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Research Article

Comparison of Dexmedetomidine and Nalbuphine on Intubating Conditions and Hemodynamic Responses During Awake Fiberoptic Intubation: A Randomized Study

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ABSTRACT

Background: The pre-requisites to a successful awake fiberoptic intubation (AFOI) include adequate psychological and pharmacological preparation of the patient. This study aims to compare two pharmacological agents, dexmedetomidine and nalbuphine, in addition to nebulization and airway topicalization, for intubating conditions during AFOI.

Methods: Sixty consenting patients belonging to ASA I/II, MPC I/II, age-group of 18-60 years weighing between 40-70 kgs requiring general anaesthesia with endotracheal intubation were randomly allocated to one of the two groups. Patients received dexmedetomidine 1µg/kg i.v. (group D) or nalbuphine 0.2 mg/kg i.v. (group N) over 10 min before intubation. Fiberoptic intubation was attempted. Intubating conditions were assessed in terms of sedation score, cough score and post-intubation score. Hemodynamic responses, lignocaine and propofol requirement were also recorded. Repeated measure ANOVA, Tukey's test, unpaired t test, Chi-square test or Fisher's exact test were used for data analysis. A $P < 0.05$ was considered significant.

Results: Sedation score ($P = 1.000$), cough score ($P = 0.165$) and post-intubation score ($P = 0.157$) were comparable among the two groups. Hemodynamic responses, propofol and lignocaine requirements were also comparable.

Conclusion: Both intravenous dexmedetomidine and nalbuphine provide good intubating condition with minimal adverse effects on haemodynamic profile during awake fibreoptic intubation.

Introduction

Awake fiberoptic intubation (AFOI) remains a safe and feasible choice for securing the airway in patients with anticipated difficult airway, unstable cervical spine injury, failed intubation and in patients where optimal positioning for laryngoscopy is either difficult to achieve or contraindicated [1]. Blunted airway reflexes, adequate sedation, anxiolysis, along with preservation of a patent airway and ventilation are some of the pre-requisites required to facilitate the procedure of awake fiberoptic intubation as well as to make the patient comfortable [2].

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A large number of pharmacological interventions are used to attenuate unfavorable responses to the procedure via topical and intravenous routes, in addition to psychological counselling. Agents like propofol, midazolam, fentanyl, etc. are commonly used alone or in combination to improve patient co-operative and comfort. Benzodiazepines when used intravenously produce anxiolysis, sedation, hypnosis as well as anterograde amnesia but can cause respiratory depression. Propofol causes amnesia along with a faster onset as well as offset of action but can cause apnea, hypotension and pain on injection [3]. Opioids such as fentanyl and remifentanil provide sedation, analgesia, blunted cardiovascular responses but are respiratory depressant.

Dexmedetomidine, an alpha-2 adrenergic agonist, provides necessary sedation and analgesia with little effect on the airway secretions. In addition, it does not possess much respiratory depressant effect. It has been found to be efficacious in providing adequate conscious sedation for awake fiberoptic intubation with very little adverse effect.

Nalbuphine acts as an antagonist at mu receptor and agonist at kappa receptor. It acts on supraspinal and spinal kappa receptors resulting in analgesia with no respiratory depression, pruritus and sedation [4]. It has been reported to be a promising agent in providing intubating conditions comparable to fentanyl when used for AFOI with minimal side effects [5].

On literature search, we could not find any study comparing dexmedetomidine and nalbuphine for AFOI. So, this study was designed to compare dexmedetomidine and nalbuphine for intubating conditions assessed by the level of sedation, cough score, tolerance to intubation and hemodynamic responses during awake fiberoptic intubation. Any requirement of additional propofol or lignocaine and the incidence of side effects like hypoxia were also studied.

