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ORIGINAL RESEARCH

Non-invasive ventilation use in status asthmaticus: 16 years of experience in a tertiary intensive care

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Abstract

Objective: To describe the use of non-invasive ventilation (NIV) in adults presenting with status asthmaticus to Middlemore Hospital Critical Care Complex (CCC, South Auckland, New Zealand) from 2000 to 2015.

Method: Retrospective review of all adult asthma admissions to the Hospital CCC between 2000 and 2015. Demographic, physiological, treatment data and blood gas results were recorded.

Results: There were 265 asthma admissions to Middlemore Hospital CCC during the study period. The median age was 34 years; 64% were female. NIV was used in 186 admissions, of which eight went on to require intubation and invasive mechanical ventilation (IMV). Twenty-three other admissions received IMV without a trial of NIV and a further 58 were managed with medical care only. The average pH for all admissions was 7.23 and the IMV group had an average pH of 6.99. Forty-five admissions presented with a Glasgow Coma Scale (GCS) score of ≤10. Twenty-five of these were managed with NIV with only one requiring subsequent intubation. The mean duration of NIV in this group was 5 h (range 1–17 h) with a mean ICU and hospital length of stay of 17 h and 3.5 days, respectively. All patients in this group effectively lowered the pCO_2 over a 2 h period with NIV having an average drop of 5.9 kPa and IMV 3.4 kPa.

Conclusion: The use of NIV appears to be safe and effective in patients with severe asthma, including selected patients with an altered level of consciousness. NIV was well tolerated with a low need for subsequent intubation.

Key words: *mechanical ventilation, non-invasive ventilation, severe asthma.*

Key findings

- One of the largest case series of NIV use in severe asthma.
- NIV appears to be safe and effective.
- NIV was well tolerated with a low need for subsequent intubation.

Introduction

Non-invasive ventilation (NIV) is an alternative to invasive mechanical ventilation (IMV) in status asthmaticus. There is good evidence for its use in chronic obstructive airways disease and acute pulmonary oedema, but the use of NIV in asthma remains contentious.[1–3] IMV in status asthmaticus has been associated with higher mortality, morbidity and longer length of stay.[4] NIV has many advantages over IMV; it is easy to initiate and stop treatment, airway reflexes are preserved, no sedation or paralysis is required, communication is easier and there is decreased rates of ventilator-associated pneumonia.[5–7]

The bronchonstriction and mucous plugging in severe asthma impairs expiratory airflow and can generate dynamic hyperinflation. Dynamic hyperinflation creates a positive pressure at end expiration from the elastic recoil of the chest wall and lung, known as intrinsic positive end expiratory pressure (iPEEP). When iPEEP is present, inspiratory effort is unrewarded by airflow until the patient has generated negative pressures greater than iPEEP. This unrewarded respiratory effort is known as the inspiratory threshold load (ITL) and is a major source of dyspnoea and increased work of breathing in patients with severe asthma.[8,9]

NIV can offset the ITL.[9] External PEEP (ePEEP) decreases the pressure gradient from the proximal airway pressure to the alveoli.[8,10] This means that alveolar pressure only needs to fall below ePEEP to initiate airflow rather than all the way to zero.[10]

Additional proposed benefits of NIV include: offsetting the mechanical disadvantage of hyperinflated lungs,[9] improved ventilation perfusion matching,[11] recruitment of lung units, bronchodilator effect[12] and enhancing the effects of bronchodilators.[13]

Despite the theoretical benefits of NIV, there is only a small number of patients in randomised controlled trials (RCTs). The Cochrane review in 2012 highlighted this paucity of evidence and advised there was no basis

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for a change in practice based on the current research.[14] Despite this, there is increasing clinical use and this study seeks to add to the reported experience of using NIV as part of the treatment for severe asthma.[15] This paper reports on all asthma admissions admitted to the Critical Care Complex (CCC) at Middlemore Hospital (MMH) between 2000 and 2015 with a focus on the use of NIV.

