MAR Pediatrics (2024) 5:3

Research Article

Retrospective Observational Study on the Safety and Effectiveness of Ketamine as a Bronchodilator in Pediatric Asthma and Bronchiolitis

Dr Sachin Padman [1]*, Dr Tejaswini A [2], Venugopal Reddy I[3]

1. Director and Consultant Paediatrician Sunrise Hospital, Kanhangad, Kerala.

2. Junior consultant in Paediatricis, Sunrise Hospital Kanhangad , Kerala.

3. Medical Director and Consultant Pediatrician Ovum Hospital, Bangalore.

***Correspondence to:** Dr Sachin Padman, Director and Consultant Paediatrician Sunrise Hospital, Kanhangad, Kerala

Copyright

© 2024: **Dr Sachin Padman**. This is an open access article distributed under the Creative Commons AttributionLicense, which permits unrestricted use, distribution, and reproduction in any medium, provided the originalwork is properly cited.

Received: 11 March 2024

Published: 15 March 2024

Introduction

Asthma is a chronic inflammatory disorder of the airways, characterized by increased airway hyper-responsiveness, recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. In India, asthma rates are officially low, but recent evidence suggests a higher prevalence. The total estimated burden of asthma is 3%, with a median prevalence of 2.4% among adults over 15. Asthma exacerbations are a frequent cause of morbidity and mortality, and response to therapy is variable. Conventional therapies like nebulized albuterol, anti-cholinergics, theophylline, epinephrine, and corticosteroids are generally effective, but some patients require invasive ventilation due to worsening respiratory distress. Anesthetic agents like ketamine, isoflurane, sevoflurane, and halothane have bronchodilator properties, but no definite dosages and guidelines have been framed for severe refractory status asthmaticus. This review discusses the effects of ketamine on respiratory mechanics, its beneficial uses in refractory status asthmaticus, and potential adverse effects in context with available data.

Inclusion/Exclusion Criteria:

Inclusion: Children diagnosed with bronchial asthma or bronchiolitis, treated with ketamine between a specific timeframe (e.g., past 5 years).

Exclusion: Children with pre-existing neurological conditions, known history of ketamine misuse, or incomplete medical records.

Data Collection: Patient Demographics (age, sex, medical history) Diagnosis & Severity of Bronchial Asthma/Bronchiolitis Conventional Treatments Received Before Ketamine Ketamine Administration details (dosage, duration, route) Respiratory Parameters (e.g., oxygen saturation, wheezing scores) Clinical Outcomes (improvement in symptoms, need for mechanical ventilation, length of hospital stay) Adverse Events (hallucinations, sedation, changes in blood pressure)

Data Analysis: Descriptive statistics for patient demographics and outcomes. Univariate and/or multivariate analysis to identify associations between: Ketamine administration and clinical outcomes. Predictors of response to ketamine (e.g., age, diagnosis, severity). Occurrence of adverse events and associated factors.

Considerations: Ethical Approval: Ensure ethical approval from your institution, addressing data privacy and confidentiality.

Data Quality: Verify the accuracy and completeness of medical records. Selection Bias: Acknowledge potential limitations due to the retrospective nature (e.g., selection bias, confounding variables). Generalizability: Consider the specific patient population and setting.

Statistical Analysis

Statistical analysis of the data was performed using SPSS 23.0. The Categorical variables were presented as frequency and percentage. The continuous variables were presented as mean ± SD. Comparison between the groups was done using ANOVA followed by Bonferroni. A p value <0.05 was considered statistically significant

Table1: Age distribution

Age	Frequency	Percent
<12months	2	10.0
1-6 years	15	75.0
7-12 years	3	15.0
Total	20	100.0

The majority of the population surveyed falls within the 1 to 6 years age range, comprising 75.0% of the total. Infants under 12 months represent 10.0%, while children aged 7 to 12 years constitute 15.0%.

Table 2: Distribution based on gender

	Frequency	Percent
Female	10	50.0
Male	10	50.0
Total	20	100.0

The population surveyed has an equal number of females and males, each making up 50.0% of the total.

Table 3:mean and SD of weight

	N	Minimum	Maximum	Mean	Std. Deviation
Weight	20	6.00	26.00	13.7300	4.83682

The weight data for the surveyed population of 20 individuals ranges from 6.00 to 26.00 units, with an average weight of 13.7300 units and a standard deviation of 4.83682 units.

