Objective: To describe our experience with ketamine sedation during infant flexible fiberoptic bronchoscopy.

Design: Retrospective chart review. Infants were sedated with midazolam and ketamine with or without fentanyl. The sedation regimen, final procedure performed, procedure duration, and complications were recorded. Complication rates between infants ≤ 6 months or > 6 months of age and between infants with upper vs lower airway symptoms were compared by χ² test with a contingency table.

Results: Fifty-nine procedures were performed in 55 patients aged 6.1 ± 3.1 months (mean ± SD). Sedation was achieved with ketamine and midazolam (n = 30) or ketamine, midazolam, and fentanyl (n = 29). Bronchoscopy with BAL was performed in 44 patients and bronchoscopy alone in 3 patients. In 11 patients, severe upper airway obstruction and/or anomalies prevented subglottic passage of the bronchoscope. One patient could not be adequately sedated. There were no major complications. Minor complications occurred in 14 patients (23.7%), most commonly mild hypoxemia (n = 9). Brief central apnea developed in three patients. Complication rates were unaffected by age or indication for bronchoscopy.

Conclusions: Infant flexible fiberoptic bronchoscopy can be safely and effectively performed using ketamine sedation. Complications, especially mild hypoxemia, appear more common in infants, likely due to smaller airway diameter. Regardless of the sedative(s) used, additional vigilance is required when performing bronchoscopy in this population.

Key words: complication; fentanyl; hypoxemia; midazolam; pediatric; procedural sedation

Flexible fiberoptic bronchoscopy has been recognized as an important tool in the evaluation and management of infant and pediatric respiratory disease for > 20 years. Subsequent to these initial reports, larger series have confirmed the safety and value of this procedure. While authors recognized the need for appropriate sedation during this procedure, few data exist regarding the safety and efficacy of specific sedation regimens. While the most commonly reported regimens include an opioid/benzodiazepine combination, other authors have suggested that ketamine, with or without a benzodiazepine, may be both safe and effective.

Ketamine is a dissociative anesthetic, chemically related to phencyclidine. Initially utilized predominantly in the operating room, increasing experience with this agent outside of the operating room has demonstrated its safety and efficacy, and has enabled it to become a popular choice for pediatric procedural sedation in both the emergency department and procedure suite. In these settings, ketamine is reported to provide excellent sedation, analgesia, and amnesia with minimal adverse respi...
Ketamine possesses bronchodilating properties\(^\text{16}\) that, combined with its favorable respiratory profile, appear to make it an ideal agent for sedation during airway manipulative procedures such as bronchoscopy. However, data regarding the safety and efficacy of ketamine in this setting are limited,\(^\text{7}\) with no data specifically addressing the infant population. This study reviews our experience with ketamine sedation in infants undergoing flexible fiberoptic bronchoscopy and discusses the safety and efficacy of this agent in this population.

**MATERIALS AND METHODS**

**Bronchoscopy**

This retrospective study was approved by the Institutional Review Board of the University of Missouri Health Sciences Center. All infants (<1 year of age) who received ketamine during sedation for flexible fiberoptic bronchoscopy between June 1999 and December 2002 were reviewed. Patients in whom bronchoscopic evaluation occurred during endotracheal intubation and/or mechanical ventilation were excluded. All bronchoscopies were performed in the pediatric ICU by a pediatric pulmonologist with the assistance of a respiratory therapist. Written, informed consent was obtained from a parent or guardian prior to each procedure. Prior to sedation, each patient received 5 mg (<6 months old) or 10 mg (>6 months old) of nebulized lidocaine with 2.5 mg of albuterol via facemask. Following topical application of lidocaine jelly, a transnasal approach was used for all procedures. Additional doses of lidocaine (5 mg or 10 mg) were applied to the vocal cords, trachea, and major bronchi as required to a maximum total lidocaine dose of 7 mg/kg. Bronchoscopy was performed with a 3.6 mm, Olympus BF3C30 bronchoscope (Olympus Corporation; Melville, NY) with a video camera adapter. BAL was performed using 0.5 to 1 mL/kg (maximum 3 mL/kg total) aliquots of nonbacteriostatic 0.9% saline solution.

