Volatile Anesthetic Rescue Therapy in Children With Acute Asthma: Innovative but Costly or Just Costly?*

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Objectives: To describe volatile anesthesia (VA) use for pediatric asthma, including complications and outcomes.

Design: Retrospective cohort study.

Setting: Children's hospitals contributing to the Pediatric Health Information System between 2004–2008.

Patients: Children 2–18 years old with a primary diagnosis code for asthma supported with mechanical ventilation.

Intervention: Those treated with VA were compared to those not treated with VA or extracorporeal membrane oxygenation. Hospital VA use was grouped as none, <5%, 5–10% and >10% among intubated children.

Measurements and Main Results: One thousand five hundred and fifty-eight patients received mechanical ventilation at 40 hospitals for asthma: 47 (3%) received VA treatment at 11 (28%) hospitals. Those receiving a VA were significantly less likely to receive inhaled b-agonists, ipratropium bromide, and heliox, but more likely to receive neuromuscular blocking agents than patients treated without VA. Length of mechanical ventilation, hospital stay (length of stay [LOS]) and charges were significantly greater for those treated with VA. Aspiration was more common but death and air leak did not differ. Patients at hospitals with VA use >10% were significantly less likely to receive inhaled b agonist, ipratropium bromide, methylxanthines, and heliox, but more likely to receive systemic b agonist, neuromuscular blocking agents compared to those treated at hospitals not using VA. LOS, duration of ventilation, and hospital charges were significantly greater for patients treated at centers with high VA use.

Conclusions: Mortality does not differ between centers that use VA or not. Patients treated at centers with high VA use had significantly increased hospital charges and increased LOS. (*Pediatr Crit Care Med* 2013; 14:343–350)

Key Words: asthma; rescue therapy; status asthmaticus; volatile (inhalational) anesthetics

Asthma, the most common chronic disease of childhood, remains a common reason for hospitalization. Despite improvements in outpatient management, intensive care for asthma exacerbations is increasing (1). Ten percent to 30% of all patients admitted to an ICU are supported with intubation and invasive mechanical ventilation (2). Although most children with respiratory failure respond to conventional therapies including bronchodilators and systemic steroids others do not, and a variety of therapies have been used including heliox, permissive hypercapnia, volatile anesthesia (VA), and extracorporeal membrane oxygenation (ECMO). The comparative effectiveness and costs of these therapies have not been evaluated (3–5).

Volatile (or inhalational) anesthetics have been used to treat status asthmaticus refractory to conventional therapies since the late 1930s (6). VAs continue to be suggested as alternatives to conventional therapy in unresponsive asthma cases as they are potent bronchodilators, decrease airway responsiveness, and attenuate bronchospasm (4, 7, 8). The mechanism for these effects is thought to be direct β adrenergic receptor stimulation leading to increased intracellular cyclic adenosine monophosphate. This increased cyclic adenosine monophosphate may bind free calcium within bronchial muscle and cause direct bronchial muscle relaxation. In addition, VAs may impede antigen-antibody–mediated enzyme production and histamine release from leukocytes (2).

Although the effects of VAs on bronchospasm are well demonstrated in patients with wheezing in the operating room, their application outside of the operating room appears limited (2). Potential for cardiovascular depression, environmental toxicity related to lack of adequate scavenging and limited clinical expertise, and the need for specialized equipment hinder their use elsewhere (9, 10).

The objective of this study is to describe current use of VAs among intubated pediatric asthma patients treated at a group

*See also p. 433.

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of pediatric hospitals that contribute administrative information to the Pediatric Health Information System (PHIS). In pursuing this objective, we also present the use of ECMO as the most invasive potential "rescue" treatment for severe asthma as a reference and comparison group with severe disease.

METHODS

We evaluated all children with a primary diagnosis code for asthma supported with invasive mechanical ventilation to determine use of VAs among this critically ill subset of children treated at U.S. Childrens' Hospitals that contribute to PHIS, collected by Children's Health Corporation of America (CHCA) (11).

