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Retrospective Study

Intensivist-based deep sedation using propofol for pediatric outpatient flexible bronchoscopy

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Abstract

AIM

To evaluate the safety and efficacy of sedating pediatric patients for outpatient flexible bronchoscopy.

METHODS

A retrospective chart review was conducted for all children, age 17 years or under who underwent flexible bronchoscopy under deep sedation in an outpatient hospital-based setting. Two sedation regimens were used; propofol only or ketamine prior to propofol. Patients were divided into three age groups; infants (less than 12 mo), toddlers (1-3 years) and children (4-17 years). Demographics, indication for bronchoscopy, sedative dosing, sedation and recovery time and adverse events were reviewed.

RESULTS

Of the total 458 bronchoscopies performed, propofol only regimen was used in 337 (74%) while propofol and ketamine was used in 121 (26%). About 99% of the procedures were successfully completed. Children in the propofol + ketamine group tend to be younger

and have lower weight compared to the propofol only group. Adverse events including transient hypoxemia and hypotension occurred in 8% and 24% respectively. Median procedure time was 10 min while the median discharge time was 35 min. There were no differences in the indication of the procedure, propofol dose, procedure or recovery time in either sedative regimen. When compared to other age groups, infants had a higher incidence of hypoxemia.

CONCLUSION

Children can be effectively sedated for outpatient flexible bronchoscopy with high rate of success. This procedure should be performed under vigilance of highly trained providers.

Key words: Pediatric flexible bronchoscopy; Propofol; Deep sedation; Procedural sedation; Sedation time; Hypoxemia

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Core tip: In this retrospective study "Intensivist-based deep sedation using propofol for pediatric outpatient flexible bronchoscopy", we are presenting our center data on pediatric patients who underwent flexible bronchoscopy under deep sedation using propofol. The study outlines our experience with intensivist-based procedural sedation as an effective strategy to facilitate successful completion of flexible bronchoscopy. This is the largest retrospective study describing the use of propofol-based procedural sedation in the outpatient settings for pediatric flexible bronchoscopy.

Abulebda K, Abu-Sultaneh S, Ahmed SS, Moser EAS, McKinney RC, Lutfi R. Intensivist-based deep sedation using propofol for pediatric outpatient flexible bronchoscopy. *World J Crit Care Med* 2017; 6(4): 179-184 Available from: URL: <http://www.wjgnet.com/2220-3141/full/v6/i4/179.htm> DOI: <http://dx.doi.org/10.5492/wjccm.v6.i4.179>

INTRODUCTION

In the last two decades, flexible bronchoscopy (FB) has become an increasingly important outpatient tool used in the evaluation of pulmonary abnormalities in children^[1,2]. As FB allows direct visualization of the patient's upper and lower airway larynx^[3], it has been used as a diagnostic and therapeutic tool for chronic cough, wheezing, cystic fibrosis and infection etiologies in immunocompetent and immunocompromised patients^[4] to diagnose various congenital or acquired pediatric airway anomalies/abnormalities.

While the need for appropriate sedation for FB is controversial in adults^[5], deep sedation is generally needed in children due to their developmental capabilities and airway anatomy in order to blunt the airway protective

reflexes and suppress the cough stimulus. Using deep sedation not only decreases a child's distress and discomfort but also significantly increases the chance of a successful completion of the procedure^[1,6]. Multiple sedation regimens and route had been evaluation including nasal, oral, intravenous and topical anesthetic^[7]. Commonly used drugs for sedation for FB include a benzodiazepine and opioids combination or ketamine with or without benzodiazepine^[6,8,9].

Propofol is an *iv* sedative-hypnotic agent that is used for induction and maintenance of deep sedation and general anesthesia^[10]. Propofol has many properties, including a rapid onset, short duration of action with rapid recovery time and minimal adverse events, which makes it an ideal agent for pediatric sedation in the outpatient setting^[11]. Emerging data support the safety and efficacy of using propofol outside the operating room for pediatric outpatient procedures by qualified physicians trained in sedation with advanced airway management^[1,12]. Additionally, with increasing numbers of pediatric patients undergoing diagnostic and therapeutic FB and the relative shortage of anesthesiologists and operating room availability, other pediatric subspecialists, such as pediatric critical care physicians, have stepped in to provide pediatric procedural sedation^[13-15].

