Original Article

A comparison of two doses of ketamine with dexmedetomidine for fiberoptic nasotracheal intubation

ABSTRACT

Background and Aims: Flexible fiber-optic intubation is considered to be the gold standard for management of difficult airway. Fiber-optic intubation does require effective sedation and blunting of airway reflexes for which various drug regimens have been utilized in the past. In a quest to find the noble drug combination, we combined ketamine and dexmedetomidine in two different doses, to evaluate the clinical efficacy and safety profile of ketamine and dexmedetomidine for fiber-optic intubation.

Materials and Methods: This prospective randomized study was conducted in 72 patients of 20–50 years' age group of either sex with the American Society of Anesthesiologists Physical Status I and II with difficult airway. We compared two doses of ketamine 20 mg (Group I) and 40 mg (Group II) with a common dose of dexmedetomidine at 1 μg/kg body weight, given as an infusion over 10 min (a solution of 50 ml with normal saline). Sedation scores, hemodynamic variables in terms of blood pressure, heart rate (HR), and oxygen saturation were studied along with 24-h postoperative patient discomfort and recall of procedure.

Results: Group II patients showed less variation from their baseline values in terms of HR (ranged between 0.73% and 4.75%) and mean arterial pressure (ranged between 0% and 3.97%) in comparison to Group I HR (ranged between 0.09% and 9.81%) and mean pressures (ranged between 0.3% and 10.38%). Discomfort during procedure ($P < 0.001$) and recall of procedure scale ($P = <0.001$) were found significantly better/lower in Group II as compared to Group I.

Conclusion: Ketamine 40 mg in comparison to 20 mg with dexmedetomidine provides better hemodynamic conditions with better tolerance and lower recall to the fiber-optic intubation.

Keywords: Conscious sedation, dexmedetomidine, difficult airway, fiber-optic intubation, ketamine

INTRODUCTION

Patients with reduced mouth opening and with difficult airway are a challenge to the anesthesiologist, which require adequate preparation and use of fiber-optic intubation for their airway maintenance. Various drugs in alone or in combination such as benzodiazepines, opioids, propofol, ketamine, and dexmedetomidine have been utilized with or without topical anesthesia of the airway for providing adequate conditions for fiber-optic intubation. An ideal anesthetic regimen for fiber-optic intubation should provide adequate sedation with stable hemodynamics, patient comfort, amnesia, and blunting of airway reflexes with spontaneous ventilation.

The favorable properties of dexmedetomidine, such as minimal respiratory depression, may provide protection against adverse

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respiratory events during awake intubation.[1] Intravenous (IV) ketamine has an opioid-sparing effect and an effective adjunct for postoperative analgesia.[2] Furthermore, the concurrent use of ketamine nullifies the bradycardia and xerostomia effects of dexmedetomidine infusion. Excellent intubating conditions for fiber-optic intubation using dexmedetomidine and ketamine have been described previously,[3,4] but no optimum dose combination of the two drugs has been described; therefore, in a quest to identify the ideal anesthetic regimen and to find the optimum dose, we combined ketamine and dexmedetomidine in two different doses, to evaluate the clinical efficacy and safety profile required for fiber-optic intubation.

MATERIALS AND METHODS

We enrolled patients after approval from the Institutional Ethical Committee (Reg. No. ECR/262/Inst/UP/2013/RR-16). All patients voluntarily signed the informed consent form. This prospective, randomized, double-blind, comparative study was conducted in 72 cooperative patients aged 15–45 years of either sex belonging to the American Society of Anesthesiologists Physical Status I and II with anticipated difficult airway (mouth opening <2 cm, thyromental distance <6.5 cm, and Mallampati Class III and IV) posted for elective surgical procedure. Uncooperative patients, patients with any type of ischemic heart disease and heart block, any known bleeding diathesis and thrombocytopenia, bradycardia (heart rate [HR] <50/min), any nasal mass, and any hypersensitivity to study drugs and patients on psychiatric medication were excluded from our study.

A sample size of 36 patients in each group was calculated with an alpha error of 5% (confidence interval 95%) and power of study of 80%. Patients were randomly allocated to Group I (dexmedetomidine 1 μg/kg + ketamine 20 mg) or Group II (dexmedetomidine 1 μg/kg + ketamine 40 mg) of 36 patients using computer-generated random table.

To achieve blinding, operation theater nurse prepared and controlled the drug infusion, a senior anesthesiologist did fiber-optic intubation and the trainee anesthesiologist did postoperative visit and documentation of data.