CHCA is a collaboration of more than 40 children's hospitals, and PHIS contains administrative data including patient demographics, diagnoses, procedures, and charges. In addition, a subset of PHIS hospitals submits "Level II" data—detailed data for billed services including pharmacy, clinical services, imaging, laboratory, supply, and room charges (12). Clinical Transaction Classification (CTC) codes are used to identify the detailed billing services received by patients (12–14). All PHIS data are de-identified and checked for reliability and validity prior to release. CTC is a proprietary system used by PHIS to categorize hospital billing for clinical, imaging, laboratory, pharmacy, supply, and other services. The centers for Medicare and Medicaid are adopting CTC for medication billing (15). However, the actual provision of a medication or service to a patient cannot be verified. The PHIS database does not contain acute physiologic information required for severity of illness scoring. The University of Utah Institutional Review Board approved the study (IRB 00032920) and granted waiver of need for informed consent.

After approval, data for all children aged 2–18 yr treated in a PHIS PICU from 2004 to 2008 with a primary diagnosis of asthma (International Classification Diseases version 9 [ICD9]-493.0, 493.1, 493.8, 493.81, 493.82, 493.9) were requested and those with any diagnosis code for cystic fibrosis (277.0, 277.00, or 277.02) or bronchiolitis (466.1–466.19, 487.1, or 491.8) excluded. For children treated in a center more than once during the study period, only the initial hospitalization was included in the analysis.

Variables

Demographic information, admission source, daily asthma therapies, and laboratory/radiographic testing based on hospital charges while in the PICU were evaluated. Procedure codes for support therapies such as ECMO (39.65–39.66), noninvasive positive airway pressure (93.90–93.99), tracheal intubation (96.04), mechanical ventilation (96.70–96.71), and complications such as air leak (512.1, 512, and 770.2), aspiration (779.16), and cardiac arrest (427.5) were ascertained by ICD9 codes. Charges for drugs administered were used to quantify therapies given including volatile anesthetics using CTC codes by day of hospital care. Because VA can only be administered to an intubated patient in the PICU, to enable scavenging of waste gas, all were coded as receiving mechanical ventilation. Six patients received VA but did not have a billing code for mechanical ventilation. However, none of these six patients underwent a surgical procedure during their hospitalization.

Outcomes

Receipt of asthma medications during PICU stay, duration of invasive ventilation, length of stay (LOS) in the hospital, complications, and mortality were evaluated.

Analysis

Among children supported with intubation and mechanical ventilation, three groups were defined: 1) those who received VA but not ECMO, 2) those who received ECMO, and 3) those who did not receive either of these two "rescue" therapies. The ECMO group was small and is presented as a comparison for an invasive "rescue" therapy, but the small sample size precluded meaningful statistical comparisons between this and the other groups. In order to describe center variation for use of VAs among intubated asthma patients who were not treated with ECMO, center use was categorized as none, < 5%, 5% to 10%, and > 10%.

Data were described using median values with 25th and 75th interquartiles or as percentages and were compared using the chi-square test, Wilcoxon ranked sign test, or the Mann-Whitney *U* test for continuous variables. Statistical significance was defined as $p < 0.05$, and all analyses were conducted using SPSS 14.0 for Windows (SPSS, Chicago, IL). A Bonferonni correction was made for multiple pairwise comparisons.

RESULTS

Among 1,558 children treated with invasive mechanical ventilation, 47 children (3%) received VA, 13 children (< 1%) were supported by ECMO, and 1 child received both VA and ECMO. Demographic and clinical features are compared between mechanically ventilated children who received these therapies for severe asthma with children treated without either rescue therapy in **Table 1**.