Methods

This randomized double blind controlled trial was undertaken after obtaining approval from the Institutional Ethical Committee - Human Research (IEC-HR) vide letter no. IEC-HR/2017/32/20, in a meeting held on Oct 7, 2017. This study was conducted at a tertiary care teaching institution in North-India between November 2017 and April 2019. The procedures adopted in the study were in accordance with the Declaration of Helsinki of 1975, as revised in 2013, for experiments on human. A written informed consent was obtained from all the participating subjects.

Sixty ASA I/II patients of either sex, with age ranging from 18 to 60 years, weight ranging from 40 to 70 kgs, with no anticipated difficulty in airway management scheduled for surgery requiring general anesthesia with endotracheal intubation were included in this study. Patients with significant neurological, hepatic, renal or pulmonary disease, having known allergies or contraindications to trial drugs or on beta blocker therapy, undergoing emergency procedures, obstetric procedures and patients with history of alcohol or drug abuse were excluded.

All the patients were premedicated with tablet alprazolam 0.5 mg on the night before surgery. Patients were advised to remain nil per mouth for 8–10 h prior to the procedure as per the institutional policy. Tablet ondansetron 4 mg and tablet ranitidine 150 mg were administered with sips of water 2 h before shifting to the operating room on the morning of surgery.

In preoperative room, nasal cavity with more room for intubation was selected. An 18-G intravenous catheter was secured. Nebulization was done with 4 ml of 2% lignocaine over 15 minutes. Topicalization was achieved by nasal pledgets soaked in lignocaine adrenaline solution. Xylometazoline (0.1%) nasal drops & 2% lignocaine jelly was applied to both the nostrils. Heart rate, blood pressure, and SpO2 were recorded at baseline, before and after topicalization.

Post nebulization and topicalization patients were shifted to operating room. Essential monitoring was instituted. Adult flexible bronchoscope was lubricated with lignocaine jelly and an appropriately sized cuffed endotracheal tube (7.0 mm ID for female patients and 8.0 mm ID for male patients) was mounted over it. Patient's tongue and hypopharynx were anesthetized using two puffs of 10% lignocaine (10 mg/puff).

Patients were then randomly assigned to receive either dexmedetomidine 1µg/kg i.v. (group D) or nalbuphine 0.2 mg/kg i.v. (group N). A computer-generated table of random numbers aided us with randomization. The study drug was diluted in 20 ml normal saline and given slowly over a period of 10 min. The anesthesiologist who prepared the study drug was not involved in further conduct of the study. The person observing the outcomes was unaware of the group allocation to ensure blinding.

At the end of study drug infusion, Ramsay sedation score (RSS) was used for assessment of sedation (1 Anxious, agitated, or restless, 2 Cooperative, oriented, or tranquil, 3 Sedated but responding to loud noise, 4 Asleep, brisk glabellar reflex, or response to loud noise, 5 Asleep, sluggish glabellar reflex, or response to loud noise, and 6 Asleep with no response to painful stimulus) [2]. Bronchoscopy was attempted through the more patent nostril if RSS ≥2 was achieved. If RSS <2, propofol was administered in boluses of 2 ml (20 mg) till RSS ≥2 was achieved. Patient was paraoxygenated throughout the procedure via a nasopharyngeal airway through the other nasal cavity. Upon visualization of vocal cords, aliquots of 2 ml (40 mg) 2% lignocaine spray were administered, if required, to facilitate further advancement of bronchoscope till carinal visualization. Tracheal intubation was completed by rail-roading it over the bronchoscope which was withdrawn thereafter. General anesthesia was now induced with propofol and vecuronium as required for the surgical procedure.

Intubating conditions were assessed in terms of cough score (1 no cough; 2 slight cough, not >2 in sequence; 3 moderate cough, 3–5 in sequence; 4 severe cough, >5 in sequence) [2]. Post intubation score determined after endotracheal intubation was used to grade the tolerance to intubation (1 cooperative; 2 minimal resistance; 3 severe resistance) [2]. Vitals including heart rate, systolic and diastolic blood pressure, mean arterial pressure and SpO2 were noted at the set time-points viz. in the preoperative area, before and after topicalization, before and after test drug, at the time of intubation, immediately after intubation, and 2, 5, 10, and 15 min after intubation. The total dose of lignocaine spray used during bronchoscopy and propofol administered during the intubation procedure were noted.

