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COMPARISON OF DEXMEDETOMIDINE-PROPOFOL WITH FENTANYL-PROPOFOL COMBINATION IN FLEXIBLE FIBREOPTIC BRONCHOSCOPY

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ABSTRACT

Background: Flexible fibreoptic brochoscopy is a widely used therapeutic and diagnostic procedure. Currently different anaesthetic agents are used for sedation during fibreoptic bronchoscopy. The primary aim of our study is to compare the respiratory and hemodynamic variables between dexmedetomidine-propofol with fentanyl-propofol during flexible bronchoscopy. Our secondary aim is to see cough reflex response, recovery time, number of propofol rescue doses used and satisfaction of bronchoscopist. **Patients and methods:** 100 patients were enrolled in the study and were randomised into two groups. [Group D (Dexmedetomidine-propofol) and Group F (Fentanyl-propofol)]. In group D, dexmedetomidine was given 1µg /kg slowly over a period of 10 minutes and group F received fentanyl 1µg/kg for sedation. An infusion of propofol at the rate of 100 µg/kg/min was started in both the groups for maintenance. Hemodynamic and respiratory parameters were recorded at baseline and at 5, 10, 15 and 20 minutes after induction and comparison was made between the two groups. Secondary objectives were cough reflex scores and discomfort level as assessed by the bronchoscopists. **Results:** The mean heart rate, systolic blood pressure and diastolic blood pressure were less in group D than Group F and were statistically significant. The mean respiratory rate and SPO_2 was statistically insignificant between the two groups. The RSS score at 5, 10 and 15 minutes between the two groups is statistically significant. The recovery time for D group was longer than the F group and was statistically significant. The development of bradycardia and hypotension was more in group D than in group F and was statistically significant. The number of propofol rescue doses between the two groups was statistically insignificant. **Conclusion:** Although Group D has better sedation score than group F during bronchoscopic procedures, but at the same time it also causes hemodynamic instability. Recovery time is also more in the group D group than group F. Therefore, we conclude that combination of fentanyl-propofol is better modality than dextmedetomidine-propofol in bronchoscopic procedures.

KEYWORDS: Dexmedetomidine-propofol, Fentanyl-propofol, bronchoscopists.

INTRODUCTION

Fibreoptic bronchoscopy is the standard procedure for the assessment, evaluation, diagnosis and management of a variety of respiratory problems. However, in view of its invasive nature, coughing, pain, dyspnea and other adverse events are usually associated.[1,2] In order to facilitate the procedure and to reduce the coughing, thereby increasing the patient compliance and comfort, patients are usually sedated during the procedure.[3,4] The use of sedatives not only can increase patients' safety and comfort[5] but also can make it easier for the bronchoscopist to perform the procedure and thus avoid extending its duration.[3] The ideal sedatives, in addition to alleviating the physiological response to airway irritation, should have a rapid onset and short duration of action with early recovery.[6] It has been the challenge for anesthesiologist to select appropriate degree of anesthesia to meet the procedural needs.[7] The most commonly used anesthetic agents include midazolam, propofol, etomidate, opioids, and inhalation anesthetics, however, each of these drugs has its limitations.[8–10] Combination of these drugs can result in severe respiratory depression, which is the most common complication and the reason of flexible bronchoscopy failure.[11,12] Therefore, to seek the reasonable combination of drugs, that can be used effectively during flexible bronchoscopy, is a must. We in our study aimed at comparing the effectiveness of a combination of most commonly used sedatives (dexmedetomidine-propofol and fentanyl-propofol) during brochoscopy.

PATIENTS AND METHODS

Our study enrolled 100 patients undergoing flexible brochoscopy with effect from April 2018 to May 2019. The patients were randomised into two groups Group D (Dexmedetomidine - Propofol Group) and Group F (Fentanyl–propofol group) by means of computer generated random numbers. The numbers in each group

were kept equal by means of permuted randomisation. All patients of ASA I and II in the age group between 18 to 60 years of both the sexes were included. Exclusion criteria included patients with ischemic heart disease, patients with heart block, severe respiratory disease, uncontrolled hypertension and patients with psychological disorders. The study protocol was approved by institutional ethical committee and was performed as per the declaration of modified Helsinki.

