

The use of non-invasive ventilation in asthma exacerbation – a two year retrospective analysis of outcomes

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ABSTRACT

Background: The use of Non-Invasive Ventilation (NIV) in acute asthma exacerbation remains controversial. Comparative data on patient characteristics that benefit from NIV in asthma exacerbation to those patients that fail NIV remains limited. Our study compares some of these patient characteristics and examines if NIV is safe and effective in carefully selected patients.

Methods: Following institutional review board approval, we extracted from the electronic medical record and conducted a retrospective chart-based review of those patients who received NIV in the emergency room for a diagnosis of asthma exacerbation from January 2017 to December 2018.

Results and Conclusion: The rate of failure of NIV overall was low, at 9.17%, with younger patients more likely to fail NIV ($P = 0.03$) and need invasive mechanical ventilation. Surprisingly, baseline asthma severity did not impact NIV failure rate, and neither did body mass index, smoking history, and a host of clinical characteristics. Understandably, the length of stay was significantly longer in the group of patients that failed NIV. There were no adverse events, such as an increased rate of barotrauma events in either group. In conclusion, this study contributes to the growing body of evidence that NIV is a safe and effective adjunct to routine care in the management of patients with asthma exacerbation.

ARTICLE HISTORY

Received 15 February 2021
Accepted 09 July 2021

KEYWORDS

Noninvasive ventilation;
bronchial asthma
exacerbation



1. Introduction

Asthma affects 1 in 10 adults in the USA, accounting for 2 million emergency department visits per year, of which about 20–30% are hospitalized [1]. Of those admitted, intensive care admissions continue to account for 10–30% of patients [2,3], despite aggressive therapy. Of those patients needing invasive mechanical ventilation, 8–22% do not survive [4,5]. Pathophysiologically, invasive mechanical ventilation (IMV) does little to address the etiology of respiratory failure in asthma, which is bronchospasm, muscle fatigue, and dynamic hyperinflation. It may, in fact, cause harm in untrained hands by contributing to dynamic hyperinflation, increased rates of barotrauma, pneumothorax, and pneumomediastinum [6,7], apart from the increased risk of infections and patient discomfort associated with invasive mechanical ventilation. Non-invasive pressure ventilation (NIV), on the other hand, goes further than IMV in addressing these defects in respiratory mechanics, oxygenation, and ventilation. NIV is the application of positive airway pressure to patients in respiratory distress, improving gas exchange and reducing work of breathing. The use of NIV is well validated in certain disease states, such as exacerbations of

chronic obstructive pulmonary disease (COPD), Congestive heart failure (CHF) [8–10]. The Pathophysiology of asthma exacerbation is in some ways similar to exacerbations of COPD, with bronchospasm and mucus plugging of airways. Consequently, clinicians believe NIV may be helpful for carefully selected patients with asthma exacerbation and respiratory failure, under close monitoring [1], although data in support of this remains scarce [11]. The largest systematic review on the topic, conducted on data from the Cochrane database [12], concluded that NIV improves respiratory rate and lung function but did not comment on its effects on the need for invasive mechanical ventilation or mortality. Thus, the use of NIV in Acute Respiratory Failure caused by Asthma exacerbation remains controversial, despite its continued use in current clinical practice.

2. Clinical rationale

The objective of our study is to compare the clinical characteristics of patients presenting with asthma exacerbation who were successfully treated with NIV with those who failed therapy, going on to

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need mechanical ventilation. Studies are now beginning to explore the impact of NIV on acute respiratory failure due to asthma exacerbation [12–14], and this study attempts to contribute to the growing body of medical literature available to clinicians.

3. Materials and methods

The study was performed at an inner-city hospital in Bronx, New York, a county known for the highest incidence of asthma in the country [15]. Following institutional review board approval, we performed an observational retrospective chart review of medical records of adults discharged from a community hospital with a diagnosis of asthma exacerbation between the years of January 2017 to December 2018. We included adult patients (age greater than 18 years) who received NIV in the emergency room for asthma exacerbation. Patients were excluded if they required urgent invasive mechanical ventilation on arrival or if the data from the chart was deemed incomplete. In addition, pregnant patients and those with a history of CHF, COPD, obstructive sleep apnea (OSA), and obesity hypoventilation syndrome (OHS) were excluded from the study, as it would not be possible to differentiate routine use of NIV from use of NIV for respiratory distress.

All patients receiving NIV also concurrently received nebulized albuterol and glucocorticoids (usually prednisone 60 mg or intravenous methylprednisolone 125 mg) as part of an escalating course of therapy. In our emergency department, the classic NIV face mask covering the nose and mouth is used for respiratory support. Patients in this study received NIV from S/T D-30 ventilatory support system (Philips Respironics; Carlsbad, CA). Adjunctive measures such as the use of Intramuscular terbutaline and epinephrine, and the use of NIV itself, were used at the discretion of the treating clinician. Failure of NIV was defined as a need for endotracheal intubation

and mechanical ventilation 48 hours after the initiation of NIV. We compared different variables such as demographic information, smoking status, baseline severity of asthma, initial heart rate (HR), respiratory rate (RR), presence of obstructive sleep apnea (OSA), and compared outcomes of the groups.