Sample size was determined assuming a difference of 25% between the two drugs to be significant. To estimate this difference at alpha = 0.5% and power = 80%, a sample size of 28 patients in each group was required. To account for 10% failure or loss to follow up, 30 patients in each group were included.

One time measured quantitative data were analyzed by unpaired students 't' test. Qualitative parameters were analyzed using Chi-square test or Fischer's exact test and McNemar's test and repeatedly measured quantitative parameters were studied using repeated measure ANOVA, followed by Tukey's test. A 'p' value of <0.05 was considered significant. All statistical analysis was done in IBM SPSS version 20.0.

Results

A total of 67 patients were screened for possible inclusion in the study, out of which 5 patients did not meet the inclusion criteria, 2 patients did not give consent for awake intubation. Remaining 60 patients completed the study protocol and were analyzed (Figure 1).

Table 1 describes the demographic profile of the two groups. Ramsay sedation score, cough score and post-intubation score are shown in (Table 2). Sedation score (P= 1.000), cough score (P = 0.165) and post-intubation score (P= 0.157) were comparable among the two groups.

Table 3 shows the requirement of aliquots of lignocaine 2% 2 ml (40 mg) and propofol 1% 2 ml (20 mg) during the procedure. There was no significant difference between the two groups (P = 0.639 and 0.587, respectively).

Heart rate changes recorded at various time intervals are shown in Figure 2 (P = 0.212). Systolic (P = 0.710), diastolic (P = 0.998) and mean (P = 0.991) arterial blood pressure changes among the study groups are shown in Figure 3. Subjects in both the groups had increased HR and BP following intubation compared to baseline. The results found were statistically similar in two groups.

There was no episode of desaturation in any of the patients throughout the study period. Hypotension was observed in one patient in group N which was promptly treated with injection mephentermine 6 mg i.v.

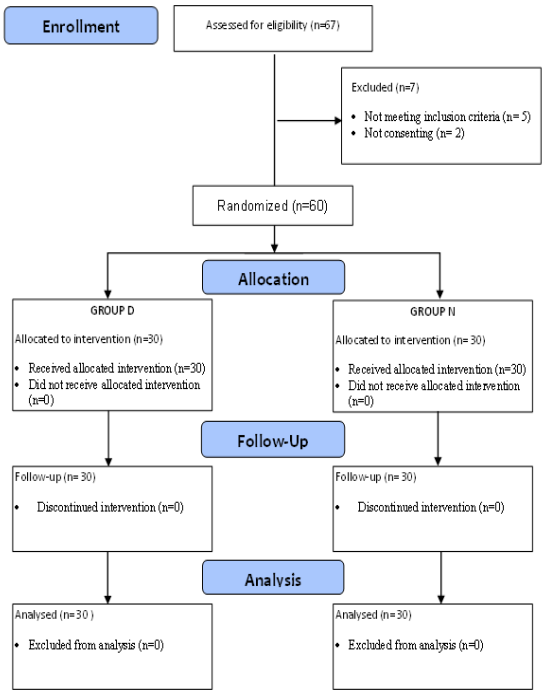

Figure 1- CONSORT flow-diagram

Table 1- Demographic profile

Parameters	Group D (n=30)	Group N (n=30)	P value
Age (years)*	32.97±9.44	27±7.28	0.074
Weight (kg)*	59.60±8.61	56.80±8.20	0.202
Height (cm)*	163.93±10.42	165.20±7.22	0.587
Gender (M:F)†	14:16	11:19	0.432
ASA grade (I:II)†	24:6	26:4	0.488
MPG (I:II)†	11:19	12:18	0.791