Methods

Data sources

MMH in South Auckland, New Zealand is the acute admitting hospital for Counties Manukau District Health Board, with a catchment population of over 530 000 people and over 116 000 ED presentations per year.[16] It has a younger, more ethnically diverse and deprived population compared to the national average.[16]

The CCC comprises a closed six bed High Dependency Unit and 12 bed Intensive Care Unit (ICU). Initial treatment of severe asthma is commenced in the ED and those patients requiring ongoing NIV or IMV are admitted to the CCC.

All patients over 15 years old admitted to MMH CCC between 2000 and 2015, who were coded as asthma, were identified in the Australian and New Zealand Intensive Care Society (ANZICS) database. Patients presenting with cardiac arrest because of asthma were excluded. We also excluded those with an alternative or significant co-existing respiratory diagnosis made during any admission or in an outpatient review that could have benefited from NIV (e.g. chronic obstructive pulmonary disease, pneumonia, bronchiectasis and congestive heart failure).

Ethics

The study was reviewed by the hospital ethics committee (Research Registration Number: 2030) and approved. It did not meet the threshold of risk requiring ethical review by the NZ Health and Disability Ethics Committee.

Data collection

A standard data collection form in Microsoft access was used. Demographic data of age, gender and ethnicity were recorded. The following clinical variables were noted: heart rate, oxygen saturations and respiratory rate, Glasgow Coma Scale (GCS) score at triage or at the time of acute deterioration. The patient's ability to speak was documented as an assessment of severity, and was classified into four groups: unable to speak, or able to speak in words, phrases or sentences. The type of ventilation, duration, time of initiation and crossover to more invasive ventilation were recorded. Respiratory rate at time of ICU admission and the use of high flow nasal oxygen from all admissions since 2006 was also recorded. The length of stay (LOS) in the CCC and hospital was documented.

All blood gases records were obtained for every CCC admissions during the study period. Available blood gases were then matched to each asthma admission and we identified those taken closest to initiation of intervention or, for the medical group, those closest to Critical Care admission. A second blood gas record taken after the first gas (range 30 min–3 h) was identified where available. Venous blood gas results were discarded.

Non-invasive ventilation

Facemask CPAP was delivered using a freestanding circuit with an attached PEEP valve whereas bi-level NIV was delivered by BiPAP Vision (Philips Respironics Inc., Murrysville, PA, USA) or via Puritan Bennet 840 (Covidien, Boulder, CO, USA).

NIV was initiated for patients who failed standard medical therapy and was started in either the ED or CCC. The use of NIV in patients with a lowered GCS was determined by a consultant at the bedside with equipment and staff available for immediate intubation. NIV settings were titrated to work of breathing and signs of clinical improvement; decreasing respiratory rate, increased ability to speak and patients feeling less breathless.

Standard asthma treatment at MMH for severe asthma includes intravenous (i.v.) and nebulised Salbutamol, inhaled Ipratropium Bromide, i.v. Magnesium and i.v. steroids. Patients who presented with a GCS ≤10 were analysed as a separate group.

Statistical analysis

The analysis was done using admissions as the base variable since some patients had more than one admission and variables such as mode of therapy, HR, RR, pH and pCO_2 varied from one admission to another. Data analysis was performed using SPSS 22.0 (IBM, Chicago, IL, USA) and was descriptive with bivariate analysis. Continuous outcomes were presented in terms of mean with standard deviation (SD) or median with interquartile range (IQR) depending on the distribution of the data. Categorical variables were presented in terms of counts and proportions. χ^2 test was carried out to assess the association between the categorical risk factors and the mode of therapy. Statistical tests were performed using either analysis of variance (ANOVA) or Kruskal–Wallis test on the continuous outcome to check for any differences between the modes of therapy. The level of significance was set at 5%.

Results

Demographic data

Initially, 337 records were identified, of which 72 met exclusion criteria because of an alternative primary reason for admission (69), cardiac arrest following asthma or admission from another hospital. This left 265 asthma admissions, from a total of 192 individual patients admitted between the years 2000 and 2015. The majority of them had one documented admission (157/192 = 82%) while multiple admissions were recorded for 35 patients, with 24 having two admissions and 11 with more than two admissions. The median age at first admission of the 192 patients was 31 (IQR 22.5–43). The median age (IQR) at

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first admission broken down by mode of therapy was: IMV (39 [24.5–57.5]), Medical (26 [19–36]), NIV (32 [23–43]) and for the failed NIV group (49 [21–59]).