All patients planned for flexible brochoscospy underwent insertion of a peripheral 20G IV canula for fluid and drug administration. Monitors were connected for ECG, non invasive BP, capnography and mean Spo2. Supplemental O_2 inhalation via nasal canula at the rate of 3 -4 litres was started before the administration of IV propofol. Oxygen desaturation or hypoxemia (defined as SpO2 of less than 90%) was avoided by increasing oxygen flow to 6 L/minute or by various other airway assistive measures like chin lift, jaw thrust and tactile and verbal stimulation.

Flexible bronchoscopy

All patients were placed in a semi-recumbent position to perform transnasal bronchoscopy by either of the two experienced bronchoscopists. Bronchoscope of same diameter was used in all patients. Prior lidocaine nebulisation was given with 4 ml of 4 % lidocaine half an hour before the procedure.

In group D, dexmedetomidine was given 1µg /kg slowly over a period of 10 minutes and group F received fentanyl 1µg/kg for sedation. An infusion of propofol at the rate of 100 µg/kg/min was started in both the groups for maintenance. If the patients showed any signs of insufficient sedation like pain or discomfort, cough reflex, additional 2 ml of 2 % lidocaine was administered in to the trachea and bronchi through the side hole of bronchoscope. Rescue doses of propofol (0.5mg/kg) were administered if the patient showed discomfort in any of the two groups.

Outcome variables

The primary study objective is to compare respiratory parameters (mean spo2, RR), hemodynamic variables (SBP, DBP, HR) and Ramsey sedation score. The secondary aim is to see cough reflex response, recovery time, number of propofol rescue doses used, bronchoscopist satisfaction and to record any adverse event.

Hemodynamic and respiratory parameters were recorded at baseline and at 5, 10, 15 and 20 minutes after induction and comparison was made between the two groups.

Secondary objectives were cough reflex scores and discomfort level as assessed by the bronchoscopists. Cough reflex score and discomfort level was assessed on a 10-point visual analogue scale (VAS) on which 0 represented no cough and discomfort and 10 represented incessant coughing and greatest possible discomfort. At the end of the procedure, bronchoscopists were asked to record their perception of the patient's cough during the procedure. The bronchoscopists were asked to use a 10‑point VAS to rate patients' discomfort associated with the procedure.

Recovery time is the time between withdrawal of a flexible bronchoscope and the moment that the patient was fully awake and conversant (Ramsey sedation score 2).

Any cardiac adverse event like hypotension or hypertension, bradycardia or conduction disturbances were recorded and managed accordingly.

Any respiratory adverse event like decreased Oxygen saturation less than 90% or respiratory rate less than 10 breaths/ minute or laryngospasm were noted and managed accordingly.

Any other complication or event was taken note of.

Statistical analysis

The type of analysis carried in our study was descriptive. Mean ± SD and Number (N) and percentage (%) are presented as results on continuous measurements and categorical measurements respectively. An unpaired t test was used for normal distribution and unpaired Mann-Whitney test for asymmetric distribution for comparison of numeric variables. For comparison of categorical variables Fisher's exact test and $\chi 2$ test was used. All these statistical tests were two sided and were referred for P Values for their significance. Any P Value less than 0.05 ($P < 0.05$) was taken to be significant.

RESULTS

The two groups were comparable in terms of age, sex, weight, ASA class, indication of bronchoscopy as is mentioned in Table 1.

Changes in hemodynamic variables.

The mean heart rate at baseline was statistically insignificant between the two groups. The mean heart rate at 5, 10 ,15 and 20 minutes was less in Group D as compared to the Group F but remained statistically significant throughout at 5,10,15 and 20 minutes. The heart rate was recorded as lowest in group D at 5 minutes. (Table 2). The mean baseline systolic arterial blood pressure between the two groups was comparable and statistically non significant (p value >0.05). The mean systolic arterial blood pressure at 5 , 10, 15 and 20 minutes was less in Group D than in Group F but the difference was statistically significant at 5, 10 15 and at 20 minutes respectively. (Table 2)

The baseline Diastolic Arterial Pressure (mmHg) between the two groups was comparable and statistically not significant. The Diastolic Arterial Pressure (mmHg)

at 5, 10, 15 and 20 minutes was less in D group as compared to the F group. The difference was statistically significant at 5 min, 10 min, 15 minutes and at 20 minutes.

