TOTAL INTRAVENOUS ANAESTHESIA USING PROPOFOL AND KETAMINE COMBINATION VERSUS PROPOFOL AND FENTANYL COMBINATION IN PATIENTS UNDERGOING BRONCHOALVEOLAR LAVAGE

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ABSTRACT

BACKGROUND

Flexible bronchoscopy being an invasive procedure can induce cough, pain etc., thus requiring deep sedation or anaesthesia to offset these adverse effects.

Aim- To compare the combination of Propofol with Ketamine (Group PK) versus combination of Propofol with Fentanyl (Group PF) for total intravenous anaesthesia (TIVA) in 100 patients.

MATERIALS AND METHODS

100 patients undergoing flexible bronchoscopy for bronchoalveolar lavage were divided into two groups- Group PK where 50 patients received propofol 2.0 mg/kg and ketamine 1.0 milligram/kg IV and Group PF where 50 patients received propofol 2.0 mg/kg and Fentanyl 1.0 microgram/kg IV in a double-blind study. The parameters measured between the groups included haemodynamics, maintenance of oxygen saturation, cough, sedation levels, need for rescue doses, recovery time as well as pulmonologist and patient satisfaction.

RESULTS

Almost all the measured parameters between Group PK and Group PF were similar and statistically insignificant. The only statistically significant difference was found in recovery time being longer in Group PK at 14.1 ± 0.32 mins compared to Group PF at 10.3 ± 1.64 mins.

CONCLUSION

We can hereby conclude that Total Intravenous Anaesthesia (TIVA) using Propofol (2 mg/kg) and Ketamine (1 mg/kg) combination versus Propofol (2 mg/kg) and Fentanyl (1 microgm/kg) combination for flexible bronchoscopy in patients undergoing bronchoalveolar lavage are similar in terms of all parameters measured, except a longer duration of recovery time for propofol-ketamine group.

KEYWORDS

Flexible Bronchoscopy, TIVA, Propofol, Ketamine, Fentanyl.

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BACKGROUND

Flexible bronchoscopy is being performed by pulmonologists to diagnose diseases of the tracheobronchial tree and obtain tissue samples or lavages for diagnosis. Some Bronchoscopists perform the procedure without sedation. But since it is an invasive procedure it can induce coughing, pain, dyspnoea and other adverse effects.[1,2] Some bronchoscopists themselves administer sedation using drugs such as midazolam to the patients to facilitate better co-operation and procedure tolerance. But this has its pitfalls such as inadequate dosage results in non-cooperation by patient, pain, cough or too deep a sedation causing apnoea requiring intervention. A study by Hatton et al suggested that although midazolam may facilitate the performance of the procedure for the operator, it does not improve patient comfort.[3] Certain other studies by Ni YL et al[4] and one by Morris et al[5] have shown that with the proper patient and drug selection, conscious sedation reduces patient discomfort and improves satisfaction in flexible bronchoscopy.

The choice of drugs should be such that they alleviate the physiological response to airway irritation during the procedure, have a rapid onset and a short duration of action in addition to allowing rapid recovery.[6] In our centre we performed a study using a combination of Propofol and ketamine versus a combination of Propofol and fentanyl as TIVA or Total intravenous anaesthesia, for performing flexible bronchoscopy for patients undergoing bronchoalveolar lavages for diagnosis of infection.

Aims and Objectives

To compare the combination of Propofol with Ketamine (Group PK) versus combination of Propofol with Fentanyl (Group PF) for total intravenous anaesthesia in 100 patients, 50 of each group in terms of intraoperative Haemodynamics,

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SpO2, cough, sedation levels, need for rescue doses of local anaesthetic and propofol, time of recovery, Pulmonologist satisfaction and patient comfort.

MATERIALS AND METHODS

This was a double-blinded, randomised, controlled trial that was done over a period of 3 years (Feb 2015 - Jan 2018), following Ethical Committee approval in 100 patients with infections for bronchoalveolar lavage.

Inclusion Criteria

Patients of either sex with ASA Grade-I and Grade-II. Patients aged between 20 - 60 years with suspected lung infections requiring bronchoalveolar lavages.

Exclusion Criteria

Nil.

Study Design

Double-blinded, randomised, controlled trial.