Patients who received VA were significantly younger than patients who did not (median age = 4.5 vs. 7 yr; $p = 0.03$) receive a rescue therapy; however, other demographic features such as gender, race/ethnicity, and insurance did not differ. When evaluating receipt of asthma therapies, use of steroids was similar among the study groups; however, receipt of inhaled albuterol (78% vs. 88%; $p = 0.001$) and ipratropium bromide (59% vs. 69%; $p = 0.02$) was significantly lower in the VA group compared with the no-rescue therapy group. Both medications are recommended therapies for acute hospitalized pediatric asthma care (16). In the case of use of therapies with less-established evidence for efficacy, use of systemic β agonists and magnesium did not vary significantly between the no-rescue therapy and the VA groups, but use of antibiotics and neuromuscular blocking agents (NMBA) was significantly more common for the VA group ($p < 0.001$). Administration of heliox was more common (23% vs. 8%) in children in the no-rescue therapy compared with the VA group.

Median days of ventilation (6 vs. 2 days; $p < 0.001$) and hospital LOS (11 vs. 7 days; $p < 0.001$) were significantly greater for the VA group compared with the no-rescue therapy group. The

TABLE 1. Children Treated With Mechanical Ventilation: Comparing Demographic and Clinical Features for Those Treated With Volatile Anesthetic Agent, Extracorporeal Membrane Oxygenation, or No-Rescue Therapy

Factor	Volatile Anesthetic Agent (No ECMO) (*n* = 46)	Conventional Ventilation Only (*n* = 1,498)	ECMO (*n* = 14)	Comparison Between Volatile Agent and Conventional Treatment (*p*)
Age (yr) (median, IQR)	4.5 (2,8)	7 (3,11)	5.5 (1,12)	0.03
Male (*n*, %)	30 (65)	930 (64)	10 (71)	0.67
Race				0.60
White (*n*, %)	14 (30)	404 (27)	1 (7)	
Black (*n*, %)	16 (35)	637 (43)	11 (78)	
Hispanic (*n*, %)	8 (17)	171 (11)	2 (14)	
Asian (*n*, %)	1 (2)	28 (2)	0	
Other (*n*, %)	2 (4)	107 (7)	0	
Missing (*n*, %)	5 (11)	151 (10)	0	
Payer				0.20
Government (*n*, %)	20 (43)	789 (53)	7 (50)	
Private (*n*, %)	14 (30)	361 (24)	5 (36)	
Other (*n*, %)	11 (24)	229 (15)	2 (14)	
Unknown (*n*, %)	1 (2)	119 (8)	0	
PICU asthma medications				
Steroids (*n*, %)	44 (96)	1,365 (91)	14 (100)	0.29
Inhaled albuterol (*n*, %)	35 (78)	1,320 (88)	14 (100)	0.001
Inhaled ipratropium (*n*, %)	27 (59)	1,040 (69)	10 (71)	0.02
Magnesium sulfate (*n*, %)	24 (52)	713 (48)	4 (29)	0.75
Methylxanthines (*n*, %)	5 (11)	200 (13)	3 (21)	0.63
Terbutaline (*n*, %)	15 (33)	541 (36)	6 (43)	0.12
Any β agonist (*n*, %)	36 (78)	1,381 (92)	14 (100)	0.002
Antibiotics (*n*, %)	46 (100)	956 (64)	8 (57)	< 0.001
Neuromuscular blocking agent (*n*, %)	40 (87)	666 (44)	6 (43)	< 0.001
Mechanical support				
Heliox (*n*, %)	4 (9)	344 (23)	1 (7)	0.02
Bilevel positive airway pressure (*n*, %)	4 (9)	109 (7)	0	0.72
Anesthetic agent (*n*, %)	46 (100)	0	1 (7)	< 0.001
Days of bilevel positive airway pressure (median, IQR)	2.5 (1,4.5)	1 (1,2)	—[a]	< 0.001
Days of ventilation (median, IQR)	6 (3,9)	2 (1,4)	7 (3,8)	< 0.001
Day of anesthetic agent (median, IQR)	1 (1,3)	—[b]	5	
Hospital length of stay (median, IQR)	11 (5,16)	7 (3,11)	7.5 (5,13)	< 0.001
Complications				
Pneumothorax (*n*, %)	0	36 (2)	1 (7)	0.29
Pneumomediastinum (*n*, %)	0	26 (2)	1 (7)	0.35

(*Continued*)