P<0.05 is significant; *values are expressed in mean±SD; †values are expressed as ratio

Table 2- Intubating conditions

Intubating conditions		Group D (n=30)	Group N (n=30)	P value
Ramsay sedation score (RSS)	1	0	0	1.000
	2	30	30	
	3	0	0	
	4	0	0	
	5	0	0	
	6	0	0	
Cough score (CS)	1	6	10	0.165
	2	19	19	
	3	5	1	
	4	0	0	
	1	11	18	0.151
	2	18	11	

Post-intubation score (PIS)	3	1	1	

Table 3- Requirements of aliquots of Lignocaine 2% 2 ml (40 mg) & Propofol 1% 2ml (20mg)

No of doses		Group D (n=30)	Group N (n=30)	P value
Lignocaine 2ml (40mg) 2%	1	2	4	0.639
	2	22	22	
	3	6	4	
	0	14	12	
Propofol 2ml (20mg)	1	6	7	0.587
	2	8	11	
	3	2	0	

P<0.05 is significant

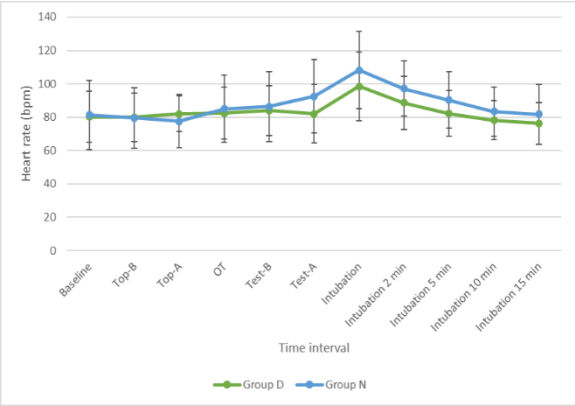

Figure 2- Heart rate changes among the study groups

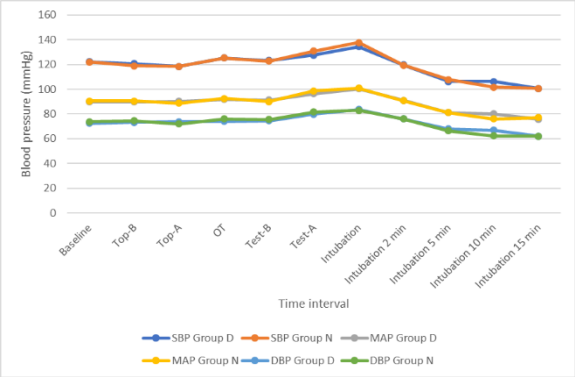

Figure 3- Blood pressure changes among the study groups

Discussion

The study results revealed that both, dexmedetomidine and nalbuphine, provided similar intubating conditions in terms of Ramsay sedation score, cough score & post-intubation score. The subsequent requirement of lignocaine and propofol boluses and hemodynamic parameters were also comparable in both the groups. There was no incidence of any clinically significant complication in either of the two groups during the conduct of this study.

In case of anticipated difficult intubation, awake intubation with preservation of respiration is the preferred technique for airway management. This requires a calm and co-operative patient with blunted airway reflexes to facilitates bronchoscopy and placement of the endotracheal tube. Dexmedetomidine is a highly selective, centrally acting α-2 agonist and an FDA approved drug for short term sedation in mechanically ventilated patients in ICU. It has hypnotic, amnestic, analgesic, anxiolytic, sympatholytic and antisialogogue effects and has a sparing effect on respiratory function, all of which are desired for AFOI. It has been recognized and used for procedural sedation in patients undergoing a variety of surgical procedure [6-9].