Ketamine is a dissociative agent that has analgesic, sedative and amnestic properties. It has been frequently used to facilitate painful procedures in children and has proven to be safe and effective in numerous studies^[16]. However, despite the reported safety of ketamine in these studies, it had been reported that high dose ketamine could result in respiratory depression and excessive salivary secretions leading to adverse respiratory events^[17].

The combination of propofol and ketamine for pediatric sedation had been reported to provide optimal hemodynamic stability and reduced adverse effects when compared to propofol alone^[18-20]. Additionally, the combination of propofol and ketamine had been shown to be beneficial in other medical fields because of allowing lower doses of propofol resulting in the reduction of the undesirable adverse effects^[20]. Many authors reported the advantages of propofol-ketamine combination in terms of hemodynamic profile and pain control in cancer patients undergoing painful procedures^[19].

The purpose of this study is to review the author institution's experiences using propofol-based deep, procedural sedation regimens for pediatric flexible bronchoscopy in an outpatient setting.

MATERIALS AND METHODS

This retrospective study was approved by the institutional review board of the Indiana University. All pediatric patients between the ages of two months to seventeen years of age undergoing deep sedation for flexible bronchoscopy from March 2007 to August 2012 were included. Patients were divided into three age groups; infants (less than 12 mo), toddlers (1-3

years) and children (4-17 years). Patients in whom flexible bronchoscopy evaluation was performed in the Pediatric Intensive Care Unit through tracheostomy or endotracheal tube were excluded. All bronchoscopies were performed at the Riley Hospital for Children at Indiana University Health System by a pediatric pulmonologist with the assistance of a respiratory therapist at our dedicated outpatient sedation room.

History and physical exam were performed and documented according to the American Academic of Pediatrics (AAP) guidelines for sedation^[21]. Written consent was obtained from the parents or guardian prior to the procedure. Sedation was performed by a sedation team consisting of a pediatric intensivist and two sedation nurses with a pediatric critical care background who monitored the patient during and after each procedure. Guidelines have been laid down by the AAP regarding monitoring, management and discharging children during procedural sedation^[21]. All patients were either classified as ASA-PS II or I per American Society of Anesthesiologists-Physical Status classification system. Patients were without any oral intake for at least 6 h prior to the procedure and had an intravenous catheter placed by sedation team. Physiologic parameters such as heart rate, respiratory rate, oxygen saturation and noninvasive blood pressure were measured every 5 min throughout the procedure and every 15 min after its completion until the patient was fully awake. Supplemental oxygen (2 L per min) was administered *via* nasal cannula to the majority of the patients (92%) before and during the procedure. Prior to sedation, each patient received viscous lidocaine to the nare, a transnasal approach was used for all procedures. Additional doses of lidocaine were applied to the vocal cords, trachea and major bronchi as required per pulmonologist.

Two sedation strategies were used; intravenous (*iv*) propofol only (P-O) and *iv* ketamine prior to *iv* propofol (K-P), solely based on the intensivist preference. When ketamine was used, it was administered as an initial bolus of 0.5 mg/kg for patients who weigh less than 20 kg and 0.25 mg/kg for patient's weight more than 20 kg. Propofol was administered as an initial bolus of 1-2 mg/kg with additional boluses of 1 mg/kg as needed to achieve deep sedation (level 3) based on University of Michigan sedation scale^[22].

Adverse events were recorded including development of hypoxemia (oxygen saturation of less than 90% for more than 30 s), hypotension (drop in systolic blood pressure below expected for age or a drop of 20% from baseline), worsening stridor from baseline, and bleeding (hemoptysis or epistaxis). Serious adverse events such endotracheal intubation, respiratory or cardiac arrest or failure to complete the procedure were also recorded.