Table 4: Duration of presenting illness

Duration	Frequency	Percent
1day	12	60.0
2days	7	35.0
3days	1	5.0
Total	20	100.0

The table summarizes the duration of presenting illness within the surveyed population. Most individuals (60.0%) reported a duration of 1 day, followed by 35.0% reporting 2 days, with only a small proportion (5.0%) indicating a duration of 3 days.

Table 5: History

	Frequency	Percent
Cogh , cold , breathing difficulty	3	15.0
Cold , breathing difficulty 1 day	2	10.0
Cold 3 days. Fever and breathing difficulty 1 day	1	5.0
Cold and breathing difficulty	1	5.0
Cold, breathing difficulty	1	5.0
Cough , cold , fever , breathing difficulty	3	15.0
Cough ,bearthing difficulty 1 day	3	15.0
Fever , cough , breathing difficulty	6	30.0
Total	20	100.0

The table illustrates the frequency and distribution of symptoms reported by the surveyed individuals. The most common symptoms were fever, cough, and breathing difficulty, which accounted for 30.0% of the cases. Other prevalent symptoms included cough, cold, and breathing difficulty, with varying durations and combinations.

Table 6: Family history of asthma / atopy

	Frequency	Percent
Father	1	5.0
Grand mother	1	5.0
Mother	2	10.0
No one	16	80.0
Total	20	100.0

The table provides insight into the family history of asthma or atopy among the surveyed population. It shows that majority, constituting 80.0% of respondents, reported no family history of asthma or atopy. Among those who did report a family history, 5.0% each for fathers and grandmothers, and 10.0% for mothers.

Table 7: Past history

	Frequency	Percent
allergic rhinitis	1	5.0
intermittent wheezer	1	5.0
nothing	10	50.0
recurrent WALRI	6	30.0
recurrent LRTI	1	5.0
recurrent WALRI , allergic rhinitis	1	5.0
Total	20	100.0

The table outlines the past medical history of the surveyed individuals. It reveals that a significant portion, accounting for 50.0%, reported no specific past medical issues. WALRI was the most commonly mentioned, comprising 30.0% of cases. Additionally, there were sporadic reports of other conditions such as allergic rhinitis, intermittent wheezing, and combinations thereof, each representing 5.0% of the total cases.

Table 8: Diagnosis

	Frequency	Percent
Aute severe asthma	1	5.0
Bronchiolitis	2	10.0
WALRI	17	85.0
Total	20	100.0

The table summarizes the diagnoses among the surveyed individuals. The majority, constituting 85.0%, were diagnosed with lower respiratory tract infections (WALRI). Additionally, 10.0% were diagnosed with bronchiolitis, while 5.0% received a diagnosis of acute severe asthma.

Table 9: Pram score

	Frequency	Percent
8.00	3	15.0
9.00	7	35.0
10.00	7	35.0
11.00	3	15.0
Total	20	100.0

The table displays PRAM (Pediatric Respiratory Assessment Measure) scores for the surveyed individuals. Scores of 9.00 and 10.00 are the most common, each representing 35.0% of cases, followed by scores of 8.00 and 11.00, each at 15.0%.

Table 10: PICU stay

	Frequency	Percent
3days	2	10.0
4days	12	60.0
5days	6	30.0
Total	20	100.0

The table provides information on the length of Pediatric Intensive Care Unit (PICU) stays for the surveyed individuals. It indicates that the majority, comprising 60.0%, had a PICU stay of 4 days, followed by 30.0% with a stay of 5 days. A smaller proportion, 10.0%, had a PICU stay of 3 days.

Table 11: treatment before admission

	Frequency	Percent
2 nd hrly SABA neb, anticholinergics ,mgso4,hydrocort, antibiotics, antiviral	19	95.0
salbutamol continous nebulization, ipravent and budecort neb, mgso4, hydrocortisone, iv antibiotics, antiviral , Ivfluids	1	5.0
Total	20	100.0

Majority of 95% were under 2 nd hrly SABA neb, anticholinergics, mgso4, hydrocort, antibiotics, antiviral.

Table 12: Ketamine initiated

	Frequency	Percent
5mic/kg/mint IV infusion	20	100.0

All individuals in the surveyed population initiated ketamine through a 5 mic/kg/min IV infusion, representing 100.0% of the cases.