Sedation was administered and supervised by a pediatric intensivist in accordance with the published guidelines of the American Academy of Pediatrics\(^\text{17}\) and institutional policy governing procedural sedation and analgesia. All patients had been without oral intake for at least 4 h prior to the start of the procedure and had an IV catheter in place. Patients were monitored by the intensivist and/or a pediatric critical care nurse. Heart rate, heart rhythm, respiratory rate, and oxygen saturation were continuously monitored. Noninvasive BP was measured every 5 min during the procedure and every 15 min afterward until the patient was awake. Supplemental oxygen via nasal cannula was provided in all cases. All patients received either atropine (0.01 mg/kg) or glycopyrrolate (0.05 to 0.01 mg/kg) as an antisylosagogue. Midazolam (0.05 to 0.1 mg/kg) was administered because of the potential for emergence reactions with ketamine and the inability of infants to report such reactions. Ketamine was administered as an initial bolus of 1 mg/kg over 1 min with additional boluses of 0.5 to 1.0 mg/kg as needed to achieve and/or maintain adequate sedation. While formal sedation scoring was not performed, sedation was deemed adequate when insertion or manipulation of the bronchoscope caused minimal or no patient movement or response. During the latter parts of the study period, patients also received a small dose of fentanyl (1 μg/kg) in an attempt to decrease coughing, which had been noted to be a frequent occurrence.

Complications were recorded including the development of hypoxemia (oxygen saturation <90% for ≥30 s), apnea, laryngospasm, increased wheezing and/or stridor compared to baseline, bleeding (epistaxis or lower airway), pneumothorax, and inadequate sedation. The procedure was interrupted or prematurely terminated at the discretion of either the intensivist or the bronchoscopist, based on the occurrence, duration, and/or severity of the above complications. When definable, the causes of hypoxemia (intrinsic disease, airway obstruction from the bronchoscope, and/or inadequate respiratory effort) were recorded.

**Data Collection**

Each patient’s chart was reviewed. Demographic information was recorded including gender, weight, age at the time of procedure, and indication for the bronchoscopy. Procedure-related information recorded included the procedure performed (laryngoscopy, bronchoscopy, or bronchoscopy with BAL), sedation regimen (agents administered and total doses received), duration of the procedure (defined as the time elapsed from initial sedative administration to completion of the procedure), duration of sedation (defined as the time elapsed from sedation administration to when the patient had returned to baseline alertness or was discharged from the pediatric ICU), and complications as outlined above. Quantitative data are presented as the mean ± SD. The effect of the addition of fentanyl on the total doses of ketamine and midazolam used was analyzed using an unpaired Student \(t\) test. As the risks of sedation-related complications are increased in younger patients, we compared the incidence of complications in patients ≤6 months old vs those >6 months old by \(x^2\) test using a contingency table. Similarly, to determine if the likelihood of complication was related to the indication for bronchoscopy, we compared the incidence of complications in patients receiving bronchoscopy for primarily upper-airway vs lower-airway symptoms. A \(p\) value of <0.05 was considered significant.

**RESULTS**

Fifty-nine sedations were performed on 55 patients during the study period. Patient characteristics are summarized in Table 1. Indications for bronchoscopy included upper-airway and lower-airway symptoms. The incidence of complications was similar in patients <6 months old and >6 months old (9/29 vs 6/26; \(p=0.63\)). Complications were more frequent in the younger patients (12/31 vs 4/26; \(p=0.018\)). The incidence of complications did not differ between patients with upper-airway symptoms and those with lower-airway symptoms (7/28 vs 13/31; \(p=0.28\)).

**Table 1—Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>6.1 ± 3.1 mo (range, 8 d to 11 mo)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>7.4 ± 1.9 (range, 3.0 to 12.0)</td>
</tr>
<tr>
<td>Female/male gender</td>
<td>23/36</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>47</td>
</tr>
<tr>
<td>African American</td>
<td>10</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD or No.*
copy included chronic wheeze (n = 27), stridor (n = 22), cystic fibrosis microbiologic surveillance (n = 9), chronic cough (n = 7), hemoptysis (n = 1), recurrent pneumonia (n = 1), and unexplained hypoxemia (n = 1). In some patients, multiple indications were present so the total number of indications exceeds the total number of procedures.