Procedure time was defined as the time between the first bolus of sedation until the bronchoscopy procedure completed. Recovery time (RT) was defined as the interval between the completions of the procedure until the patient's level of conscious was back to baseline. Discharge time (DT) was defined as the interval between

the start of sedation until the patient was discharged home.

Outcomes analyzed included: Propofol dose, hypoxemia, hypotension, procedure and recovery times, and time to discharge. For the two sedation strategies, bivariate analyses were conducted using χ^2 and Wilcoxon Sum Rank Tests. For the three age groups, bivariate analyses were conducted using χ^2 and Kruskal-Wallis Tests.

RESULTS

During the study period, a total of 458 bronchoscopies were performed, of which 454 (99.1%) were successfully completed. Patients' demographics and indications for bronchoscopy are summarized in (Table 1). Of the 458 flexible bronchoscopies performed, 337 patients (73.6%) were sedated using propofol only strategy and 121 patients (26.4%) using propofol and ketamine. Children in the (K-P) group tend to be younger and have lower weight compared to the (P-O) group. Four cases (< 1%) (3 in the P-O group, 1 in the K-P group) were terminated early. Two patients (< 0.5%) were admitted to the pediatric intensive care unit; one toddler in the P-O group and one child in the K-P group. One of the four patients required endotracheal intubation; two other patients required fluid resuscitation and one patient had a brief bradycardic episode. Both admitted patients were discharged home in the first 24 h of admission. Transient hypoxemia occurred in 8.3% of patients while hypotension in 23.6%. Prolonged hypoxemia necessitating the need for bag/mask ventilation happened in 5.1% of all patients (Table 2). There was no significant difference in propofol dosage, adverse effects or sedation times using the two sedation strategies (P-O or K-P) (Table 2). Analysis of the three age groups showed significantly higher hypoxemia in infants compared to toddlers and children (Table 3). A logistic regression of age groups predicting hypoxemia showed that infants have significantly higher odds of hypoxemia compared to toddlers ($P < 0.0001$, OR: 13.56, 95%CI: 3.92, 46.91), and compared to children ($P < 0.0001$, OR: 10.96, 95%CI: 3.65, 32.91). However, children and toddlers do not have significantly different odds of hypoxemia ($P = 0.62$).

DISCUSSION

FB is an essential diagnostic and therapeutic modality commonly used in various congenital and acquired pediatric pulmonary disorders^[9,23].

To the best of our knowledge, this is the largest retrospective study describing the use of propofol with or without ketamine for procedural sedation in the outpatient settings for pediatric FB.

Between 2007 and 2012, we have used propofol as the main intravenous sedative agent for pediatric outpatient for FB. Propofol was well tolerated in the majority of pediatric patients undergoing the FB. Compared with the study of

Table 1 Demographics and indications of bronchoscopy in patients

Variable	Overall (n = 458)	Propofol only (n = 337)	Propofol ketamine (n = 121)	P value
Age, yr	5.0 (2.5, 9.1)	5.6 (2.8, 9.8)	3.4 (1.9, 6.6)	< 0.0001
Age group, n (%)				
Infant (< 12 mo)	15 (3.3)	6 (1.8)	9 (7.4)	< 0.0001
Toddler (1-3 yr)	132 (28.8)	84 (24.9)	48 (39.7)	
Child (4-17 yr)	311 (67.9)	247 (73.3)	64 (52.9)	
Weight (kg)	18.1 (13.1, 31.8)	20.0 (14.4, 33.0)	14.7 (11.2, 26.0)	< 0.0001
Female gender, n (%)	198 (43.2)	143 (42.4)	55 (45.5)	0.57
Diagnosis, n (%)				
Cystic fibrosis	38 (8.3)	29 (8.6)	9 (7.4)	
Cough	93 (20.3)	62 (18.4)	31 (25.6)	0.38
Wheezing	108 (23.6)	87 (25.8)	21 (17.4)	
Stridor	56 (12.2)	41 (12.2)	15 (12.4)	
Pneumonia	57 (12.4)	42 (12.5)	15 (12.4)	
Tachypnea	106 (23.1)	76 (22.6)	30 (24.8)	