TABLE 1. (*Continued*). Children Treated With Mechanical Ventilation: Comparing Demographic and Clinical Features for Those Treated With Volatile Anesthetic Agent, Extracorporeal Membrane Oxygenation, or No-Rescue Therapy

Factor	Volatile Anesthetic Agent (No ECMO) (*n* = 46)	Conventional Ventilation Only (*n* = 1,498)	ECMO (*n* = 14)	Comparison Between Volatile Agent and Conventional Treatment (*p*)
Aspiration pneumonia (*n*, %)	3 (6)	29 (2)	1 (7)	0.03
Cardiac arrest (*n*, %)	0	55 (4)	0	0.19
Death (*n*, %)	1 (2)	31 (2)	0	0.32
Hospital charges				
Charges (median, IQR)	$91K (39K,166K)	$35K (19K,71K)	$43K (8K,182K)	< 0.001

ECMO = extracorporeal membrane oxygenation; IQR = interquartile range.
[a]The "ECMO" group didn't receive any bilevel positive airway pressure.
[b]The "conventional ventilation only" group didn't receive any volatile anesthetic.
Any β agonist includes inhaled albuterol, levalbuterol, terbutaline, and intravenous terbutaline.

median duration of VA use was 1 day (interquartile range = 1,3 days). The child treated with both ECMO and VA was treated for 5 days with VA.

Complications such as air leak and cardiac arrest were uncommon and did not differ between study groups; however, aspiration pneumonia was significantly more common in those treated with VA compared with the no-rescue therapy group (6% vs. 2%; $p = 0.03$). Overall 32 children died from asthma; however, rates of death did not vary between groups. Hospital charges were significantly higher for the VA group compared with the no-rescue therapy group (median $91K vs. $35K; $p < 0.001$).

When evaluating procedures done on the first day of VA administration, we found that two patients in the volatile agent group had a tonsillectomy and nine patients in the ventilation only group had procedures (tonsillectomy, palate repair, or abdominal procedures) that suggest some patients may have had surgery complicated by bronchospasm; however, this represents < 1% of the cohort.

Seven hospitals used ECMO in some of the intubated asthma patients compared with 11 hospitals that used VA. Two centers used both "rescue' therapies for severe asthma. PICUs that administered VA ranged in size from 20 to more than 70 beds. Eight of the 11 centers that used VA did so < 10% of the time and one hospital reported VA administration to all intubated asthma patients. **Table 2** categorizes center variation for volatile anesthetic use (VAU) among intubated asthma patients not treated with ECMO as none, < 5%, 5% to 10%, and > 10%.

Use of medical therapies differed between centers grouped by VAU. Although use of steroids was similar across all VAU groups, use of inhaled albuterol was lowest in the > 10% VAU group compared with other groups (60% vs. 89% to 93%) and significantly differed from hospitals that did not use VA (89%; $p < 0.001$). Receipt of inhaled ipratropium bromide also varied significantly by VAU groups but not in a consistent manner. Use of second tier (16, 17) asthma medications showed variation such that patients treated at centers that did not use VA received significantly more methylxanthines (16% vs. 10% to 5%; $p = 0.01$), but it showed a general trend for increased use of antibiotics (61% at no use VAU vs. 87% at > 10% VAU centers) and NMBA (44% at no use VAU vs. 77% at > 10% VAU centers) at centers with greater VAU. Patients treated at centers with more than 10% VAU received significantly less heliox compared with those treated at no VAU centers (22% vs. 2%; $p < 0.001$). Use of bilevel positive airway pressure did not differ by VAU group.

The median duration of VAU was 1 day and did not differ by VAU group. Median length of mechanical ventilation (median 2 vs. 3 days; $p < 0.001$), duration of NMBA use (median 2 vs. 3 days; $p < 0.001$), and hospital LOS (median 4 vs. 7 days; $p = 0.002$) were significantly less at hospitals that did not use VA in intubated asthmatics compared with the highest VAU centers but did not differ significantly from centers with lesser VAU. Likewise rate of aspiration pneumonia was greatest at centers using VA in more than 10% of ventilated asthmatics (6% vs. 2% to 4%; $p = 0.011$). Use of blood gases and radiographic testing increased as VAU increased. Median hospital charges for patients treated at a no VAU center was $34K compared with $66K for those treated at centers with > 10% VAU.