In all instances, the procedure was scheduled with the intent of performing bronchoscopy with BAL. Of the 59 sedations, bronchoscopy with BAL was performed in 44 patients. In three patients, BAL was not possible due to the development of airway obstruction with hypoxemia on advancement of the bronchoscope below the vocal cords. In 11 patients, laryngoscopy alone was performed as severe upper airway obstruction from laryngomalacia (n = 7), subglottic stenosis (n = 3), laryngospasm (n = 2), and/or laryngeal polyp (n = 1) prevented passage of the bronchoscope below the vocal cords. In one patient, the procedure was canceled when adequate sedation could not be achieved.

In 58 of 59 instances, sedation was excellent and a diagnostically adequate procedure was easily completed. Airway pathology was identified in 57 of the 58 procedures completed (Table 2). In all patients undergoing bronchoscopy for stridor or chronic wheeze, specific anatomic pathologic changes were identified; in all patients undergoing bronchoscopy for cystic fibrosis microbiologic surveillance, bacterial growth was accompanied by evidence of acute inflammation.

Sedation was achieved with a regimen of ketamine and midazolam (n = 30) or ketamine, midazolam, and fentanyl (n = 29). The cumulative doses of each drug used are recorded in Table 3. The addition of fentanyl had no effect on the doses of ketamine or midazolam used. The depth of sedation achieved was adequate as defined above, and the procedure was easily performed in all but one patient, a 6-month-old boy with chronic wheeze who remained active and agitated after receiving 0.09 mg/kg of midazolam, 0.9 µg/kg of fentanyl, and 4.7 mg/kg of ketamine. This procedure was canceled and performed under general anesthesia at a later date. In three patients, ongoing sedation was provided to facilitate the performance of additional procedures including gastrostomy and insertion of a percutaneous IV central catheter (n = 1). The mean procedure duration was 19.4 ± 6.9 min (range, 9 to 45 min). This decreased to 18.5 ± 5.3 min (range, 9 to 30 min) when removing the three patients in whom additional procedures were performed. The mean duration of sedation was 104.2 ± 36.6 min.

There were no major complications. Sixteen minor complications were observed in 14 of 59 sedations (23.7%). Complications occurred in 8 of 33 patients (24.2%) ≤ 6 months old and 6 of 26 patients (23.1%) > 6 months old (p = not significant). The distribution of complications in these two age groups is shown in Table 4. The most common complication was hypoxemia (9 of 16 complications, 56.3%). In all instances, the procedure was temporarily suspended but hypoxemia resolved rapidly with withdrawal of the bronchoscope from the trachea, administration of supplemental oxygen, and/or brief (<15 s) bag valve mask ventilation. Bronchoscopy with BAL was subsequently performed in five of these cases, bron-
chonchoscopy without BAL in three cases, and laryngoscopy in one case. In eight of nine instances (89%), hypoxemia did not develop until after passage of the bronchoscope into the lower airways. In all cases, hypoxemia was accompanied by an increase in respiratory rate, work of breathing, and retractions, suggesting an obstructive etiology. Hypoxemia occurred in 4 of 22 patients (18.2%) undergoing evaluation of upper airway symptoms and 5 of 37 patients (13.5%) undergoing evaluation of lower airway symptoms (p = not significant). Central apnea (> 20 s) without hypoxemia developed in three patients aged 1.5 months, 1.5 months, and 7 months. In all three infants, apnea developed almost immediately after the initial bolus of ketamine was administered and was managed with brief bag valve mask ventilation. In all three infants, the procedure was subsequently performed without incident. Two patients became apneic after receiving midazolam and ketamine, while the third patient had received midazolam, fentanyl, and ketamine. Laryngospasm without hypoxemia developed in two patients. This resolved rapidly but prevented passage of the bronchoscope below the vocal cords. Mild epistaxis controlled with pressure developed in one patient, and postprocedure stridor developed in another patient, which resolved with a single treatment of nebulized L-epinephrine. No procedure-related morbidities occurred. No patient required endotracheal intubation, although one patient underwent urgent tracheostomy after the procedure identified critical subglottic stenosis. However, he had tolerated both the sedation and the procedure (laryngoscopy only) without complication.

**DISCUSSION**

The value of flexible fiberoptic bronchoscopy in the pediatric patient is well recognized, particularly in the younger patient where the common indications for bronchoscopy (eg, "noisy breathing," chronic wheeze) are more likely to be associated with abnormal findings. While most authors acknowledge the need for appropriate sedation during bronchoscopy in this population, few data exist regarding the effectiveness and safety of specific sedative agents or sedation regimens, including ketamine.