On the preoperative visit, a day before surgery, a patient was counseled for the nasotracheal fiber-optic intubation approach and no premedication was prescribed. Patients were advised fasting for solids for 6 h and clear liquids for 2 h. On the day of surgery, after arrival at the theater, a 20-gauge IV cannulation was performed in both the forearms under local anesthesia. Routine monitoring devices such as 5-lead electrocardiogram (ECG), HR, noninvasive blood pressure, mean arterial pressure (MAP), and oxygen saturation (SpO_2) were recorded. Once the patients were comfortable to the surroundings, two drops of a vasoconstrictor (xylometazoline 0.1%) were administered in both the nostrils.

Oxygen supplementation with nasal prong was started at 4 L/min and was continued throughout the procedure. Injection glycopyrrolate 0.2 mg IV was given 5 min before administering the study drugs. Groups I and II patients received dose of dexmedetomidine at 1 mcg/kg over 10 min in 50-mL normal saline using infusion pump (Injectomat Agilia® Fresenius Kabi India) connected with the right forearm IV cannula. Group I patients received ketamine 20 mg over 10 min in 10-mL normal saline using infusion pump (Injectomat Agilia® Fresenius Kabi India) connected with the left forearm IV cannula, and Group II patients received ketamine 40 mg over 10 min in 10-mL normal saline using infusion pump (Injectomat Agilia® Fresenius Kabi India) connected with the left forearm IV cannula. Hence, each patient had two infusion pumps. Once the dose of the drugs was infused, sedation score was assessed by modified Observer Assessment of Alertness/Sedation (Oaa/S) scale as given 5 = responds readily to name spoken in the normal tone, 4 = lethargic response to the name spoken in normal tone, 3 = responds only after name spoken loudly or repeatedly, 2 = response only after mild prodding or shaking, and 1 = does not respond to mild prodding or shaking.[5]

An endotracheal tube (ETT) of appropriate size was mounted over the fiberscope (Karl Storz, working length: 65 cm, distal tip diameter: 3.7 mm) and introduced through the selected nostril with appropriate lubricating gel, immediately after 10 min of study drug infusions. After visualization of the glottis and vocal cords, the fiber optic was maneuvered across the vocal cord into the trachea, and ETT was passed over it into the trachea and positioned just above the carina. Fiber-optic bronchoscope was withdrawn appreciating the tracheal rings and the ETT inside the trachea. Cuff was inflated and ETT was adequately secured. General anesthesia was induced as per common institutional protocol.

The primary outcome was measured in terms of hemodynamic stability (MAP, HR, SpO_2, and ECG) and sedation score in terms of OAA/S scale. Hemodynamic variables were assessed at different time intervals. Baseline, every 2 min after start of drug, fiberscopy beginning, ETT in nasopharynx, ETT in glottis, 5 min after intubation and at 10 min after intubation. Other parameters that were studied were (i) ease of intubation (1 = easy, 2 = moderate, and 3 = difficult), (ii) cough (1 = none, 2 or slight = if no >2 coughs in sequence, 3 or moderate = 3–5 coughs in sequence occurred, and 4 or severe = if >5 cough in sequence occurred), and (iii) patient tolerance to intubation by facial grimace score (FGS)

1 = no grimace, 2 = minimal grimace, 3 = mild grimace, 4 = moderate grimace, 5 = severe grimace, and 6 = very severe grimace).[6]

On the first postoperative day, a patient was assessed in terms of (i) discomfort during procedure (1 = none no discomfort at all, 2 = mild discomfort or just comfortable, 3 = moderate discomfort or tolerable, and 4 = severe discomfort or completely intolerable), (ii) recall or memory of fiberscopy procedure (1 = no recall after the infusion, 2 = partial or cannot recall full procedure exactly, and 3 = full or remember the procedure), and (iii) any adverse side effects such as hoarseness and sore throat.

The statistical analysis was done using SPSS (Statistical Package for the Social Sciences) version 21.0 Statistical Analysis Software (IBM Inc, Chicago, USA). The values were represented in number (%) and mean ± standard deviation. Hemodynamic variables were analyzed using Student's *t*-test and paired *t*-test. Sedation score and FGS were analyzed using Mann–Whitney U-test. Ease of intubation, level of recall, discomfort, and adverse events were analyzed using the Chi-square test.

RESULTS

All the patients were successfully nasally intubated using the fiber-optic bronchoscope. The demographic profile parameters and baseline hemodynamics were similar in both the groups [Table 1].

Hemodynamic variables in terms of mean HR decreased continuously in both the groups [Figure 1]. There was a significant difference in mean HR in comparison to baseline values in Group I at all points ($P < 0.001$) except at 2 min ($P = 0.147$), while in Group II, mean HR in comparison to baseline values showed a significant difference only after 6 min ($P < 0.003$) of drug infusion and thereafter ($P < 0.001$) at all observational points. Group II patients showed less variation from their baseline values in terms of HR (ranged between 0.73% and 4.75%) in comparison to Group I HR (ranged between 0.09% and 9.81%).