DISCUSSION

In this cohort of children mechanically ventilated for asthma, overall use of VA as a "rescue" therapy was 3% but varied greatly with some centers not using VA while others administered it to more than 10% of intubated asthmatics. Treatment with VA was associated with increased monitoring including blood gases, radiographs, prolonged LOS, and increased charges. Patients treated with VA were significantly less likely to receive inhaled β agonists and anticholinergic medications that are recommended therapies for acute asthma (16, 17). Aspiration pneumonia was significantly more common compared with intubated asthmatic children not treated with VA, but mortality was similar. Although aspiration pneumonia was associated

TABLE 2. Demographic and Clinical Features of Children Who Received Care at Centers by Use of Volatile Agent Use Among Intubated Children With Asthma

Feature	No Volatile Use ($n = 1,046$)	< 5% volatile Use ($n = 295$)	5.1% to 10% Volatile Use ($n = 116$)	> 10% Volatile Use ($n = 87$)	Comparison Across All Groups (p)	Comparison Group 0% and > 10% (p)
Number of centers	29	5	4	2		
Volatile use (n, %)	0	9 (3)	9 (8)	29 (33)	< 0.001	< 0.001
Age (yr) (median, IQR)	7 (3,11)	6 (2,12)	7 (2,11)	7 (4,11)	0.67	0.95
Male (n, %)	649 (62)	175 (60)	81 (70)	55 (63)	0.28	0.94
Average number of patients per center (median:range)	37 (30:2–200)	59 (40:20–97)	23 (36:11–49)	35 (19–50)	< 0.001	0.97
PICU number of beds: median (min, max)	40 (20, 83)	32 (23, 71)	42 (38, 83)	23 (20, 81)		
Race					< 0.001	< 0.001
White (n, %)	279 (27)	100 (34)	21 (18)	18 (22)		
Black (n, %)	484 (46)	89 (30)	33 (28)	48 (55)		
Hispanic (n, %)	89 (9)	46 (16)	38 (33)	6 (7)		
Asian (n, %)	15 (1)	7 (2)	7 (6)	0		
Other (n, %)	69 (7)	18 (6)	15 (13)	7 (8)		
Missing (n, %)	125 (12)	35 (12)	2 (2)	8 (10)		
Payor					< 0.001	< 0.001
Government (n, %)	572 (55)	152 (52)	54 (47)	31 (36)		
Private (n, %)	226 (22)	98 (33)	23 (20)	28 (32)		
Other (n, %)	154 (15)	33 (11)	31 (27)	22 (25)		
Missing (n, %)	94 (9)	10 (4)	8 (7)	6 (7)		
PICU asthma medications						
Steroids (n, %)	955 (91)	264 (90)	109 (94)	81 (92)	0.52	0.84
Inhaled albuterol (n, %)	926 (89)	273 (93)	103 (89)	52 (60)	< 0.001	< 0.001
Inhaled ipratropium (n, %)	709 (68)	239 (81)	66 (57)	53 (60)	< 0.001	0.14
Magnesium sulfate (n, %)	485 (46)	152 (51)	52 (43)	47 (54)	0.21	0.13
Methylxanthines (n, %)	163 (16)	31 (11)	6 (5)	5 (6)	< 0.001	0.01
Terbutaline (n, %)	372 (36)	80 (27)	62 (53)	42 (48)	< 0.001	< 0.001
Any β agonist (n, %)	979 (94)	281 (95)	108 (93)	63 (72)	< 0.001	< 0.001
Antibiotics (n, %)	666 (64)	174 (59)	91 (78)	71 (80)	< 0.001	< 0.001
Neuromuscular blocking agents (n, %)	456 (44)	99 (34)	83 (72)	67 (77)	< 0.001	< 0.001
Mechanical support						
Bilevel positive airway pressure (n, %)	82 (8)	16 (5)	8 (7)	7 (8)	0.47	0.95
Heliox (n, %)	226 (22)	107 (36)	13 (11)	2 (2)	< 0.001	< 0.001
Days of bilevel positive airway pressure (median, IQR)	1 (1,2)	2 (1,3)	2 (1,8)	1 (1,3)	0.36	0.85