Changes in respiratory variables

The mean baseline respiratory rates (breaths per minute) of the two groups were comparable and the differences were not statistically significant. The mean respiratory rate at 5, 10, 15 and 20 minutes was lower in group F compared to group D and the difference was statistically insignificant throughout the procedure till 20 minutes [P value >0.05]. (Table 2)

The mean baseline SpO2% between the two groups was comparable and the difference was not statistically significant. The mean SpO2% in F group was lower as compared to D group but was statistically significant only at 5 minutes of the procedure. The mean SpO2% at 10, 15 and 20 minutes was comparable and statistically insignificant between the two groups (Table 2).

Hemodynamic and respiratory parameters were recorded at the baseline and found to be statistically insignificant.

RSS score at baseline and at 5,10, 15 and 20 minutes in two groups is shown in Table 2. The RSS score at 5, 10 and 15 minutes between the two groups is statistically significant.

VAS Score, additional lidocaine administration, and recovery times.

There were no significant differences in VAS scores for coughing and discomfort between the two groups as rated by bronchoscopists (Fig. 5). There was also no significant difference between the two groups regarding the number of times that additional lidocaine was necessary. (Table 3) The recovery times for D group was longer than the F group and was statistically significant. (p value <0.05) [Table 3].

Adverse events: The development of adverse cardiac events like hypotension was statistically significant between the two groups (Group D =7 cases and Group F =1 case) and there was also a significant difference in bradycardia between the two groups (13 in Group D and 3 in Group F). Two patients in the group F developed severe hypoxemia which was not statistically significant between the two groups. The number of propofol rescue doses between the two groups was statistically insignificant. [Table 3]

Table 1.

Parameter	Group D	Group F	P value
Age	49.77±7.60	50.47±6.94	>0.05
Sex, Male/female (%)	28/22, (54/46)	26/24,(52/48)	>0.05
BMI	23.21±3.06	22.69±3.17	>0.05
ASA class, I II	 34 16	 30 20	>0.05
Duration of bronchoscopy	21.50±5.93	22.30±6.75	>0.05
Indication of bronchoscopy 1, BAL 2,Transbronchial biopsy 3, Inspection 4, others	 15 20 10 5	 17 19 11 3	>0.05
Type of bronchoscopy 1, Infection 2, Haemoptysis 3,Suspicion of malignancy 4,Others	 18 22 9 1	 15 20 14 2	>0.05

Table 2.

Time interval	Parameters		Group D		Group F		P value
			Mean	S.D	Mean	S.D	
Baseline	Heart rate		88.07	6.234	89.50	5.333	>0.05
	SABP		120.2	10.12	116.4	11.23	>0.05
	DABP		84.24	4.616	82.34	3.89	>0.05
	RR		13.01	1.42	12.24	1.30	>0.05
	SPO_2		97.30	0.6	97.21	0.5	>0.05
	RSS	1	27	54	25	50	>0.05
		2	23	46	25	50	
5 minute	Heart rate		78.49	6.203	83.06	5.501	<0.05
	SABP		105.20	4.965	112.2	10.24	<0.05
	DABP		73.80	4.06	80.30	4.50	<0.05
	RR		12.99	1.1	12.05	1.0	>0.05
	SPO_2		98.01	0.8	95.01	0.7	<0.05
	RSS	3	3	6	15	30	<0.05
		4-5	47	94	35	70	
10 Minute	Heart rate		79.05	7.01	84.08	5.61	<0.05
	SABP		106.30	4.995	114.2	10.98	<0.05
	DABP		74.05	4.07	82.03	4.56	<0.05
	RR		13.02	1.2	11.95	1.1	>0.05
	SPO_2		99.60	1.0	99.50	0.9	>0.05
	RSS	3	4	8	17	34	<0.05
		4-5	46	92	33	66	
15 Minute	Heart rate		80.55	7.02	86.06	5.80	<0.05
	SABP		108.20	5.02	117.4	11.02	<0.05
	DABP		75.05	4.58	83.58	4.67	<0.05
	RR		13.30	1.30	12.85	1.34	>0.05
	SPO_2		99.68	1.2	99.50	1.02	>0.05
	RSS	3	3	7.5	12	27.90	<0.05
		4-5	37	92.5	31	72.10	
20 minute	Heart rate		81.00	7.05	87.08	5.82	<0.05
	SABP		110.20	6.05	120.23	12.0	<0.05
	DABP		76.06	4.98	85.99	4.98	<0.05
	RR		13.58	1.31	13.00	1.36	>0.05
	SPO_2		99.70	1.3	99.60	1.12	>0.05
	RSS	3	0	0	1	8.32	> 0.05
		4-5	9	100	10	91.78	