MAP in Group I showed a declining trend in comparison to the baseline values at all times of observation ($P < 0.001$) which was statistically significant except at 2 min ($P = 0.108$). MAP in Group II showed an uprising trend in comparison to baseline values at all times ($P < 0.001$, at 10 min after intubation $P = 0.033$) which was statistically significant except at 4 min ($P = 0.612$). Group II patients showed less variation from their baseline values in terms of MAP (ranged between 0% and 3.97%) in comparison to Group I mean pressures (ranged between 0.3% and 10.38%) [Figure 1].

Table 1: Distribution of participants according to demographic profile and baseline hemodynamic parameters

Parameters	Group I ($n=36$)	Group II ($n=36$)	*P*	Significance
Age (years)	37.28±5.91	39.53±4.67	0.240	NS
Sex (male/female)	32/4	34/2	0.394	NS
Height (cm)	166±3	165±3	0.450	NS
Weight (kg)	57.67±2.33	56.97±2.67	0.243	NS
BMI (kg/m^2)	20.94±0.57	20.83±0.53	0.370	NS
ASA PS (I/II)	0/36	0/36	0.999	NS
Mouth opening (cm)	1.47±0.46	1.40±0.44	0.518	NS
Thyromental distance (cm)	6.39±0.21	6.40±0.20	0.775	NS
Baseline HR (beats/min)	96.25±8.87	95.42±12.87	0.750	NS
Baseline MAP (mm Hg)	102.01±3.82	100.50±4.14	0.113	NS

The values are mean±SD or number of patients. $P<0.05$ is statistically significant. ASA PS: American Society of Anesthesiologists Physical Status, NS: Not significant, MAP: Mean arterial pressure, HR: Heart rate, BMI: Body mass index, SD: Standard deviation

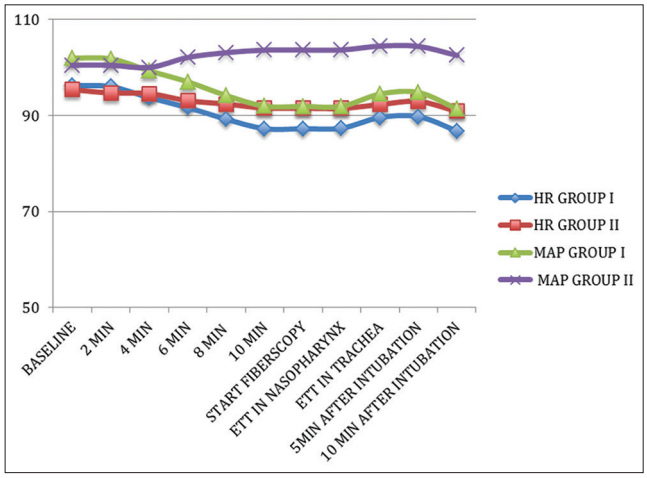

Figure 1: Comparison of hemodynamic parameters in terms of mean heart rate and mean arterial pressure

Sedation score was measured with OAA/S, and patient tolerance to intubation was measured using the FGS and cough [Table 2]. Patients of Group II were deeply sedated and showed better tolerance to intubation as compared to Group I ($P < 0.001$). Cough was less severe in terms of grading described before in Group II as compared to Group I, and the difference was statistically significant ($P = 0.023$). Significantly higher proportion of patients of Group II was easy to intubate in comparison to Group I ($P = 0.041$).

On the first postoperative day, patients of both the groups were assessed for recall of procedure, discomfort level, and any side effects [Table 3]. There was lesser recall of

Table 2: Parameter during fiber-optic intubation

Parameter	Group I	Group II	*P* (Mann-Whitney U test)
OAA/S	3.89±0.78	2.19±0.95	<0.001
FGS	2.42±0.50	1.64±0.49	<0.001
Cough (1/2/3/4)	27/7/2/0	35/1/0/0	0.023*
Ease of intubation (1/2/3)	28/8/0	34/2/0	0.041*

*Chi-square test, $P<0.05$ significant, Cough (1: None, 2 or slight: If no more than 2 coughs in sequence, 3 or moderate: 3-5 coughs in sequence occurred, and 4 or severe: If >5 cough in sequence occurred), ease of intubation (1: Easy, 2: Moderate, and 3: Difficult). Data are mean±SD or number of patients. OAA/S: Modified Observer Assessment of Alertness/Sedation, FGS: Facial grimace score, SD: Standard deviation