Many researchers have used dexmedetomidine in a dose of 1 µg/kg and found it to be effective in providing good intubating conditions, sedation and stable hemodynamics [2,10-11]. On the other hand studies using dexmedetomidine in higher doses ranging from 1-2 µg/kg i.v. have reported apnea and hypertensive episodes [12-13]. In lower doses of 0.25-0.5 µg/kg, a hypotensive response has been observed.[13] We used a dose of 1 µg/kg administered over 10 minutes as it has been found that when given slowly over 10 min, the biphasic BP response to dexmedetomidine is reduced [14].

Nalbuphine has been studied by many authors for its effect on intubating conditions and it has been found that at a dose of 0.2 mg/kg, it provides satisfactory intubating condition and sedation with stable hemodynamics [5,15-17]. Sharma K et al used nalbuphine in dose of 0.3 mg/kg and concluded it was better in attenuating vasopressor response to laryngoscopy. However, there was 12.5% incidence of respiratory depression in the group [18]. Recently, nalbuphine was used in a dose of 0.2 mg/kg for AFOI having similar effect as fentanyl with minimal side-effects [5]. Hence, we decided to use the same dose in this study as well.

In the present study, we found the RSS of 2 in all patients at the end of the test drug infusion. However, Mondal et al and Yousuf et al achieved a higher level of sedation (RSS=3) in all subjects with the same dose of dexmedetomidine [2,10]. Mondal et al gave both a bolus and an infusion of dexmedetomidine in their study accounting for higher sedation scores [2]. With nalbuphine in doses similar to present study, Chaudhari et al reported an RSS of 2.13±0.48 which is comparable to this study [17].

In this study, both the groups had median cough score of 2. The results are in concurrence with the studies by Mondal et al and Yousuf et al. [2,10]. However, Mourad et al in his study had more favourable cough score (CS=1) in most patients. This could be because the author had

used infusion of 0.5 µg/kg/hour in addition to bolus dose of 1 µg/kg dexmedetomidine [19].

In our study, tolerance to intubation was assessed by post intubation score (PIS). There was no statistically significant difference in the scores between the two groups. All but one patient in the two groups had PIS less than or equal to 2, i.e., minimal resistance to intubation. This is in concurrence with the studies by Mondal et al and Yousuf et al. [2,10].

The requirements of lignocaine 2% and propofol 1% to facilitate easy advancement of FOB through the glottic opening was similar in the two groups (p value>0.05). Hence, we can say that both the drugs provided comparable intubating conditions.

Hemodynamic parameters recorded at various time intervals from baseline to first 15 minutes after intubation were found to be statistically similar in two groups. Subjects in both the groups had increased HR and BP following intubation compared to baseline. This is in concurrence with the previous studies where either dexmedetomidine & nalbuphine was used for attenuation of intubation response [16,18]. Chalam KS et al, had more favorable hemodynamic parameters in his study, probably due to addition of infusion dose following bolus dose of dexmedetomidine [20].

The oxygenation during the AFOI was assessed by recording the SpO2 by pulse oximetry in both the groups. There was no episode of desaturation in any of the patient. None of the previous studies also describe clinically significant desaturation with use of any of these drugs in doses similar to our study [5,10,11,14,16-18].

This study has certain limitations. The patients included had no anticipated airway difficulty. Further studies can be conducted in patients with anticipated difficult airway to know the efficacy of the two drugs. We studied only a total of 60 patients. A larger patient population can be studied.

Conclusion

From the above study, we conclude that both intravenous dexmedetomidine 1 µg/kg and nalbuphine 0.2 mg/kg infused over 10 minutes, along with adequate airway topicalization and boluses of injection lignocaine and propofol, provided a calm and cooperative patient leading to favorable intubating conditions with minimal adverse effects on hemodynamic profile during awake fiberoptic intubation.

Thus, both, dexmedetomidine and nalbuphine, are safe and efficacious for awake fiberoptic intubation. Further studies involving a larger patient population with anticipated difficult airway are recommended.

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