Analysis was performed using Stata statistical software (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). We compared categorical variables with the chi-squared test, and continuous variables are reported as mean values \pm standard error. Mean values are compared using the student -T-test if a normal distribution is detected. A 2-tailed $p < 0.05$ was considered significant. We compared age, sex, history of drug use and smoking, baseline severity of asthma, initial heart rate(HR) and respiratory rate(RR), length of hospital and ICU stay between those with successful versus failed NIV.

4. Results

We reviewed charts through our Electronic Medical Record, beginning from January 2017 to December 2018. Patients with a concomitant diagnosis of CHF, COPD, obesity, hypoventilation syndrome, and those with incomplete data were excluded. We then reviewed 230 charts of patients with an admitting diagnosis of asthma exacerbation that received non-invasive ventilation as part of disease management during the study period. After excluding patients who did not meet inclusion criteria, we analyzed 109 patients' baseline characteristics and other pre-determined variables.

The baseline characteristics of both groups were found to be similar, as demonstrated in Table 1. Younger patients were more likely to present with a severe exacerbation of their asthma and were more likely to need mechanical ventilation ($p = 0.03$, effect size of 0.66). The effect size was calculated at 0.66,

Table 1. Baseline characteristics of patients.

Characteristics	N = 109	IMV (N = 10, 9%)	NIV (N = 99, 91%)	OR (95% CI)	p
Demographics					
Mean Age	53.74 \pm 15.6	44.7 \pm 14.78	54.66 \pm 15.45	-	0.054
Age < 49 years	42 (39)	7 (17)	35 (83)	4.27 (1.04–17.54)	0.03* EFFECT SIZE = 0.66
Age 50 years and above	67 (61)	3 (5)	64 (95)		
Gender					
Male	35 (32)	3 (9)	32 (91)	0.9 (0.22–3.7)	0.5
Female	74 (68)	7 (9.5)	67 (90.5)		
Clinical characteristics					
CCS					
Mean	2.19 \pm 2.34	2.5 \pm 3.13	2.16 \pm 2.27	-	0.74
0 to 2	69 (63)	6 (9)	63 (91)	0.86 (0.23–3.24)	0.52
3 and above	40 (37)	4 (10)	36 (90)		
BMI					
Mean	33.3 \pm 13.04	31.33 \pm 10.9	33.5 \pm 13.4	-	0.6
Underweight	2 (2)	0	2 (100)	-	-
Normal	21 (19)	3 (14)	18 (86)	Ref	-
Overweight(BMI >25)	30 (28)	3 (10)	27 (90)	0.66 (0.12–3.6)	0.64
Obese (BMI>30)	56(51)	4 (7)	52 (93)	0.46 (0.09–2.2)	0.34

IMV = Mechanical Ventilation; NIV – Non Invasive ventilation; BMI – Body Mass Index, CCS – Charleston Comorbidity Score; OR – Odds Ratio.

Table 2.

Characteristics	N = 109(%)	IMV (N = 10, 9%)	NIV (N = 99, 91%)	OR (95% CI)	p
Severity of asthma					
Not documented	17 (16)	4 (24)	13 (76)	-	-
Intermittent	9 (8)	1 (11)	8 (89)	Ref	-
Mild persistent	9 (8)	1 (11)	8 (89)	1.00 (0.05–18.9)	0.99
Moderate persistent	20 (18)	1 (5)	19 (95)	0.42 (0.02–7.5)	0.55
Severe persistent	54 (50)	3 (6)	51 (94)	0.47(0.04–5.09)	0.53
HR		110.6 ± 21.60	104.72 ± 18.99	-	0.35
60–100	44 (40)	5 (12)	39 (88)	1.54 (0.42–5.66)	0.32
Above 100	65 (60)	5 (8)	60 (92)		
RR	25.9 ± 5.6	27.9 ± 8.2	25.7 ± 5.2	-	0.42
Estimated PF/ Best PF	435.68 ± 78.9	453.33 ± 123.42	434.84 ± 77.66	-	0.69
PEFR					
Mean	212.89 ± 72.14	216 ± 70.3	100	-	-
≤100	6 (6)	2 (33)	4 (67)	-	-
101–150	11 (10)	0	11 (100)	-	-
151–200	17 (15)	0	17 (100)	-	-
201–250	15 (14)	0	15 (100)	-	-
251–300	13 (12)	0	13 (100)	-	-
301–350	1 (1)	0	1 (100)	-	-
>351	1 (1)	0	1 (100)	-	-
NA	45 (41)	8 (18)	37 (82)	-	-
PEFR 100 cutoff					
≤100	6 (6)	2 (43)	4 (57)	-	0.02
Above 100	58 (53)	0	58 (100)		
Smoking					
Never smoker	52 (48)	5 (10)	47 (90)	Ref	-
Active smoker	21 (19.3)	1 (5)	20 (95)	0.851 (0.21–3.4)	0.82
Former smoker	36 (33)	4 (11)	32 (88)	0.4 (0.04–3.8)	0.42
OSA	25 (23)	2 (8)	23 (92)	0.83 (0.16–4.17)	0.58
ABG after NIV use					
No ABG performed	23 (20)	0	23 (100)	-	-
Poor response	11 (10)	10 (91)	1 (9)		
Good response	75 (69)	0	75 (100)		
Outcomes					
Mortality	0	0	0	-	-
LOS	3.78 ± 5.14	12.56 ± 11.61	2.89 ± 2.84	-	0.02