Table 2 Average doses, sedation times and adverse events

Variable	Overall (n = 458)	Propofol only (n = 337)	Propofol ketamine (n = 121)	P value
Propofol dose (mg/kg)	4.1 (2.7, 5.6)	4.2 (2.7, 5.6)	3.7 (2.8, 5.2)	0.3
Procedure time (min)	10 (6, 15)	10 (7, 12)	10 (5, 15)	0.3
Recovery time (min)	25 (20, 30)	25 (20, 30)	25 (20, 35)	0.63
Time to discharge (min)	35 (30, 43)	35 (30, 40)	35 (30, 45)	0.31
Respiratory events				
Prophylactic use of O ₂ supplementation prior to bronchoscopy, n (%)	423 (92.4)	311 (92.3)	112 (92.6)	0.92
Hypoxemia, n (%)	38 (8.3)	29 (8.6)	9 (7.4)	0.69
BMV/significant desaturation ¹ , n (%)				0.58
Neither	413 (91.2)	302 (90.7)	111 (92.5)	
BMV + significant desaturation	23 (5.1)	16 (4.8)	7 (5.8)	
Significant desaturation only	16 (3.5)	14 (4.2)	2 (1.7)	
BMV use only	1 (0.2)	1 (0.3)	0 (0)	
Cardiac events				
Start MBP	77.7 (70.3, 86.7)	78.3 (71.3, 86.3)	76.3 (68.0, 88.7)	0.58
End MBP	70.3 (63.0, 78.7)	71.0 (64.0, 79.3)	68.7 (61.7, 76.3)	0.04
Difference in MBP	-7.5 (-17.0, 2.0)	-6.7 (-16.0, 2.7)	-8.7 (-19.0, 0.7)	0.12
% Change MBP from start of procedure	-9.8 (-20.0, 3.0)	-9.2 (-18.8, 4.3)	-10.5 (-22.8, 0.7)	0.12
Blood pressure drop more than 20% from the baseline (hypotension)	108 (23.6%)	76 (22.6%)	32 (26.4%)	0.4

¹Significant desaturation defined as oxygen saturation of less than 90% for more than 30 s. BMV: Bag mask ventilation; MBP: Mean arterial blood pressure.

Hasan and Reddy, our RT and discharge time DT were significantly shorter (26.7 ± 14.3 min vs 40 ± 18 min) and (37.6 ± 16.1 min vs 80 ± 44 min) respectively^[24]. These findings can be due to the variability in indications and the practice of FB in pediatrics. Additionally, our propofol dose used is in line with the findings in another study to evaluate the use of propofol in pediatric FB^[1] with no significant difference between three age groups or sedation regimens.

The routine administration of small dose ketamine prior to propofol has been shown in some studies to be beneficial in maintaining hemodynamic stability and decreasing side effect profile of propofol^[18,19]. We used ketamine prior to propofol in only one fourth of our patient population but we did not observe significant difference in the adverse events between two groups. Also, we observed no difference in the average propofol dose between the groups. Additionally, RT and DT were similar in both groups. It is unclear whether there is

truly no difference when adding ketamine to propofol or if it was due to small sample size or could be related to the fact that ketamine dose is too low to achieve anesthetic effect.

In term of adverse events and comparing to the data from the Pediatric Sedation Research Consortium on propofol sedation, we observed higher incidence of transient hypoxemia, hypoxemia required bag/mask ventilation and unexpected hospital admission in our study (8% vs 1.4%, 5% vs 1%, 0.4% vs 0.07% respectively)^[14]. The higher incidence of these adverse events could be related to the nature of the procedure. Additionally, the pediatric research consortium data did not include pediatric patients who undergo this category of procedures. However, our findings are consistent with other reported data of complications of FB in children^[3,25]. Our infants group had a significantly higher incidence of transient hypoxemia in infants compared to toddlers