(*Continued*)

TABLE 2. (*Continued*). Demographic and Clinical Features of Children Who Received Care at Centers by Use of Volatile Agent Use Among Intubated Children With Asthma

Feature	No Volatile Use (*n* = 1,046)	< 5% volatile Use (*n* = 295)	5.1% to 10% Volatile Use (*n* = 116)	> 10% Volatile Use (*n* = 87)	Comparison Across All Groups (*p*)	Comparison Group 0% and > 10% (*p*)
Days of ventilation (median, IQR)	2 (1,4)	1 (1.3)	2 (1,4)	3 (1,7)	< 0.001	< 0.001
Days of anesthesia (median, IQR)	–	1 (1,1)	1 (1,2)	1 (1,4)	0.024	
Days of neuromuscular blocking agent (median, IQR)	2 (1,3)	1 (1,2)	2 (1,4)	3 (1,7)	< 0.001	< 0.001
Days in hospital (median, IQR)	4 (6,8)	6 (2,12)	6 (4,9)	7 (4,13)	< 0.001	0.002
Complications						
Aspiration pneumonia (*n*, %)	17 (2)	5 (2)	5 (4)	5 (6)	0.39	0.011
Pneumothorax (*n*, %)	28 (3)	7 (2)	2 (2)	2 (2)	0.61	0.33
Cardiac arrest (*n*, %)	8 (1)	0	1 (1)	0	0.46	0.47
Tests in PICU						
Blood gases (median, IQR)	6 (2,25)	8 (3,25)	12 (4,28)	16 (3,80)	< 0.001	< 0.001
Chest radiographs (median, IQR)	6 (2,20)	4 (1,12)	12 (2,30)	23 (2,64)	< 0.001	< 0.001
Electrolytes (median, IQR)	6 (3,15)	4 (1,5)	12 (5,29)	5 (1,39)	< 0.001	0.53
Magnesium levels (median, IQR)	6 (3,21)	5 (2,16)	8 (4,14)	14 (2,28)	0.023	0.51
Hospital charges						
Charges (median, IQR)	$34K ($19,72K)	$29 K ($16,52K)	$65K (34,91K),	$66K ($37,109K)	< 0.001	< 0.001

IQR = interquartile range.
Any β agonist includes inhaled albuterol, levalbuterol, terbutaline, and intravenous terbutaline.

with administration of VA, this observation cannot distinguish whether the event occurred with intubation or during a different time point in care. Aspiration pneumonia may also be indicative of severity of illness.

Substantial variation in asthma care was present in our data; however, this variation has been previously reported using several databases (18–20). Only 11 of 40 centers administered VA for severe asthma, and its use did not appear related to PICU bed size. The use of VA may reflect several factors including the clinical experience of PICU physicians and ease of administering VA in the PICU, such as availability of appropriate ventilator and scavenging equipment, anesthesiologist presence during the period of volatile anesthetic administration, and billing for these services. Given the rarity of use, PICU providers without this expertise should seek consultation from anesthesiologists and develop systems for medication delivery and staff education prior to use for a critically ill patient.

Centers with greatest use of VA had significantly longer duration of mechanical ventilation and LOS and higher charges for intubated patients compared with children treated at centers that did not use VA for care of critical asthma. It is possible that children who received VA may have been more severely ill than children who did not receive VA. We did not demonstrate a clear benefit from administration of VA; however, the PHIS database does not contain severity of illness information, so this analysis cannot evaluate appropriateness of VA use for individual patients. Asthmatic children treated with ECMO had lower median charges than those treated with VA while duration of ventilation and LOS were similar for these two "severe" groups treated with a "rescue" therapy. Acute complications were infrequent as was death and did not differ between children treated with a "rescue" therapy or not.