The safety and efficacy of ketamine sedation for a variety of pediatric procedures has been well documented. Its main advantages are the combination of excellent sedation, analgesia, and amnesia with minimal respiratory depression. However, as bronchoscopy involves direct manipulation of the airways, unique sedation needs exist that must take into account the additional risks of airway obstruction, irritation, or perforation, which may lead to hypoxemia, hemorrhage, or pneumothorax. It has been suggested that ketamine, due to its favorable cardiorespiratory profile and bronchodilator properties, may be the optimal agent for pediatric bronchoscopic sedation. However, Slonin and Ognibene reported an increased incidence of complications during bronchoscopy in children sedated with ketamine, compared to other sedatives, and concluded that ketamine may be associated with an increased risk of complications during this procedure. To our knowledge, ours is the first report to specifically assess the safety and outcomes of ketamine sedation during flexible bronchoscopy in infants. Our data suggest that, with appropriate monitoring and vigilance, bronchoscopy with ketamine may be safely performed in this population.

Whereas the need for sedation during adult bronchoscopy appears somewhat controversial, its value during pediatric procedures is well accepted. While we did not specifically record sedation scores, ketamine provided a depth of sedation that allowed the procedure to be easily completed in all but one instance. This is important since inadequate sedation, with patient agitation and movement during the procedure, could increase the risk of morbidities, such as airway injury, pneumothorax, and hemorrhage.

Ketamine also proved to be both a safe and effective agent for use in patients with upper airway symptoms and pathology in whom the risks of airway compromise during sedation are increased. Of the 22 patients undergoing bronchoscopy for evaluation of stridor, the incidence of hypoxemia (18%) was similar to that observed for the overall group (15%). More interestingly, in the 11 patients with such severe upper airway obstruction that passage of the bronchoscope below the vocal cords was not possible, hypoxemia occurred in only 1 patient, a 6 month old with severe laryngomalacia. This suggests that the development of hypoxemia in our upper airway obstructed patients was more related to
the added obstruction associated with passage of the bronchoscope below the vocal cords, rather than the sedation regimen itself. While it is certainly possible that the use of sedation worsened the underlying obstruction, there is a well-recognized risk of sedation in general and this is not unique to ketamine.

The incidence of complications (24%) reported here is higher than the 3 to 5% incidence reported in some series\(^2\,^4\) and may, again, lead some to question the safety of ketamine for this application. However, other series using different sedative regimens have reported complication rates similar to ours. Godfrey et al\(^3\) reported a complication rate of 20% during 200 fiberoptic bronchoscopies in children sedated with pethidine and midazolam. Stacey and Hurley\(^9\) reported a 28% complication rate in 105 pediatric bronchoscopies performed under inhalational anesthetic, and Abadaco et al\(^10\) reported a 24% incidence of complications during 105 pediatric bronchoscopies using an IM combination of meperidine, promethazine, and chlorpromazine for sedation. These studies, like ours, reported hypoxemia as the most common complication, whereas neither Wood\(^1\) nor Barbato et al\(^4\) reported this as a complication, which may have also contributed to their lower complication rates. Removal of hypoxicemic episodes from our analysis decreases our complication rate to 8.5% (5 of 59 patients), which is more consistent with the 3 to 5% reported in these two series.\(^2\,^4\)

Previous studies\(^7\,^9\) have also observed that the incidence of complications, including hypoxemia, was increased in the younger patient. While complication rates for specific age groups (infants vs toddlers vs older children vs adolescents for example) in these studies were not reported, our population included only infants, which should account, at least in part, for our higher complication rate. A number of factors contribute to this age difference. First, the older child may do well with lighter sedation with or without nonpharmacologic techniques, whereas deeper levels of sedation tend to be required in the younger patient. This would increase the likelihood of respiratory depression and hypoxemia, as infants are more sensitive to the respiratory depressing effects of sedatives, including ketamine. In a review of sedation-related events in 1,140 children sedated for a variety of procedures, Malviya et al\(^11\) reported a 20% and 10% incidence of respiratory events in children < 1 month and 1 to 12 months of age, respectively, compared to an incidence of 3 to 5% in children ≥ 1 year old. Our cohort included only two infants < 1 month old, making a comparison with these figures impossible. However, it is still interesting that our complication rate did not differ between infants ≤ 6 months old and those > 6 months old. While infrequent, apnea with ketamine has also been most often reported in the younger patient.\(^13\,^14\) Central apnea developed immediately following the initial bolus of ketamine in three patients in this series (5%), aged 1.5 months, 1.5 months, and 7 months. However, pretreatment with midazolam (n = 3) with or without fentanyl (n = 1) may have also contributed to this.