Table 3 Analysis of adverse events, propofol dose and sedation times in three age groups

Variable	Infants (<i>n</i> = 15)	Toddlers (<i>n</i> = 132)	Children (<i>n</i> = 311)	<i>P</i> value
Hypoxemia, <i>n</i> (%)	7 (46.7)	8 (6.1)	23 (7.4)	< 0.0001
Hypotension, <i>n</i> (%)	2 (13.3)	35 (26.5)	71 (22.9)	0.45
Propofol only regimen, <i>n</i> (%)	6 (40.0)	84 (63.6)	247 (79.4)	< 0.0001
Propofol dose (mg/kg)	4.3 (2.4, 5.4)	4.34 (3.3, 5.3)	3.7 (2.5, 5.7)	0.06
Recovery time (min)	25 (15, 30)	25 (20, 35)	25 (20, 30)	0.39
Procedure time (min)	10 (7, 15)	10 (5, 11.5)	10 (8, 15)	0.16
Time to discharge (min)	35 (25, 40)	35 (30, 45)	35 (30, 40)	0.56

and children (46.7%, 6% and 7% respectively). While infants are only 3% of our study population. This could be due to some difficulty in delivering O₂ by nasal prongs to younger children or due to their low functional residual capacity. Given the high incidence of transient hypoxemia, infants might benefit from having their bronchoscopies performed under general anesthesia with a secure airway. Two children in our study had major unexpected complications requiring hospital admission (0.4%). Both were discharged home in the next day.

Our study has a number of limitations, including its retrospective nature and the fact that it was conducted at a single institution. As a retrospective report, there are many variables that are impossible to control and any comparison of our techniques is really made impossible by the possible bias that is introduced by how our sedation providers may have chosen to deliver sedation to one patient vs another. In regards to the sedation regimen used or the need for oxygen supplementation, it was chosen by the attending physician based on personal preference and experience. However, statistical analysis showed no difference between the two sedation regimens. Lastly, we did not compare the efficacy, adverse events and the cost of performing these procedures as an outpatient setting to the operation room setting under general anesthesia, future study comparing both settings with tightly controlled protocols and well defined outcomes would provide important information. The purpose of this study was not to compare between these two approaches, rather to describe our experience using propofol based sedation regimen for pediatric outpatient flexible bronchoscopy as an alternative approach that might be applied in certain institutions.

In conclusion, children can be sedated using propofol based sedation regimen for flexible bronchoscopy vs a pediatric intensivist-based team in an outpatient setting with expediency and high rate of success. Given the nature of the procedure, we observed a higher incidence of transient hypoxemia especially in infants and an overall higher incidence of hypoxemia compared to other procedures done under the same setting. This approach can be appealing since it provides an alternative valuable option to general anesthesia with a short recovery and discharge time. Given the higher incidence of anticipated adverse events, the use of this sedation strategy should be restricted to practitioners highly trained in pediatric airway and cardiorespiratory monitoring and

management. Future study comparing this strategy to general anesthesia to determine any economical and workflow advantages and monitor adverse events is warranted.

COMMENTS

Background

Flexible bronchoscopy (FB) has become an increasingly important outpatient tool used in the evaluation of pulmonary abnormalities in children. FB is often considered to be invasive procedure, therefore, deep sedation is usually required. Multiple sedation regimens and route had been evaluation including nasal, oral, intravenous and topical anesthetic with variable efficacy and safety profiles.

Research frontiers

Evaluating the safety and efficacy of sedating pediatric patients for flexible bronchoscopy using propofol based sedation regimens in an outpatient setting.

Innovations and breakthroughs

This is the largest retrospective study describing the use of propofol with or without ketamine for deep sedation in the outpatient settings for pediatric flexible bronchoscopy.

Applications

Although the approach was efficacious and safe, they did not compare the efficacy, adverse events and the cost of performing this approach as an outpatient setting to the operation room setting under general anesthesia, future study comparing both settings with tightly controlled protocols and well defined outcomes would provide important information.

Peer-review

The paper is good, nicely framed and written.

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