Table13:Duration of Ketamine infusion

	Frequency	Percent
<=50 hours	18	90
>50 hours	2	10
Total	20	100.0

The table presents the duration of ketamine infusion among the surveyed individuals. The majority, accounting for 90.0% of cases, had infusions lasting 50 hours or less. Conversely, 10.0% had infusions lasting more than 50 hours.

Table 14:Temperature

	Frequency	Percent
Febrile	1	5.0
Normal	19	95.0
Total	20	100.0

The table illustrates the distribution of temperature status among the surveyed individuals. The vast majority, comprising 95.0% of cases, exhibited normal temperature levels, while only 5.0% were classified as febrile.

Table 15: RR

RR	Mean	Std. Deviation	F value	P value
At admission	53.650	5.518		
Before ketamine	51.250	5.169		
4hours after ketamine	36.000	4.779		
48 hours of admission	27.750	2.221	17.000	P<0.001

The respiratory rate (RR) data indicates significant fluctuations over different time points. the mean RR was 53.650 ± 5.518 breaths per minute , Before ketamine administration, the RR remained elevated at 51.250 ± 5.169 breaths per minute. However, following ketamine infusion, a substantial reduction in RR was observed, with the mean dropping to 36.000 ± 4.779 breaths per minute after 4 hours and further decreasing to 27.750 ± 2.221 breaths per minute 48 hours post-admission.

Table 16: Multiple comparison of RR

(I) factor1		Mean Difference (I-J)	Std. Error	P value	95% Confidence Interval for Difference[b]	
					Lower Bound	Upper Bound
At admission	Before ketamine	2.400*	.483	.001	.977	3.823
	4hours after ketamine	17.650*	1.286	.000	13.864	21.436
	48 hours of admission	25.900*	1.174	.000	22.444	29.356
Before ketamine	4hours after ketamine	15.250*	1.285	.000	11.466	19.034
	48 hours of admission	23.500*	1.053	.000	20.401	26.599
4hours after ketamine	48 hours of admission	8.250*	.940	.000	5.483	11.017

The p-values in the multiple comparison table indicate the statistical significance of the differences in respiratory rate (RR) between various time points. In each comparison, the p-value is less than 0.05, indicating that the observed differences are statistically significant.

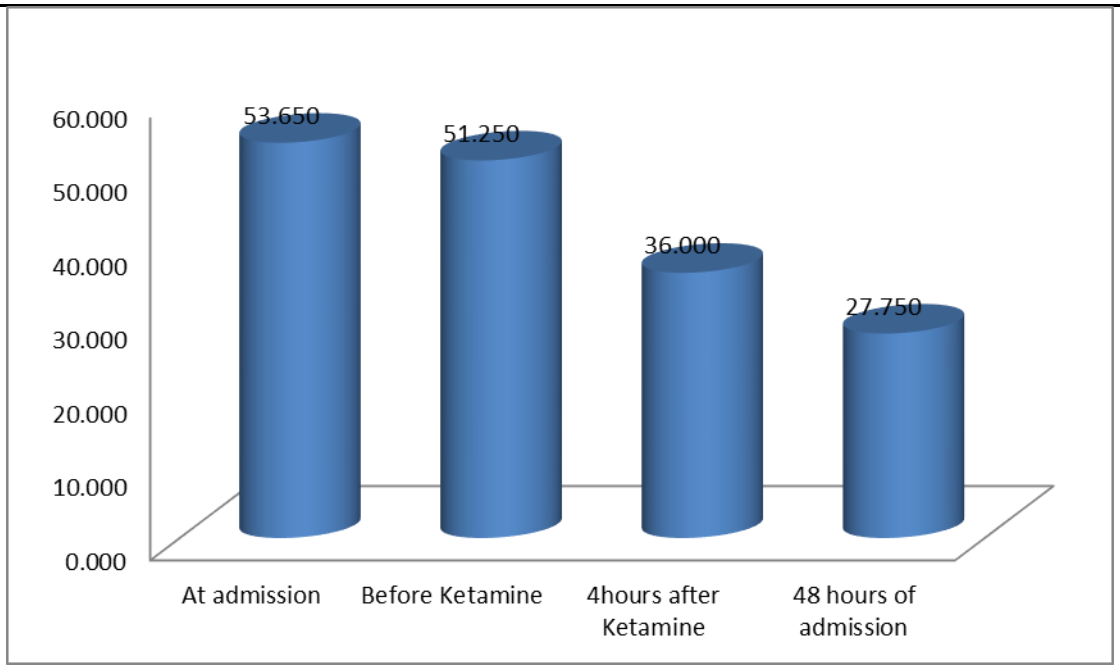

Figure 1

Table 17 : HR

HR	Mean	Std. Deviation		
At admission	159.100	9.619	401.540	p<0.001
Before Ketamine	164.700	9.342		
4hours after Ketamine	156.600	8.762		
48 hours of admission	103.400	5.688		