a value consistent with a medium to large effect size, which in essence, confirms that the difference between the two groups is likely significant. Other baseline characteristics for patients in both groups appeared comparable. Gender, body mass index (BMI), and Charleston Comorbidity Score (CCS) did not seem to influence the need for invasive mechanical ventilation in this study (Table 2).

Initial heart rate (HR), Initial respiratory rate (RR), smoking history, history of obstructive sleep apnea (OSA), and baseline severity of asthma did not have an impact on the need of mechanical ventilation in this study. Arterial blood gas (ABG) analysis was used frequently (80%) by physicians, as a means of assessing response to NIV. Of the total number of patients in the study, 69% experienced improved ventilation on their ABG, while 10% of patients sustained a worsening in ventilation. Unsurprisingly, 91% of patients who sustained worsening in their ABG progressed to needing invasive mechanical ventilation.

Mean HR and Mean RR were comparable among groups, suggesting factors such as accessory muscle use, altered mental status, worsening ventilation, and acidosis helped determine the need of employing mechanical ventilation, as is recommended.

There were no adverse events related to the use of NIV on indicators of increased risk of barotrauma

such as pneumomediastinum and pneumothorax. Of the 109 patients placed on NIV, nine patients failed to respond and were placed on Invasive mechanical ventilation (IMV) within 48 hours of admission. Understandably, patients who failed NIV had a longer duration of hospital stay (12.56 ± 11.61 vs. 2.89 ± 2.84).

5. Discussion and conclusions

Over the last two decades, the use of NIV has increased considerably. It has progressed from its use as a standard of care in exacerbations of COPD and cardiogenic pulmonary edema [16,17], to being used increasingly as a short trial in most forms of acute respiratory failure, regardless of etiology. Clinicians employ NIV to decrease the need for invasive mechanical ventilation and its accompanying adverse effects, even as the supporting evidence for its use in diseases such as asthma is weak [18,19]. Nevertheless, the rate of use of NIV in asthma has been increasing over the last decade. A study on a nationwide inpatient dataset demonstrated an increase in NIV use for asthma exacerbation from 0.3% in 2000 to 1.9% in 2009 [19]. Another recent study on 14,000 patients in 98 U.S. hospitals demonstrated an increase in NIV use from 2.3% in 2009 to

4.7% in 201 [20]. Stefan and colleagues [21] propose three possible reasons for the increased use of NIV, in indications for which we may not have the strongest evidence base (such as asthma exacerbations). These include a) pathophysiological similarities between asthma and COPD exacerbations b) increased familiarity among clinicians and respiratory therapists with the NIV devices, monitoring and expected outcomes c) the ability and ease of deployment of NIV in units outside the intensive care unit, allows clinicians to use NIV earlier on in the course of the exacerbation.

Failure rate of NIV for Asthma exacerbation has consistently improved from prior studies from 19.4% in a study from 2015 [13] to about 9.17% in our study. The data from our study suggests that younger patients are at significantly higher risk ($p = 0.03$) of failing NIV (and consequently needing invasive mechanical ventilation). Other factors such as gender, body mass index, smoking status, and baseline severity of asthma did not seem to influence the failure rate of NIV among our patients. Other large studies have reported a failure rate of as low as 4.7% [1]. This suggests that clinicians may now be more experienced with the use of NIV for asthma and perform better in patient selection and monitoring during NIV use. Our study also demonstrates a decreased length of stay (understandably so) for patients treated with NIV compared to patients who failed NIV. This is consistent with the findings of a recent study about NIV use for asthma exacerbation in 58 U.S. hospitals, where hospitals with the highest quartile of NIV use had a significantly shorter length of stay but no difference in case fatality rates [21]. This may be, in part, be due to the severity of the exacerbation in patients needing invasive mechanical ventilation, but the role of NIV (in select patients) in reducing the length of stay by breaking the vicious cycle of respiratory mechanics in asthma exacerbation is becoming increasingly difficult to deny.