Table 3.

Parameter	Group D		Group F		P value
	Mean	SD	Mean	SD	
Anaesthesia onset time	7.05	1.2	9.03	1.5	<0.05
Recovery time	10.74	1.73	8.62	1.61	<0.05
Additional 2ml of 1% Lidocaine	n=50		N=50		>0.05
0	23		24		
1	24		22		
>2	3		4		
No of propofol rescue doses used	1.930	0.89	2.30	1.52	>0.05
Cough and discomfort score	Assessed by bronchoscopist		>0.05		

DISCUSSION

The two groups were comparable in terms of age, sex distribution, BMI, ASA status, diagnosis, duration of surgery, the procedure performed and mean baseline hemodynamic and respiratory parameters.

The Mean heart rate, Systolic Arterial Pressure (SABP) and Diastolic Arterial Pressure (DABP) during the procedure was less in DP group as compared to the FP group. Intraoperative mean systolic and diastolic blood pressure and heart rate in DP group were lower than their baseline values and the corresponding values in FP group. A significant decrease in the heart rate from

baseline following dexmedetomidine infusion in children undergoing MRI examination were also reported by Korugulu A et al.[13] Tosun Z et al[14] who compared the effects of dexmedetomidine-ketamine [DK] and propofol-ketamine [PK] combinations on hemodynamics, sedation level, and the recovery period in pediatric patients undergoing cardiac catheterization also reported similar results.

Hypotension and bradycardia have been reported in dexmedetomidine infusions, particularly with high bolus dosing regimens, in patients with pre-existing cardiac problems and a loading dose infusion given over 10 minutes.[15-18] These results also co-relate well with the study of Ragab A et al,[20] who compared the effects of dexmedetomidine/ morphine/ propofol with benzodiazepines/ morphine/propofol as adjuncts to local anesthesia during rhinoplasty–on analgesia, sedation, respiratory and hemodynamics variables.

Hypotension is commonly reported with Dexmedetomidine therapy due to its sympatholytic effect.[20-23] Hyo-Seok Na et al[24] found that dexmedetomidine use resulted in significantly lower systolic blood pressures compared to propofol and alfentanil when used for monitored anaesthesia care. Parikh DA et al[25] reported that intraoperative heart rate and mean arterial pressure following dexmedetomidine therapy were lower than the baseline values and the corresponding values in Midazolam-Fentanyl therapy (P Value < 0.05) during tympanoplasty.

The mean respiratory rate was more stable in the D group than the F group. The mean respiratory rate was lower in the F group than the D group throughout the procedure but was statistically insignificant [p value >0.05]. The mean SpO_2 between the two groups was comparable throughout the procedure except at 5 minutes. The mean SpO_2 at 5 minutes was lower in the F group than the D group and was statistically significant. Moreover, the mean SpO_2 was more stable in the D group than F group during the procedure. Dexmedetomidine does not cause respiratory depression because its mechanism is not mediated by the γ- amino butyric acid system.[15, 26-28] Cooper L et al[29] in their randomised controlled trial on dexmedetomidine also reported that it is effective in achieving adequate levels of sedation without increasing the rate of respiratory depression or decreasing oxygen saturation compared with standard therapy (midazolam and opioids). Na HS et al[24] in their study reported that although dexmedetomidine provided a more stable respiratory rate intraoperatively, the effects of dexmedetomidine as well as propofol and alfentanil on respiratory rate were comparable when used for monitored anaesthesia care. Anchalee Techanivate et al[30] in their study found that all patients maintained a normal respiratory rate and oxygen saturation during the procedure with no differences in the respiratory end points of two groups i.e. Group P (fentanyl/propofol) and Group D (dexmedetomidine/fentanyl with propofol).