Table 1 shows the demographic data and physiological observations for the patients. The heart rate and respiratory rate are consistent with severe asthma exacerbations. Table 2 shows the work of breathing assessment based on patient's ability to speak; 80% of all admissions could speak in single words per breath or were unable to speak.

The asthma admissions over the study period vary per year from 7 to 28 patients. In the medical therapy group since 2006, 62.5% patients received high flow nasal prong (HFNP) oxygen.

Non-invasive ventilation

The median duration of NIV therapy was 5 h with an IQR of 2–11 h. Most patients having NIV had it commenced within 2 h of arrival to hospital; median time to initiation was 1.42 h (IQR 0.25–6.93 h). Sixteen of the NIV group had NIV for an hour or less. Most NIV admissions received CPAP alone but 23 (13%) of the NIV group received BiPAP at some stage. Seven of these patients received BiPAP alone. The median CPAP setting was 10 cm H_2O (IQR 7.5–10).

Invasive mechanical ventilation

Thirty-one (11.7%) admissions received IMV with a median duration of 10 h (IQR 6.5–13). The median time to intubation was 0.35 h (IQR 0.02–1.82) and five (16%) of the IMV group were intubated prehospital. No patient had multiple admissions requiring IMV.

Of the IMV group, eight patients had trials of NIV (one had BiPAP, seven had CPAP) prior to invasive ventilation (failure rate of 4.5%). Characteristics of patients who failed NIV were: an older median age (49 years), a higher pCO_2 (median 14.1 kPa) and more acidaemia (median pH 7.01) (Table 3). Table 3 displays the significant differences in pCO_2 levels and pH between the different modes.

Low GCS group

Table 4 shows the numbers of admissions presenting with a GCS ≤10. One of the low GCS patients failed NIV therapy and required intubated.

The blood gas data in Table 4 shows the patients in the low GCS were severely hypercapnic and acidotic with a median pH of 7.02 (IQR 6.86–7.07). Both NIV and IMV were effective in lowering the pCO_2 over the 2 h: NIV had an average drop of 5.9 kPa (SD 4.6) and 3.4 kPa for IMV (SD 4.9).

Table 5 compares asthma admissions to MMH and CCC between ethnic groups from 2000 to 2015. It also shows ethnic proportions of the catchment population and New Zealand from the 2013 census data.

No serious complications were documented; there was one reported pneumothorax, which at the time was attributed to central venous catheter insertion.

Discussion

This study lends support to the increasing evidence that NIV is a safe treatment option in the management of severe asthma. Over the same period at MMH there were 20 448 patients admitted with a primary diagnosis of asthma; 1.3% required admission to CCC and 0.16% required IMV.

TABLE 1. *Baseline physiological and demographic characteristics for 265 admissions, 2000–2015*

	MED	NIV	IMV	Total	*P*-value
Number of admissions (%)	58 (21.9)	176 (66.4)	31 (11.7)	265	
Female	34 (58%)	118 (67%)	21 (67%)	173 (65%)	
Male	24 (41%)	57 (32%)	10 (32%)	91 (34%)	
Heart rate (/min), mean (SD), valid *N*	128 ± 19.5, 57	131 ± 21.4, 175	129 ± 28.7, 23	130 ± 22, 255	0.567
Respiratory rate (/min), mean (SD), valid *N*	32 ± 8.8, 57	32 ± 9.3, 175	25 ± 11.7, 23	32 ± 9.6, 255	0.005
Duration of therapy (h), median (IQR)		5.25 (3.5–11)	10 (6.5–13)		
CCC LOS (days), median (IQR)	0.72 (0.54–1.11)	0.88 (0.53–1.4)	0.92 (0.51–1.7)	0.85 (0.53–1.32)	0.133
Hospital LOS (days), median (IQR)	3.1 (2.6–4.3)	3.6 (2.5–5.2)	4.1 (2.6–5.2)	3.5 (2.5–5.0)	0.175†

†Non-parametric test (Kruskal–Wallis test). CCC, Critical Care Complex; IMV, invasive mechanical ventilation; LOS, length of stay; MED, medical therapy; *N*, number of admissions; NIV, non-invasive ventilation; SD, standard deviation.