Preoperative Period

Pre-anaesthesia evaluation included a detailed history and physical examination to rule out co-morbidities and to optimise the patient. Routine blood investigations included a Haemoglobin percentage, blood sugar, urea, creatinine, bleeding time, clotting time, blood grouping-typing and ECG. The anaesthetic procedure was explained to the patient and informed written consent was obtained.

The patients were allocated to either of the two groups by randomisation using manual lottery method, details of which are not revealed to the patient. Depending on the group, ketamine 1.0 milligram/kg or Fentanyl 1.0 microgram/kg body weight was loaded, diluted to 5 mL and handed over to the anaesthesiologist administering anaesthesia, who was not aware of the drug contained in the syringe.

Equipment Used

18-G Cannulae, IV fluid Normal saline, Drugs, Disposable plastic syringes, BPL Multiparameter Monitor with ECG, SpO_2, HR, NIBP, RR monitoring, Anaesthesia machine, Resuscitation Equipment as standby.

Intraoperative Period

On being shifted to the operating room, intravenous cannulation was done using 18-G cannulae and IV fluid Normal saline started @ 100 mL/hour. The patient was connected to the monitor and baseline readings of Electrocardiogram (ECG), Oxygen saturation (SpO_2), Heart rate (HR), Non-invasive blood pressure (NIBP) and respiratory rate (RR) was obtained. The readings were obtained every five minutes till shift out from procedure room. The patient was then premeditated with injection glycopyrrolate 0.2 mg + injection ondansetron 4 mg + injection midazolam 1 mg. These patients were assigned to either one of the two groups that received drugs as appropriate.

Group PK- 50 patients received propofol 2.0 mg/kg and ketamine 1.0 milligram/kg IV.

Group PF

50 patients received propofol 2.0 mg/kg and Fentanyl 1.0 microgram/kg IV.

The induction parameters were non-responsiveness to verbal commands and loss of eyelash reflex. Spontaneous respiration was maintained with 100% O2 using face mask and Bain's circuit with assistance, increased oxygen delivery and airway manoeuvres in times of apnoea- absence of breathing attempts for greater than or equal to 20 seconds or hypoventilation with respiratory rate < 8/minute or desaturation or hypoxaemia when SpO2 was < 90% for > 30 sec.[7]

Throughout the procedure, the patient received supplemental oxygen at a rate of 4 L/min via nasal cannula. In case of Hypotension or BP < 90/50 mmHg, a bolus of 5 mg ephedrine was given; for Bradycardia (HR < 60 beats/min) 0.3 mg atropine; for Hypertension (SBP > 180 mmHg or DBP > 100 mmHg) and tachycardia (HR > 100 beats/min and/or variation of > 20% from baseline value). Rescue doses of boluses of local anaesthetic spray 2 mL of 1% lidocaine through the side hole of the flexible bronchoscope and bolus of propofol 20 mg IV was given. The number of rescue doses were noted.

Flexible bronchoscopy was performed by an experienced bronchoscopist who used a bronchoscope of the same diameter to perform transnasal bronchoscopy in all patients. As a routine, all patients received sprays of 2 mL of 1% lidocaine over the vocal cords, trachea and both main bronchi. No inhaled lidocaine was administered prior to the procedure.[8]

In addition to monitoring HR, NIBP and SpO2 at every 5 mins intervals; cough, level of sedation, duration of procedure and recovery were noted. The entire procedure lasted over 15 – 20 mins. At the end of the procedure, the bronchoscopist was asked to use a 10-point VAS to rate patient's discomfort during the procedure, where 0 represented no discomfort and 10 represented maximum discomfort. The patient was asked to rate their discomfort using the same 10-point VAS, two hours after the end of the procedure.

Sedation is assessed by using various scales. The modified Wilson scale is a variant of the Ramsay[9] and Wilson[10] scales is simple to use with an inter-rater agreement of 84%.[11] But for more precision, the observer's assessment of alertness/sedation (OAA/S) was chosen, as it has an inter-rater agreement that varies between 85% and 96% depending on the level of sedation[12] where scores corresponding to sedation levels are 5 - alert, 4 - light, 3 - moderate, 2 - deep and 1 - unconscious.

Statistical Methods

A convenience sample size of fifty patients in each group was chosen based on the inflow of patients at our centre. Our study was similar to studies by Grendelmeier et al who investigated the safety of sedation with propofol in flexible bronchoscopy[13] in a large group and another smaller randomised study by Feng Yuan et al[14] using Dexmedetomidine-Fentanyl versus Propofol-Fentanyl in flexible bronchoscopy with 50 participants in each group.