In our study the baseline Ramsay Sedation Scores of the two groups were comparable and the difference was not statistically significant (P Value 0.84). Higher Ramsay Sedation Scores in our study were observed in the DP group as compared to the FP group during the procedure (P> 0.05) and returned to statistically insignificant difference at 20 min (P Value > 1.00). Ali AR et al[31] in their comparative study of propofol/dexmedetomidine group and propofol/fentanyl group in children undergoing ESWL reported a better sedation analgesia profile in propofol/dexmedetomidine group. Ragab A et al[20] and Koroglu A et al[13] in their study also recorded a better level and higher rate of adequate sedation intraoperatively in the dexmedetomidine group. Comparable results were found by Dere K et al,[32] who concluded that RSS scores in Dexmedetomidine group were significantly higher than the midazolam/fentanyl group at the 10 and 15 minute in patients undergoing colonoscopy under conscious sedation.

The recovery times for D group was longer than the F group and was statistically significant in our study. Waleed MA et al[33] in their comparative study 39 have reported a longer recovery in their study in patients receiving dexmedetomidine. Ryu JH et al[34] in a randomised study 40 also recorded a recovery time of 18.4 min in the dexmedetomidine propofol group, which is relatively longer than our study. Anchalee Techanivate et al[30] in their study found longer recovery times in Group P (fentanyl / Propofol) as compared to group Group D (dexmedetomidine/fentanyl with Propofol) (Group D vs Group P: 6min vs 10.2 min, P Value 0.038).

In the present study, the average number of propofol rescue doses (bolus of 0.5 mg/kg whenever patient showed discomfort) used during the procedure were statistically insignificant. Ali AR et al[31] in their study reported that propofol/dexmedetomidine combination was accompanied with less propofol consumption, prolonged analgesia and lower incidence of intraprocedural and postprocedural complications compared to propofol/fentanyl group. . Tosun Z et al[14] also reported that the number of patients who required additional propofol was significantly higher in the PF group compared to the PK group (50% VS 17 %, P Value <0.01).

Hypotension and bradycardia is commonly reported with dexmedetomidine therapy due to its sympatholytic effect.[20-23] Ayden Arden et al[35] reported 5% incidence of bradycardia which required treatment using propofol/fentanyl in children for ESWL. Hyo-Seok Na et al[24] reported a 3.2 % incidence of adverse cardiac events with dexmedetomidine infusion. Arboledas FJ et al [36] reported no adverse cardiac events in patients in whom sedoanalgesia was performed using Fentanyl/Propofol. Ryu JH et al[34] reported no adverse

cardiac events in 35 patients undergoing flexible brochoscopy using dexmedemidine-propofol sedation analgesia protocol.

In our study, 2 patients in the fentanyl propofol group had an adverse respiratory event (Desaturaton i.e., SpO2<90%, respiratory rate < 10 breaths/min) and none of the patients in demedetomidine-propofol group developed any adverse event but difference was not statistically significant (P Value 0.242). Dexmedetomidine is unique in that it does not cause respiratory depression, because its mechanism is not mediated by the γ-aminobutyric acid system.[15,26-28] Ayden Erden et al[35] reported 25% incidence of desaturation using propofol/fentanyl in children for ESWL. Alados-Arboledas FJ et al[36] reported no adverse respiratory events in patients in whom sedoanalgesia was performed using fentanyl/propofol.

In the present study, higher percentage of operator satisfaction (bronchoscopist) was observed in patients who underwent bronchoscopy using fentanyl/propofol protocol (Group F), however the difference was not statistically significant (P Value 0.078).

CONCLUSION

In conclusion, with the exception of few adverse respiratory events, the present study found that fentanyl-propofol (Group F) was superior to dexemedetomidine-propofol (Group D) in providing satisfactory sedation and stable hemodynamics during flexible bronchoscopy. Furthermore, propofol-fentanyl had lesser recovery time and better operator satisfaction.

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