The mean heart rate (HR) and its standard deviation (SD) at different intervals are as follows:

At admission: 159.100 ± 9.619 beats per minute,Before Ketamine: 164.700 ± 9.342 beats per minute,4 hours after Ketamine: 156.600 ± 8.762 beats per minute,48 hours post-admission: 103.400 ± 5.688 beats per minute.These values indicate statistically significant changes in HR over time.

Table 18: Multiple comparison in HR

(I) factor1		Mean Difference (I-J)	Std. Error	p value	95% Confidence Interval for Difference[b]	
					Lower Bound	Upper Bound
At admission	Before ketamine	-5.600	2.233	.128	-12.174	.974
	4hours after ketamine	2.500	2.328	1.000	-4.353	9.353
	48 hours of admission	55.700*	2.496	.000	48.351	63.049
Before ketamine	4hours after ketamine	8.100*	1.126	.000	4.785	11.415
	48 hours of admission	61.300*	1.963	.000	55.521	67.079
4hours after ketamine	48 hours of admission	53.200*	1.617	.000	48.441	57.959

The statistically significant p-values ($p < 0.05$) indicate meaningful differences in heart rate (HR) between various time points. These findings suggest notable changes in HR over time, particularly higher HR levels observed 48 hours after admission compared to earlier time points.

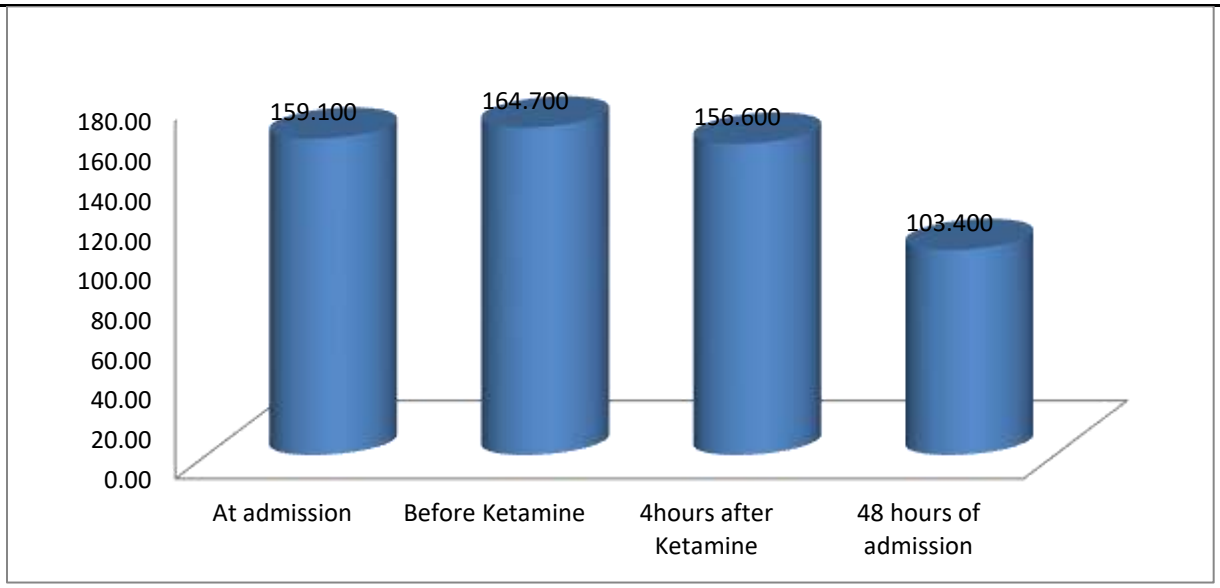

Figure 2

Table 19:SPO2

SPO2	Mean	Std. Deviation	F value	p value
At admisiion	84.550	8.300	18.000	p<0.001
before Ketamine	95.450	1.761		
4hours after Ketamine	98.850	0.745		

At admission, the mean SpO2 (blood oxygen saturation level) was 84.550% with a standard deviation of 8.300. This significantly improved to 95.450% before ketamine administration. Following ketamine infusion, there was a further increase in SpO2, reaching 98.850% 4 hours afterward. These changes were statistically significant, as indicated by the F-value of 18.000 and p-value of less than 0.001.