A statistical analysis was performed using the Statistical Package for Social Sciences (SPSS for Windows version 18.0. Continuous outcomes and Categorical data were examined and analysed with the student's t-test or the Fisher's exact test or chi-square test as appropriate. A "p" - value of < 0.05 was considered as statistically significant.

	Group PK (n=50)	Group PF (n=50)	Significance
Age	42.06± 0.62	41.58± 0.97	Not significant
Gender Males/Females	31(62)/ 19(38)	34(68)/ 16(32)	Not significant
Body Mass Index, kg/m2	21.36±3.15	22.21±3.11	Not significant
ASA Class I/ II	21(42)/ 29(58)	24(48)/ 26(52)	Not significant
Duration of Procedure	18.53±2.02	19.12 ±1.91	Not significant
Indications for Flexible Bronchoscopy	Bronchoalveolar lavage	Bronchoalveolar lavage	Not significant

Table 1. Demographic and Baseline Characteristics of Patients undergoing Flexible Bronchoscopy

Values presented with in ( ) as percentage %.

	Group PK (n=50)	Group PF (n=50)	"P" value	Significance
Haemodynamics:				
Heart Rate varying more than 20% from baseline				
Tachycardia	22 (44)	18 (36)	0.2320	Not significant
Bradycardia	0	4 (8)	1.0000	Not significant
Systolic Blood Pressure Varying more than 20% from Baseline				
Hypertension	27 (54)	22 (44)	0.2112	Not significant
Hypotension	5 (10)	8 (16)	0.7576	Not significant
Diastolic Blood Pressure Varying more than 20% from Baseline				
Hypertension	28 (56)	25 (50)	0.3079	Not significant
Hypotension	5 (10)	8 (16)	0.7576	Not significant
Oxygen Saturation:				
SpO2 between 90% - 93%	28 (56)	35 (70)	0.7936	Not significant
SpO2 falling below 90% (hypoxaemia) and apnoea	0	0		Not significant
Cough	12 (24)	15 (30)	0.6790	Not significant
Sedation Scoring- MOAS/S (5, 4, 3, 2, 1)				
5th minute	0/2/3/40/5	0/4/6/38/2	0.3814	Not significant
10th minute	0/0/2/45/3	0/0/3/44/3	0.4298	Not significant
Rescue Doses				
0	24 (48)	22 (44)	0.3472	Not significant
1	16 (32)	17 (34)	0.5238	Not significant
More than 2	10 (20)	11 (22)	0.5304	Not significant
Time of Recovery	14.1± 0.32 mins	10.3±1.64 mins	Less than 0.0001	Significant
Pulmonologist Satisfaction (VAS score 2 or less than 2)	49/50 (98)	48/50 (96)	0.4328	Not significant
Patient Comfort (VAS score 2 or less than 2)	46/50 (92)	48/50 (96)	0.5552	Not significant

Table 2. Intra- and Post-Operative Parameters

Values presented with in ( ) as percentage %.

RESULTS

Comparison of Age, Gender, Body mass index, ASA class, indications for bronchoscopy and duration of procedure revealed no statistically significant differences between the two groups. Similarly, on comparison of haemodynamics, SpO_2 changes, cough, sedation scores, need for rescue dose and pulmonologist and patient satisfaction there was no statistical difference. The time of recovery alone was statistically significant with longer time taken for recovery in Group PK or ketamine group compared to Group PF or fentanyl group.

DISCUSSION

Total Intravenous Anaesthesia (TIVA) for bronchoscopy is gaining popularity as it facilitates patient co-operation, comfort and safety, as also making it easier and comfortable for the bronchoscopist. Ambulatory anaesthesia, wherein the patient is admitted and discharged on the same day can also be achieved with TIVA. We used a combination of propofol 2.0 mg/kg and ketamine 1.0 milligram/kg IV for one group of 50 patients (Group PK) and another 50 patients received a combination of propofol 2.0 mg/kg and Fentanyl 1.0 microgram/kg IV (Group PF).