An asthma exacerbation is a condition of airflow limitation caused by bronchial wall inflammation and edema, mucus plugging, and smooth muscle-induced bronchoconstriction. The airflow limitation is most pronounced in the expiratory phase, leading to increased end-expiratory lung volumes and positive end-expiratory pressure (PEEP) associated with the retained volume at the end of exhalation. The accumulation of small amounts of end-expiratory lung volume with every respiratory cycle is referred to as dynamic hyperinflation or 'Breath-Stacking.' Both these mechanisms contribute to increased work of breathing, progressive fatigue, and the sensation of dyspnea. In effect, the patient needs to overcome the end-expiratory PEEP by exerting increasing amounts of energy to generate a large enough negative intrathoracic pressure to draw sufficient tidal

volumes across smaller diameters of airways. This process eventually results in progressive muscle fatigue and hypercarbic respiratory failure.

The application of NIV has been used in this situation, as it is thought to break the vicious cycle by applying extrinsic pressure, decreasing the pressure gradient over which the patient needs to breathe, thereby decreasing muscle fatigue, improving alveolar ventilation, and improving gas exchange [21,22,23]. Patients who fail NIV have been managed with invasive mechanical ventilation (IMV). Prior studies have shown that IMV in asthma exacerbation is associated with a longer duration of ICU and hospital stay, a higher rate of complications including barotrauma, nosocomial infections, and increased mortality [4,24–26]. Due to the easy availability and application of NIV, its potential benefits of being able to offload respiratory muscles and improve gas exchange, it is increasingly being used (with good reason, we argue) in asthma exacerbation to decrease the need for invasive mechanical ventilation, decrease the length of stay and potentially decreasing morbidity and mortality [27]

Our study, though pragmatic, is limited by its retrospective chart review design, preventing us from being able to report on bedside clinical assessments on severity of illness. Some selection bias on the part of practicing clinicians in the emergency room may play a role in patient selection, but we hope that the power of the study would correct for large variations in practice. Thirdly, we were only privy to therapy administered within the emergency room (ER) and could not access therapy received prior to ER presentation. Nevertheless, this study also has many strengths. It's pragmatic design grants insight into clinician practice patterns in one of the busiest emergency rooms in the country, catering to a community with one of the largest prevalence of uncontrolled asthma in the USA [15]. It demonstrates that NIV is being used relatively safely in select patients with asthma exacerbations under close observation to reduce the length of hospitalization, reduce the need for invasive mechanical ventilation and its associated complications. The data shows that the younger patients with asthma exacerbation is more likely to need invasive mechanical ventilation, compared to older patients. Length of stay is significantly lower in patients treated with NIV as compared to those who failed NIV use. Larger prospective randomized study designs are warranted in order to further study patient characteristics that are likely to benefit from NIV in severe asthma exacerbations and status asthmaticus.

6. Clinical implications and future directions

Our study builds upon a growing body of evidence [4,20,22–27] that non-invasive ventilation is

increasingly being used in patients with asthma exacerbation, under close observation for a clinical decline, in which case, invasive mechanical ventilation is indicated. After consideration for correct patient selection, NIV is proving to be a relatively safe and effective complement to standard medical management of bronchial asthma exacerbation, decreasing the need for invasive mechanical ventilation and complications associated with it. Future studies may investigate differences in the duration of steroids between patients who received NIV and patients who failed NIV and progressed to requiring mechanical ventilation. Future randomized controlled trials on the use of NIV in bronchial asthma exacerbation will further elucidate the risk factors associated with failure of NIV, and those associated with more favorable outcomes.

Acknowledgments

Each of the Authors participated in curation of literature, formulation of the manuscript from conception to design, analysis and finished product. Dr. Vidya Menon played a supervisory role, as Senior Author, in the conception of the topic, editing, analysis, revision of intellectual content, and in literature review. Thank you for taking the time to evaluate our submission.

Disclosure statement

The Author(s) report no conflicts of Interests.

Funding

The Authors do not report the receipt of any form of funding for the project.

Author notes

The work has been reviewed and approved by all co-authors. It is not currently being considered for publication in any other journal.

Abbreviations

NIV: Noninvasive Ventilation; COPD: chronic obstructive pulmonary disease; CHF: Congestive heart failure; OSA: Obstructive Sleep Apnea; OHS: Obesity Hypoventilation Syndrome; HR: Heart rate; RR: Respiratory Rate; MV: Invasive mechanical ventilation; BMI: Body Mass Index; PEEP: Positive End Expiratory Pressure; ER: Emergency room

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