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TABLE 2. *Work of breathing assessment for the 265 admissions*

	MED	NIV	IMV	All patients	*P*-value
Able to speak in full sentences, *n* (%)	5 (9)	3 (2)	0	8 (3)	<0.0001†
Speaks in phrases, *n* (%)	11 (19)	33 (19)	0	44 (17)	
Speaks in words, *n* (%)	32 (55)	83 (47)	8 (26)	123 (46)	
Unable to speak, *n* (%)	10 (17)	57 (32)	23 (74)	90 (34)	

†χ^2 test of association. IMV, invasive mechanical ventilation; MED, medical therapy; NIV, non-invasive ventilation.

TABLE 3. *Single blood gases results taken within 2 h of intervention based on 228 admissions*

	MED (*n* = 48)	NIV (*n* = 151)	IMV (*n* = 29)	Total	*P*-value	Failed NIV (*n* = 7)
pCO_2 (kPa), median (IQR)	5.15 (4.3–6.1)	6.2 (5–8.95)	14.6 (9.5–17.3)	6.25 (5.0–9.85)	<0.0001†	14.1 (11.6–16.8)
pH, median (IQR)	7.32 (7.29–7.36)	7.28 (7.19–7.33)	7.01 (6.86–7.1)	7.28 (7.15–7.33)	<0.0001†	7.01 (6.9–7.14)

†Non-parametric test (Kruskal–Wallis test). Failed NIV, group of patients that had NIV prior to IMV they are also included in the IMV group; IMV, invasive mechanical ventilation; MED, medical therapy; *n*, number of admissions within each mode of therapy who have a blood gas within 2 h of starting therapy or time of admission for the medical therapy group; NIV, non-invasive ventilation.

There was a difference between our catchment population ethnicity and CCC admission rates. This is consistent with NZ health statistics showing much higher hospital admission rates in Maori and Pacific Islander asthmatics.[9,17] The male : female skew in admissions is in keeping with the known gender bias in adult asthma incidence.[18]

Other studies of NIV in asthma also report low or no complication rates.[19–21] The haemodynamic effects of positive pressure ventilation are also less marked in spontaneous breathing patients.[8]

The rates of IMV (11.7%) in our study were lower than previous studies but our total (IMV and NIV) rate of ventilation was 78%.[22–24] More recent data reports a trend for lower rates of IMV use.[25] Within our study the IMV rates for the first 6 years was 16.1% and dropped to 9.3% in

TABLE 4. *Length of stay, duration of therapy and blood gases for the admissions in the low GCS group*†

	MED (*n* = 1)	NIV (*n* = 16)	IMV (*n* = 16)	Total (*n* = 33)	*P*-value
Duration therapy (h), median (IQR)		4 (2–7.5)	7.5 (5–11.8)		
Hospital LOS (days), median (IQR)	1.94	3.28 (2.43–4.10)	3.57 (2.64–4.43)	3.32 (2.54–4.41)	
CCC LOS (days), median (IQR)	0.29	0.56 (0.39–0.97)	0.67 (0.42–1.42)	0.57 (0.42–1.15)	
Initial pCO_2 (kPa), median (IQR)	13.0	15.6 (12–16.5)	15.3 (9.3–17.6)	15.4 (11.5–16.8)	0.906‡
2nd pCO_2 (kPa), median (IQR)	5.5	8.5 (6–11.6)	10.9 (9.55–13.3)	9.8 (7.8–13.1)	0.068‡
Initial pH, median (IQR)	7.08	7.03 (6.95–7.06)	6.94 (6.81–7.08)	7.02 (6.86–7.07)	0.455‡
2nd pH, median (IQR)	7.36	7.21 (7.1–7.26)	7.07 (7.01–7.12)	7.11 (7.06–7.24)	0.007‡

†The median time between starting the intervention and the first blood gas was 11.9 min (IQR -1.0–28.5 min). ‡Non-parametric test (Kruskal–Wallis test). CCC, Critical Care Complex; IMV, invasive mechanical ventilation; LOS, length of stay; MED, medical therapy; *n*, number of admissions within each mode of therapy who had GCS <10 and two blood gases available; NIV, non-invasive ventilation.