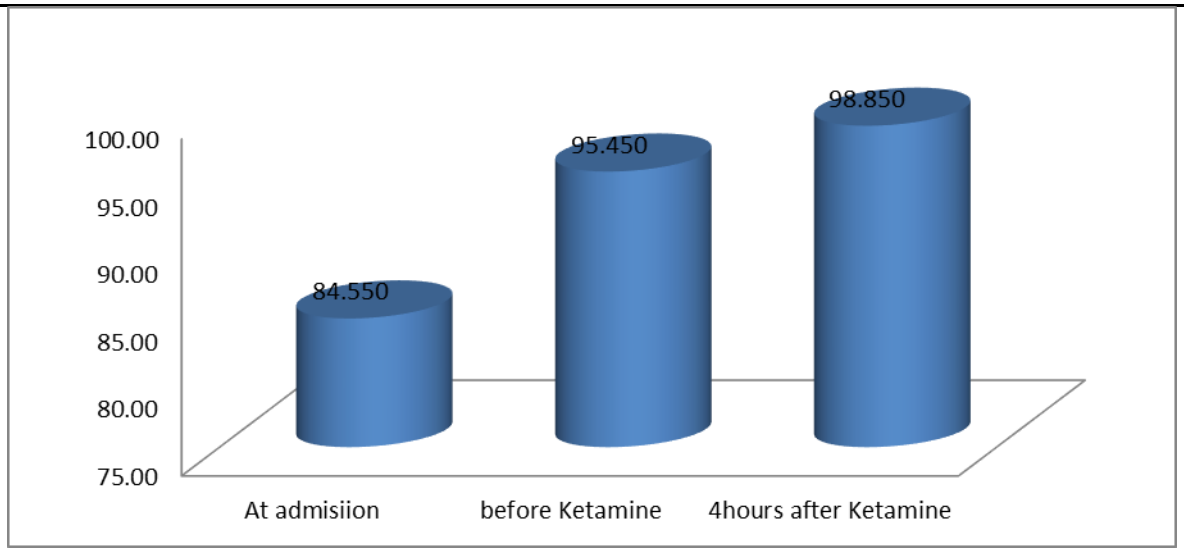

Figure 3

Table 20 : Multiple comparison in SPO2

(I) factor1		Mean Difference (I-J)	Std. Error	p value	95% Confidence Interval for Difference[b]	
					Lower Bound	Upper Bound
At admisiion	before Ketamine	-10.900*	1.664	.000	-15.267	-6.533
	4hours after Ketamine	-14.300*	1.860	.000	-19.182	-9.418
before Ketamine	4hours after Ketamine	-3.400*	.380	.000	-4.397	-2.403

The multiple comparison table for SpO2 (blood oxygen saturation levels) indicates significant differences between various time points. Before ketamine administration, there was a significant decrease in SpO2 levels compared to admission, with a mean difference of -10.900%. However, 4 hours after ketamine infusion, there was a significant increase in SpO2 levels compared to both admission and before ketamine administration, with mean differences of -14.300% and -3.400%, respectively.

Table 21: Adverse, Hallucination, HT, disorientation, trachebrochial secretators and Glycopyyrolate received

		Frequency	Percent
Adverse event	Brochial secretion	1	5.0
	Tracheo bronchial secretion	6	30.0
	No	13	65.0
Hallicination	No	20	100.0
Hyper tension	No	20	100.0
Disorientation	No	20	100.0
Tracheobronchial secretions	No	13	65.0
	Yes	7	35.0
Glycopyyrolate received	No	13	65.0
	Yes	7	35.0

Among adverse events, tracheo bronchial secretion was the most commonly reported, accounting for 30.0% of cases, followed by brochial secretion at 5.0%. the majority of individuals (65.0%) did not experience any adverse events. Regarding specific medical conditions, all surveyed individuals reported no occurrences of hallucination, hypertension, or disorientation. However, tracheobronchial secretions were noted in 35.0% of cases, while 7 individuals (35.0%) received glycopyrrolate.

