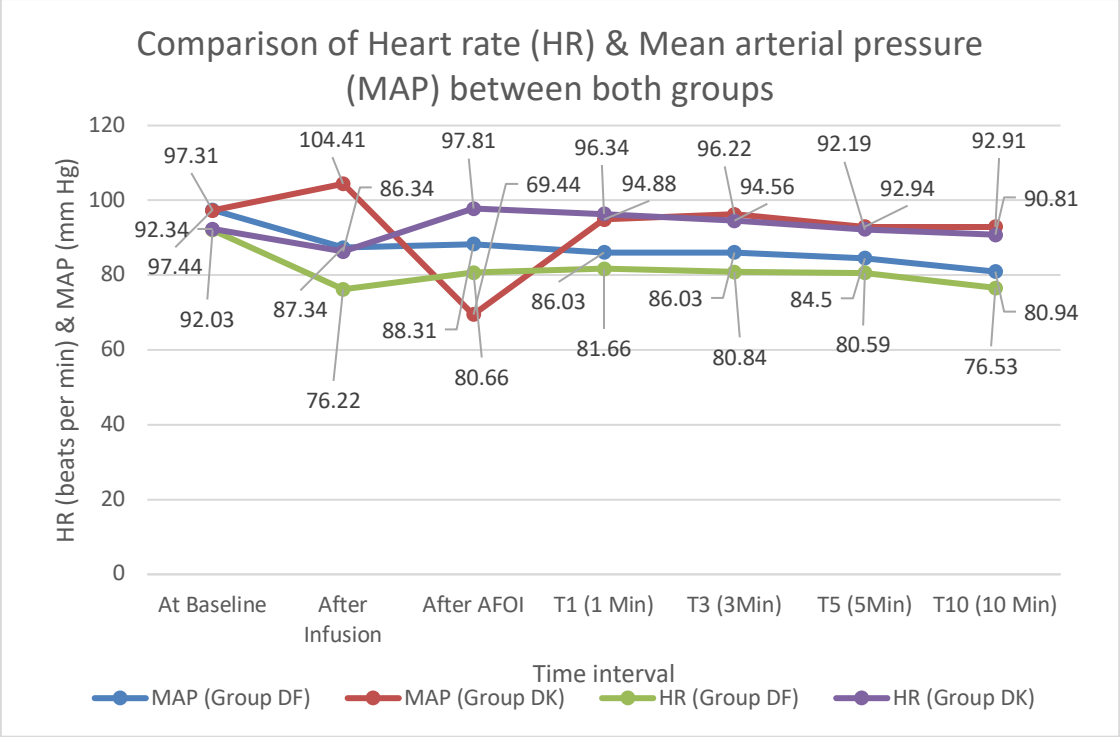

Fig 2: Comparison of heart rate (HR) and mean arterial pressure (MAP) between groups

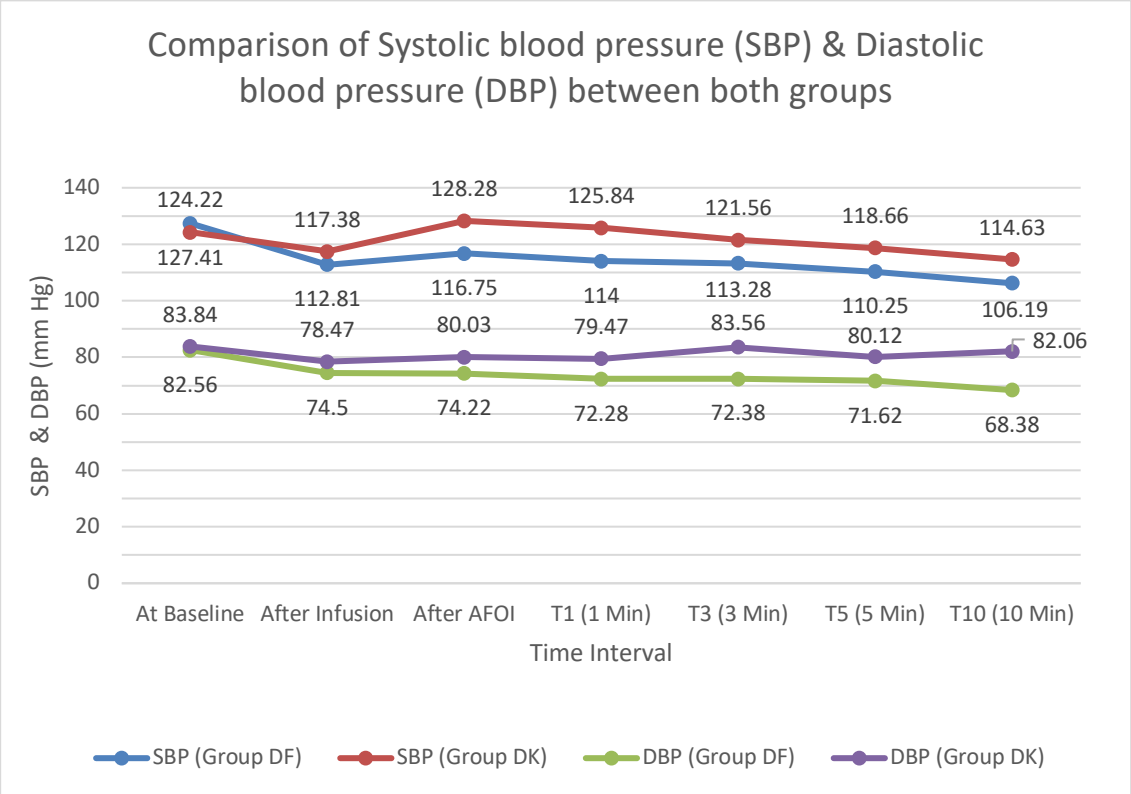

Figure 3: Comparison of systolic blood pressure (SBP) and diastolic blood pressure (DBP) between groups

Discussion

AFOI is the gold standard technique for endotracheal intubation in difficult airway scenarios. Performing AFOI without sedation impose technical difficulties due to uncooperativeness of the patient, imparts a very unpleasant experience to the patient and causes severe haemodynamic disturbances in form of tachycardia, hypertension, arrythmias and even

may cause myocardial ischemia and infarction [4]. Selection of sedative drugs for AFOI must impose a delicate equilibrium between patient comfort, cooperation, suppression of airway reflexes, sedation with minimal cardiorespiratory compromise.