Although our study is weakened by lack of physiologic and laboratory data, some inferences can be made regarding

frequency of VAU. Centers with the greatest use of VA (> 10%) treated significantly fewer patients with recommended asthma medications. These differences in medication use were most pronounced for inhaled β2 agonists, which may reflect concern about interrupting the volatile anesthetic to enable aerosolized drug delivery or a provider preference for VA over standard inhaled asthma medications among intubated patients. However, current recommended anesthetic management for bronchospasm includes systemic steroids and inhaled β2 agonists (21). Patients treated at centers with > 10%VAU had significantly greater median LOS and charges compared with children treated at centers that did not use VA for asthma. However, centers with lower VAU were equally likely to administer recommended medications compared with centers with no VAU, and the median LOS and charges were similar to those treated at centers with no VAU.

The documented experience with VA as a "rescue" therapy in children with severe asthma is confined to a few case reports and case series spanning the past 20 years. These are summarized in **Table 3**. Our study augments these reports by documenting low mortality risk and data about cost of care.

Although this study has the advantage of a large sample of children mechanically ventilated in pediatric ICUs for severe asthma, the PHIS database has limitations. The specific volatile anesthetic used for each case was not provided. Although older reports in the literature suggest that isoflurane may reduce dynamic compliance (a measure of small airway resistance) more than halothane (32, 33), more recent studies demonstrate no difference in the bronchodilating properties of the VAs currently in clinical use: halothane, isoflurane, sevoflurane, and desflurane (34). However, because these studies have not been conducted in humans, it is theoretically possible that one agent may be preferable to another in select patient groups.

Our assessment of exposure to various asthma treatments was based on billing; however, it is possible that some patients received medications but were not billed for those treatments. The ascertainment of asthma medications relied on pharmacy charges that we cannot verify. For instance, clinical practice suggests that all children with asthma receive β agonist treatment, but our data did not capture administration to all patients. Our data may have not captured all charges for these medications. Additionally, we selected patients based on their primary diagnosis code for asthma. Use of ECMO was captured by ICD procedure codes, whereas VA use was assessed by CTC. Because diagnosis and procedure codes are used for billing, the ascertainment for exposure to ECMO may differ compared with ascertainment for VA. We also cannot be sure if the individual patient actually received a charged therapy. It is possible that despite having a primary diagnosis code for asthma supported with invasive mechanical ventilation, being billed for VA, a PICU bed, and mechanical ventilation, some subjects may have been included who were not intubated for their asthma exacerbation. Another major limitation is that the pharmacy and procedure data are recorded by calendar day that prevents assessment of the sequence of care within a given day.

Given the limitations discussed above, it is difficult to explicitly answer the question in our title. However, certain conclusions can be drawn. VAs are being used in some PICUs nationally as a rescue therapy for severe childhood asthma leading to ventilatory failure requiring mechanical ventilation. Mortality does not differ between centers regardless of the use of VA for asthma. Use of VA was associated with substantially increased cost of care, compared with even ECMO. Increasing VAU was associated with greater duration of ventilation, hospital LOS, and testing with blood gases and radiographs.

TABLE 3. Use of Volatile Anesthetics in Children With Asthma

Study Reference	Year	Study Type	Number of Patients	Medication
Revell et al (9)	1988	Case report	1	Isoflurane
Johnston et al (22)	1990	Case series	2	Isoflurane
DeNichola et al (23)	1990	Case report	1	Halothane
Habre et al (24)	1996	Case series	60	Halothane
Miyagi et al (25)	1997	Case report	1	Isoflurane
Rice et al (26)	1998	Letter to editor/case report	2	Isoflurane
Habre et al (27)	1999	Case-control	44	Sevoflurane
Wheeler et al (5)	2000	Case series	6	Isoflurane
Mazzeo et al (28)	2004	Case report	1	Sevoflurane
Restrepo et al (29)	2005	Case report	1	Halothane
Shankar et al (30)	2006	Case series	10	Isoflurane
Watanabe et al (31)	2008	Case report	1	Sevoflurane

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