Table 3: Parameters measured during the first postoperative day

Parameter	Group I (*n*=36)	Group II (*n*=36)	*P*
Patient's recall, 1/2/3, (percentage values)	0/10/26, (0/27.8/72.2)	13/22/1, (36.1/61.1/2.8)	<0.001*
Discomfort during procedure, 1/2/3/4 (percentage values)	0/20/16/0, (0/55.6/44.4/0)	13/23/0/0, (36.1/63.9/0/0)	<0.001*
Hoarseness	0	0	-
Sore throat	0	0	-

*Chi-square test, $P<0.05$: Significant. Values are in numbers, Recall or memory of fiberscopy procedure (1: No recall after the infusion, 2: Partial or cannot recall full procedure exactly, and 3: Full or remember the procedure), discomfort during procedure (1: None no discomfort at all, 2: Mild discomfort or just comfortable, 3: Moderate discomfort or tolerable, and 4: Severe discomfort or completely intolerable)

fiberscopy procedure in Group II as compared to Group I and was statistically significant ($P < 0.001$), whereas the level of discomfort was more and statistically significant ($P < 0.001$) in Group I as compared to Group II. There was no incidence of any side effects in both the groups.

DISCUSSION

Management of anticipated difficult airway clearly underlines the importance of awake fiber-optic intubation. Judicious use of sedation with minimum effect on airway tone and respiratory efforts of the patient is one of the prerequisites for successful awake nasotracheal fiber-optic intubation.[7] Achieving cardiovascular stability during airway manipulation is one of the goals of management.

Due to the antagonistic hemodynamic effects, procedural sedation with dexmedetomidine and ketamine has been utilized extensively in pediatric cardiac catheterization, imaging, endoscopies, and airway maintenance with stable hemodynamics.[4,8-10]

With this study, we have studied two different fixed-dose combinations of dexmedetomidine and ketamine for awake fiber-optic nasotracheal intubation. All the patients were successfully intubated in both the groups using fiber-optic technique.

Group II patients showed less variation from their baseline values in terms of HR (ranged between 0.73% and 4.75%) in comparison to Group I HR (ranged between 0.09% and 9.81%). There was a progressive decline in HR in both the groups as compared to baseline values similar to a study by Sinha *et al.*[4] Dexmedetomidine, because of its sympatholytic and vagomimetic actions, is approved with a warning about hypotension, bradycardia, and sinus arrest and should be used only in a monitored situation.[11] Yildiz *et al*.[12] noted an increase in mean HR during laryngoscopy and intubation in their study. Neither there was any incidence of bradycardia nor there was an increase in HR in both the groups as compared to baseline values, which indicate the adequacy of the anesthetic depth.

Group II patients showed less variation from their baseline values in terms of MAP (ranged between 0% and 3.97%) in comparison to Group I mean pressures (ranged between 0.3% and 10.38%). MAP values in Group I showed a continuous decline as compared to baseline values similar to study by Sinha *et al.*,[4] but in Group II, due to increased dose of ketamine, there was an increase in MAP values as compared to baseline after 6 min of infusion. None of the patients in either group had any fall or rise of MAP and HR of >11% of baseline values. The opposing action of ketamine and dexmedetomidine on cardiac and sympathetic system probably resulted in a more stable hemodynamic response.[3]

Group II patients had better tolerance to tube as assessed by FGS and were deeply sedated in comparison to Group I and were statistically significant ($P < 0.001$). The sedative effects of the combination of ketamine and dexmedetomidine were found to be additive at the endpoints of hypnosis and anesthesia.[3] About 97.2% patients of Group II had no episode cough as compared to 75% of Group I patients and were significant ($P = 0.023$). Achieving good analgesia and sedation under spontaneous ventilation with minimal cough without the use of opioids or propofol appears to be one of the main advantages of this technique. The use of propofol and remifentanil for nasotracheal intubation raises incidences of airway obstruction.[13,14]

About 72.2% (26/36) patients in Group I could recall the complete procedure on the next day as compared to 2.8% (1/36) patients of Group II which was statistically significant ($P < 0.001$), and this could be explained because of lesser dose of ketamine in Group I and also because of infusion of drugs for only 10-min duration in both the groups. Tsai *et al.*[13] and Hall *et al.*[15] also reported higher incidence of recall in dexmedetomidine group. Similarly, 36.1% (13/36) of patients of Group II did

not face any discomfort during the procedure, whereas 55.6% (20/36) of Group I had mild discomfort during the procedure, and this difference was statistically significant ($P < 0.001$).

Limitation of our study could be the small sample size of patients belonging to normal body mass index (BMI). We suggest larger randomized controlled trials in overweight patients with higher BMI.

CONCLUSION

With our study, we conclude that 40-mg ketamine with dexmedetomidine is an attractive option for awake fiber-optic nasotracheal intubation in difficult airway even in the absence of topical anesthesia with minimal complications and better hemodynamic stability.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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