Propofol is a common induction agent, which is non-opioid and non-barbiturate sedative hypnotic. Its rapid onset, offset of action and smooth recovery make propofol very appealing, but dose-dependent respiratory depression and hypoxaemia are possible.[15,16,17] A dose of 2 mg/kg of propofol was chosen, as it was found to be a satisfactory induction dose by Briggs et al as compared to lower doses.[18] But if used as a sole agent the dose requirement is higher, which may be associated with haemodynamic and respiratory effects like hypotension, bradycardia, apnoea or hypoventilation.[19] These effects may be decreased or even offset by using it with other agents such as ketamine. A variety of sedatives including benzodiazepines, opioids and propofol have been used for bronchoscopy. However, certain studies have shown that following the use of sedatives, recovery times are longer and more desaturations occur.[20,21]

Ketamine which is water soluble intravenous anaesthetic belongs to phencyclidine group of drugs and having hypnotic, analgesic and amnesic properties.[22] Administering a small dose of other anaesthetic agent to reduce the total dose of the induction agent is known as co-induction and it provides haemodynamic stability.[23] In our study, we gave the entire dose of 2 mg/kg propofol and hence did not measure the dose reduction of propofol when used with a co-induction agent. Certain studies[24] have proved that co-induction of ketamine with propofol produces lesser fall in blood pressures

compared to induction with propofol alone, something that was observed in our study also though haemodynamic stability was maintained with both groups. A comparison of combination of propofol-fentanyl and propofol with ketamine in 18 patients who underwent non-cardiac surgery was done by Guit et al[25] who concluded that propofol ketamine combination resulted in haemodynamically stable anaesthesia without the need for additional analgesics. In ketamine group, the occurrence of tachycardia and hypertension was higher compared to fentanyl group, whereas bradycardia and hypotension was more in fentanyl group, but both being statistically insignificant. This is similar to effects seen in certain other studies such as by Fernando et al.[26,27] This can be explained by the fact that fentanyl can cause hypotension and bradycardia due to activation of the Bezold-Jarisch reflex triggered by a reduced cardiac venous return in combination with affective mechanisms such as pain or fear and Propofol being venodilatory. But the number of patients in which it occurred was less as the stimulation due to bronchoscopic procedure persists producing a counter adrenergic drive. According to a study by Adachi et al,[28] haemodynamic responses during flexible bronchoscopy reflect an increase in HR and blood pressure. Ketamine is also a very economical drug compared to fentanyl, dexmedetomidine or butorphanol and fentanyl being a commonly used opioid analgesic.

Fall in saturation between 90% - 93% occurred in both the groups, slightly more in fentanyl group compared to ketamine group, but statistically insignificant. This difference is attributed to the respiratory stimulant effect of ketamine compared to fentanyl, which being an opioid causes depression of respiratory centres in the brain. Otherwise, there was no hypoxaemia or apnoea. This is similar to studies by Fernando[27] and Ramakrishna.[29]

There was no statistical differences in cough, sedation scores and need for rescue doses in both the groups. Recovery time alone was statistically significant with recovery in ketamine group being 14.1 ± 0.32 mins compared to 10.3 ± 1.64 mins in fentanyl group. According to the study conducted by Knox et al[30] in 1970, recovery of anaesthesia with ketamine induction lasted for 13.2 +/- 1.25 minutes.

The 10-point VAS scores for comfort as recorded by the bronchoscopist and patients showed no difference between the groups. Emergence delirium can be a matter of concern in ketamine group, but in our study, post-operative behaviour was normal in all patients and none of the patients had emergence delirium in the ketamine group. This is similar to a study conducted by Sherry N Rizk and Enas M Samir.[31] The aetiology of Emergence delirium after ketamine administration is not clear with the probable mechanism being a variable rate of neurological recovery of neurons in the brain, which is circumvented on co-induction with Propofol and thus eliminating its occurrence in the Propofol-Ketamine group.

Limitations of our Study

We did not have a group receiving propofol sedation alone. Secondly, decrease in induction dose of propofol when used with ketamine or fentanyl was not studied.

CONCLUSION

We can hereby conclude that sedation using a combination of Propofol (2 mg/kg) and Ketamine (1 mg/kg) versus combination of Propofol (2 mg/kg) and Fentanyl (1 microgm/kg) for flexible bronchoscopy in patients undergoing bronchoalveolar lavage are similar in terms of haemodynamics, maintenance of oxygen saturation, cough, sedation levels, need for rescue doses as well as pulmonologist and patient satisfaction. The only difference being in the longer duration of recovery time for propofol-ketamine group.

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