Discussion

The majority of the population surveyed was between 1 and 6 years old, with 75.0% of the total being males and 10.0% females. The weight data for the 20 individuals ranged from 6.00 to 26.00 units, with an average weight of 13.7300 units and a standard deviation of 4.83682 units. The duration of presenting illness was most common (60.0%), with most individuals reporting a duration of 1 day. The most common symptoms were fever, cough, and breathing difficulty, accounting for 30.0% of cases.

The majority of respondents (80.0%) reported no family history of asthma or atopy. A significant portion (50.0%) reported no specific past medical issues. WALRI was the most commonly mentioned condition,

comprising 30.0% of cases. Other conditions such as allergic rhinitis, intermittent wheezing, and combinations thereof represented 5.0% of the total cases.

The majority (85.0%) were diagnosed with lower respiratory tract infections (WALRI), bronchiolitis, and acute severe asthma. PRAM scores were the most common, representing 35.0% of cases, followed by scores of 8.00 and 11.00, each at 15.0%. The length of Pediatric Intensive Care Unit (PICU) stays was the most common, with 60.0% having a stay of 4 days, 30.0% with a stay of 5 days, and a smaller proportion (10) having a stay of 3 days.

All individuals initiated ketamine through a 5 mic/kg/min IV infusion, representing 100.0% of the cases. The mean heart rate (HR) data indicated significant fluctuations over different time points, with the mean dropping to 36.000 ± 4.779 breaths per minute after 4 hours and further decreasing to 27.750 ± 2.221 breaths per minute 48 hours post-admission.

At admission, the mean SpO2 (blood oxygen saturation level) was 84.550%, significantly improved to 95.450% before ketamine administration. Following ketamine infusion, there was a further increase in SpO2 levels, reaching 98.850% 4 hours afterward.

Among adverse events, tracheo bronchial secretion was the most commonly reported, accounting for 30.0% of cases. The majority of individuals (65.0%) did not experience any adverse events. Regarding specific medical conditions, all surveyed individuals reported no occurrences of hallucination, hypertension, or disorientation. However, tracheobronchial secretions were noted in 35.0% of cases, while 7 individuals (35.0%) received glycopyrrolate.

Conclusion

Ketamine is a versatile and inexpensive drug used as a bronchodilator in severe status asthmaticus refractory to routine medications. It has been found to eliminate the need for mechanical ventilation in various studies due to its limited side effects. However, its use in asthma is debated due to a lack of randomized studies and information on its optimum dose. Physicians typically administer bolus doses ranging from 0.1-2 mg/kg and continuous infusions from 0.15 to 2.5 mg/kg/hr. Most studies have small sample sizes and lack control groups,

and the dosage and duration of conventional medication are not mentioned. Reporting bias is likely, and ketamine is considered a potent bronchodilator for refractory status asthmaticus. Further well-designed studies are needed to identify its role in acute asthma.

References

1. Ebert B, Mikkelsen S, Thorkildsen C, Borgbjerg FM. Norketamine, the main metabolite of ketamine, is a non-competitive NMDA receptor antagonist in the rat cortex and spinal cord. Eur J Pharmacol. 1997;333:99–104. [PubMed] [Google Scholar]

2. Grant IS, Nimmo WS, McNicol LR, Clements JS. Ketamine disposition in children and adults. Br J Anaesth. 1983;55:1107–11. [PubMed] [Google Scholar]

3. Qureshi FA, Mellis PT, McFadden MA. Efficacy of oral ketamine for providing sedation and analgesia to children requiring laceration repair. Pediatr Emerg Care. 1995;11:93–7. [PubMed] [Google Scholar]

4. Roelofse JA, Joubert JJ, Swart LC, Stander I, Roelofse PG. An evaluation of the effect of oral ketamine and standard oral premedication in the sedation of paediatric dental patients. J Dent Assoc S Afr. 1996;51:197–201. [PubMed] [Google Scholar]

5. Bourke DL, MAlit LA, Smith TC. Respiratory interactions of ketamine and morphine. Anesthesiology. 1987;66:153–6. [PubMed] [Google Scholar]

6. Hamza J, Ecoffey C, Gross JB. Ventilatory response to CO2 following intravenous ketamine in children. Anesthesiology. 1989;70:422–25. [PubMed] [Google Scholar]

7. Mankikian B, Cantineau JP, Sartene R, Clergue F, Viars P. Ventilatory pattern of chest wall mechanics during ketamine anesthesia in humans. Anesthesiology. 1986;65:492–99. [PubMed] [Google Scholar]