Dexmedetomidine, a centrally acting α2 agonist, is preferred drug for achieving sedation during AFOI at many centres due to its various benefits like arousable sedation, anxiolysis, analgesia, decreased secretions (for better visualization), no or minimal respiratory depression. However, its use can produce cardiovascular depression leading to bradycardia & hypotension which are easily treatable but can be deleterious in patients with cardiovascular compromise. The dose of dexmedetomidine for AFOI should be adequate to inhibit airway reflexes but without causing airway collapse. Combining dexmedetomidine with other drugs like fentanyl or ketamine can help in reducing dose & potential side effects of dexmedetomidine.

Fentanyl provides analgesia, maintains cardiovascular stability & reduces the discomfort during passage of bronchoscope. However, it causes dose dependent respiratory depression. [11]

Ketamine, a NMDA antagonist, preserves patient's respiratory drive along with producing analgesic effect. [8] Ketamine's bronchodilatory effect offers additional advantage in patients undergoing AFOI [12].

There is paucity of literature comparing effect of dexmedetomidine fentanyl combination with dexmedetomidine ketamine combination administered intravenously for optimizing intubating conditions during AFOI. The present study was undertaken to evaluate & compare the effect of combination of dexmedetomidine with fentanyl and dexmedetomidine with ketamine on optimizing intubating conditions during AFOI.

The results of present study revealed the superiority of dexmedetomidine with fentanyl combination over dexmedetomidine with ketamine combination in blunting airway reflexes, improving intubating conditions, ensuring haemodynamic stability and improving overall patient satisfaction.

Haemodynamic stability is of utmost importance during AFOI. In our study, patients administered dexmedetomidine-fentanyl combination consistently exhibited lower HR and MAP post study drug infusion & during AFOI, indicating better cardiovascular stability. Fentanyl's potent suppression of sympathetic responses, when combined with dexmedetomidine's central α_2 receptor agonistic action provided enhanced haemodynamic stability. Ketamine's sympathomimetic effects, while beneficial in some contexts, resulted in significantly higher HR & MAP in group DK. Acharya R et al had also demonstrated that dexmedetomidine with fentanyl combination avoids excessive bradycardia & hypotension while maintaining efficacy. [11]

In our study, significantly higher number of patients in Group DF exhibited better vocal cord position and intubating conditions, allowing faster and smoother intubation. Cough severity was lower in the DF group, where none of the patients showed Grade IV cough, compared to 15.6% in DK ($p<0.001$). This reinforces fentanyl's established antitussive effect, essential for a successful AFOI.

Group DK patients demonstrated more cough reflex and longer intubation times, potentially due to ketamine-induced secretions and sympathetic surge, corroborating prior observations by Srinivas et al.[13] Even though ketamine preserves airway reflexes and ventilatory effort, its stimulatory profile appears less favourable than fentanyl in suppressing cough and facilitating intubation. Decreased inhibition of airway reflexes also resulted in enhanced instillation of lignocaine during AFOI by SAYGO technique in group DK ($p<0.05$).

While both groups had similar sedation scores, SpO_2 levels were better in Group DF post-infusion and post-intubation ($p = 0.009$ and 0.029 respectively). This could reflect the more stable airway and less frequent coughing episodes, allowing uninterrupted oxygenation.

The incidence of adverse events was low in both groups. Group receiving dexmedetomidine-ketamine combination had a slightly higher incidence of minor bleeding and local injury, which may be attributed to increased coughing and patient movement during intubation. No episodes of desaturation, arrhythmia, or regurgitation were observed in either group, emphasizing the overall safety of both regimens. Importantly, no patient in either group required rescue sedation or conversion to general anaesthesia before securing the airway.

Group DF scored significantly better inpatient satisfaction and postoperative recall, with 40.6% of patients rating their experience as Grade I compared to only 9.4% in DK. The smoother intubation, lesser discomfort, and more stable haemodynamics likely contributed to this outcome. These results echo those of Srinivas et al [13], who also emphasized the importance of patient tolerance and minimal recall for overall success in AFOI procedures.

Our study had its own limitations. Our study was a single centre trial and had a modest sample size. The patients included had normal airway belonging to MPG I & MPG II. Thus, the efficacy of these agents was not assessed for AFOI in difficult

airway scenario. There is a possibility that midazolam premedication offered a synergistic action although the sedation protocol remained constant across all participants. Moreover, the feasibility of this trial was not assessed in emergency cases. Further, different doses of study drugs were not evaluated in the present study. Dose response studies should be undertaken in future to find the optimum dose of study drugs for facilitating AFOI.

Conclusion

IV dexmedetomidine-fentanyl provides better conditions for AFOI as compared to IV dexmedetomidine-ketamine by ensuring better vocal cord relaxation, more favourable intubating conditions, improved patient cooperation, fewer airway reflexes, superior haemodynamic control and higher patient satisfaction along with reducing procedure time and decreasing requirement of local anaesthetic agent.

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