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TABLE 5. *Ethnicity data: comparing CMDHB versus New Zealand ethnicity and asthma admissions to hospital versus admission to the Critical Care Complex*†

	Asian (%)	Caucasian (%)	Maori (%)	PI (%)
New Zealand population	14	64	16	6
CMDHB catchment population	24	38	16	21
Middlemore CCC asthma admissions 2000–2015	11	21	31	37
Middlemore Hospital asthma admissions 2000–2015	7	32	29	32

†New Zealand has the fourth highest hospital admission rates for asthma of OECD countries. CCC, Critical Care Complex; CMDHB, Counties Manukau District Health Board;[16] PI, Pacific Islanders.

the final 10 years. Our study shows shorter CCC and hospital LOS than most published international data.[21,22] However, an American database study had similar LOS for their NIV patients of 4.1 days.[15]

Our blood gas data was consistent with severe asthma and the median pH is lower than other studies.[21,26] Previous studies have also shown that NIV is effective in decreasing arterial carbon dioxide in severe asthma and can be as effective as IMV.[19,26] The lower drop in pCO_2 in intubated patients compared to those treated with NIV is likely due to IMV patients being hypo-ventilated to prevent gas trapping. NIV is being used in sicker populations as earlier studies of NIV in asthma often had patients with normal pCO_2 levels.[27,28]

Coma is normally a contraindication to NIV, but there have been previous reports of its successful use in the literature.[26] We have described 25 cases with decreased GCS (≤10) that were managed with NIV and without any reported cases of aspiration pneumonia. The low GCS group had rapid correction of hypercapnia and shorter CCC LOS than the higher GCS group. CPAP may be a safe option in selected patients with low GCS. Its safety depends on having experienced staff available for immediate intubation if required.

Our failure rate for NIV was 4.5%, similar to a large American retrospective cohort[15] from an electronic medical record database but less than other studies.[15,20,26] Leatherman reports a failure rate of 17% across five studies.[29] Failure rate needs to take into consideration the initial asthma severity and timing of the study as earlier studies appear to have higher failure rates. Our patients who failed NIV had similar physiological data as the IMV group.

In this series of patients, there were no reported deaths. Pallin *et al.* reported much higher mortality (41% in patients requiring IMV) but 88% of the patients were intubated in the setting of cardiopulmonary resuscitation.[21] Overall in the previous decade (2000s), the reported mortality averaged 6.8% for intubated asthmatic, prior to this it was 10.7%.[30] In experienced centres, mortality is often lower and deaths occur from prehospital hypoxia.[22,23,29] With the more recent data we need to review the statement that an 'unacceptably high fraction of patients with acute severe asthma die from complications of invasive ventilation'.[4]

Limitations

The main limitations of the study are the retrospective nature, non-randomised and being performed at a single institution. As it was retrospective there is small amount of missing data (Table 1) and some asthma admissions may have been overlooked if there were coding errors. The authors were not blinded to the study objectives. The accuracy of data collection was not checked by an independent data extractor. The blood gas data was abstracted from a database of all blood gases recorded within the hospital. The model that performed the abstraction ignored the mode of therapy received by the patient. Some patients did not have blood gases taken or the timing of the blood gases was not appropriate. While smoking history was not included in the study, all clinical notes were reviewed and patients were excluded if they were ever diagnosed with chronic obstructive pulmonary disease. MMH has a history of using NIV in asthma since the mid-1990s and the staff are familiar with its use.

There are many difficulties in doing a RCT of NIV against standard therapy in status asthmaticus. Despite the lack of trials, it is a standard practice in some institutions to trial NIV in acute asthma and there may be no clinical equipoise in experienced units. Future research could look at HFNP versus NIV and cross over to more invasive therapy (following treatment failure). However, the low mortality and morbidity in recent studies of IMV suggests there may be incentive to compare standard care and IMV versus standard care and NIV.

Conclusion

This is the largest reported case series of NIV use in status asthmaticus. Our physiologic and demographic data are consistent with severe asthma. NIV was used in severely unwell patients including some high-risk patients with lowered GCS. Patients treated with NIV did not appear to have any significant adverse effects, LOS was short and our IMV rates were lower than other studies.

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Competing interests

None declared.

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