8. Shulman D, Beardsmore CS, Aronson HB, Godfrey S. The effect of ketamine on the functional residual capacity in young children. Anesthesiology. 1985;62:551–56. [PubMed] [Google Scholar]

9. Betts EK, Parkin CE. Use of ketamine in an asthmatic child. Anesth Analg. 1971;50:420–1. [PubMed] [Google Scholar]

10. Corssen G, Gutierrez J, Reves JG, Huber FC., Jr Ketamine in the anesthetic management of asthmatic patients. Anesth Analg Curr Res. 1972;51:588–96. [PubMed] [Google Scholar]

11. Youssef-Ahmed MZ, Silver P, Nimkoff L, Sagy M. Continuous infusion of ketamine in mechanically ventilated children with refractory bronchospasm. Intensive Care Med. 1996;22:972–6. [PubMed] [Google Scholar]

12. Hemmingsen C, Nielsen PK, Odorico J. Ketamine in the treatment of bronchospasm during mechanical ventilation. Am J Emerg Med. 1994;12:417–20. [PubMed] [Google Scholar]

13. Shlamovitz GZ, Hawthorne T. Intravenous ketamine in a dissociating Dose as a temporizing measure to avoid mechanical ventilation in adult patient with severe asthma exacerbation. J Emerg Med. 2008;41:492–4. [PubMed] [Google Scholar]

14. Strube PJ, Hallam PL. Ketamine by continuous infusion in status asthmaticus. Anaesthesia. 1986;41:1017–9. [PubMed] [Google Scholar]

15. Jahangir SM, Islam F, Chowdhury SN, Aziz L, Ghani MA. Ketamine infusion for postoperative analgesia: A prospective cohort study in asthmatics. Bangladesh Med Res Counc Bull. 1993;19:21–7. [PubMed] [Google Scholar]

16. Achar MN, Achar KN. Efficacy of ketamine infusion in refractory asthma complicated by acute myocardial infarction. Anaesth Intensive Care. 1993;21:115–7. [PubMed] [Google Scholar]

17. Park GR, Manara AR, Mendel L, Bateman PE. Ketamine infusion. Its use as a sedative, inotrope and bronchodilator in a critically ill patient. Anaesthesia. 1987;42:980–3. [PubMed] [Google Scholar]

18. Huber FC, Jr, Reves JG, Gutierrez J, Corssen G. Ketamine: Its effect on airway resistance in man. South Med J. 1972;65:1176–80. [PubMed] [Google Scholar]

19. Petrillo TM, Fortenberry JD, Linzer JF, Simon HK. Emergency department use of ketamine in pediatric status asthmaticus. J Asthma. 2001;38:657–64. [PubMed] [Google Scholar]

20. Heshmati F, Zeinali MB, Noroozinia H, Abbacivash R, Mahoori A. Use of ketamine in severe status asthmaticus in intensive care unit. Iran J Allergy Asthma Immunol. 2003;2:175–80. [PubMed] [Google Scholar]

21. Howton JC, Rose J, Duffy S, Zoltanski T, Levitt MA. Randomized, double-blind, placebo-controlled trial of intravenous ketamine in acute asthma. Ann Emerg Med. 1996;27:170–5. [PubMed] [Google Scholar]

22. Allen JY, Macias CG. The efficacy of ketamine in pediatric emergency department patients who present with acute severe asthma. Ann Emerg Med. 2005;4:43–50. [PubMed] [Google Scholar]

23. Rock MJ, Reyes de la Rocha S, L'Hommedieu CS, Truemper E. Use of ketamine in asthmatic children to treat respiratory failure refractory to conventional therapy. Crit Care Med. 1986;14:514–16. [PubMed] [Google Scholar]

24. Fisher MM. Ketamine hydrochloride in severe bronchospasm. Anesthesia. 1977;32:771–2. [PubMed] [Google Scholar]

25. Turnpenny PD, Nash SF. Ketamine in severe acute asthma. Arch Emerg Med. 1991;8:291–2. [PMC free article] [PubMed] [Google Scholar]

26. Hemming A, MacKenzie I, Finfer S. Response to ketamine in status asthmaticus resistant to maximal medical treatment. Thorax. 1994;49:90–1. [PMC free article] [PubMed] [Google Scholar]

27. Galbis-Reig D, Rasansky MA. A case presentation and literature review of successful ketamine administration in a patient with refractory status asthmaticus. Internet J Intern Med. 2004;5:31. [Google Scholar].