Due to the physical manipulation of the airways, the relative risk of adverse respiratory events during bronchoscopy should also be increased. This is especially true in the younger child, in whom the bronchoscope is relatively larger compared to the airway diameter than in an older child, increasing the risk of significant airway obstruction on entering the trachea or more distal airways. While previous studies have not commented on the etiology of hypoxemia during bronchoscopy, eight of nine patients who did so in our series did so after the bronchoscope had been passed into the trachea. In each instance, hypoxemia was associated with an increase in respiratory rate, work of breathing, and retractions, suggesting that the development of significant airway obstruction from the bronchoscope was the most significant contributor to hypoxemia. The fact that bronchoscope we used is 3.6 mm in diameter, compared to an average infant tracheal diameter of 5.3 ± 1.0 mm,\(^2\) likely contributed to the development of obstruction. It is possible that use of a smaller bronchoscope would have decreased our incidence of hypoxicemic and/or obstructive events. The additional finding that most (80%) of our patients had obstructive pathology would have further contributed to the development of obstructive hypoxemia.

Therefore, when evaluating the safety of a particular sedation regimen, it must be determined if complications are the result of the sedation, the procedure itself, or patient characteristics. Slonin and Ogubene\(^7\) concluded that the use of ketamine sedation for pediatric flexible bronchoscopy "may contribute to procedure-related complications." However, the authors also stated that they preferred to use ketamine in the younger child in order to achieve a deeper level of sedation and to facilitate a more controlled procedure, while both of these factors (younger age and deeper sedation) increase the risk of complications independent of the sedative used. They further reported that many of their complications occurred in patients who were HIV positive. Previous studies have reported complication rates of 29%\(^2\) and 24%\(^2\) during bronchoscopy in this population, suggesting that this is another high-risk group. Together, these observations raise the question of whether the higher complication rate reported in ketamine-sedated children in this study\(^7\) was truly related to ketamine itself or to its use in high-risk populations. In this series, 10 of the com-

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complications that occurred (hypoxemia after passage of the bronchoscope below the vocal cords \( n = 8 \), epistaxis \( n = 1 \), and stridor \( n = 1 \)) appear to have been more related to the procedure than the sedation itself, decreasing the apparent rate of purely sedation-related complications.

By some standards, the 24% rate we report might appear high, even though no events were associated with significant morbidity. This may prompt the question of what should the “acceptable complication rate” for procedural sedation be. This is an extremely important question. To answer it, one must first separate procedure-related complications from sedation-related complications, as discussed above. Additionally, this requires consensus regarding the definition of “complication,” which remains controversial. For example, Pena and Krauss\(^{23}\) evaluated the incidence of complications during procedural sedation/analgesia in 1,150 pediatric emergency department patients. The authors defined complications simply as “adverse events that negatively affected outcome or delayed recovery,” which is somewhat arbitrary. Conversely, in an evaluation of procedural sedation-related complications in 1,140 children, Malviya et al\(^{21}\) utilized more rigorous definitions of complications. While the reported complication rate was greater in the latter study (20.1% vs 2.3%), it is unclear whether this was related to sedation practices, sedative agents, or simply the definitions used. In other words, reported complication rates are dependent on the \textit{a priori} definitions used, making comparisons between studies and acceptability thresholds difficult. That the question, then, remains largely unanswered underscores the need for multicenter and multidisciplinary collaboration to adequately define and then effectively evaluate the incidence of complications and adverse events in a much larger pediatric sample size than has been published to date.

In conclusion, we report here the safe and efficacious use of ketamine sedation to facilitate flexible fiberoptic bronchoscopy in infants. This sedation regimen enabled the performance of a diagnostically adequate procedure in all but one patient. While we report a relatively high complication rate, it is consistent with other reports and our series comprises a higher risk population. While no significant morbidity occurred, our data do suggest that sedation for bronchoscopy in the infant, regardless of the sedative regimen employed, mandates vigilant patient evaluation throughout the procedure and the presence of personnel skilled in emergent airway management. This study further suggests that factors other than sedative regimen should be considered when evaluating the etiology of complications during pediatric bronchoscopy.

References