Effectiveness and safety of noninvasive positive-pressure ventilation in hypercapnia respiratory failure secondary to acute exacerbation of chronic obstructive pulmonary disease

Ali O. Abdel Aziz[a], Islam M. Abdel El Bary[a], Mohammad T. Abdel Fattah[a], Mohamd A. Magdy[a], Ashraf M. Osman[b]

Background Patients with acute respiratory acidosis caused by an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) constitute the group that benefits most from noninvasive positive-pressure ventilation (NIPPV). However, there are some patients who do not respond to NIPPV. Studies from the west report variable failure rates. Delays in recognizing nonresponders can increase hospital morbidity and mortality.

Objective The aim of this study was to assess the effectiveness and safety of NIPPV in patients with acute hypercapnia respiratory failure (AHRF) secondary to AECOPD.

Patients and methods This was a prospective observational study of 119 consecutive chronic obstructive pulmonary disease patients who were admitted with a diagnosis of AHRF and in whom NIPPV was applied.

Results The overall success rate of NIPPV in the studied group was 94%. Mortality and duration of hospitalization were significantly higher in the failure group (P=0.0001 and 0.002, respectively). The most encountered complications were air leak (29%) and mask discomfort (24%).
Comparison between the success and the failure group at the time of hospital admission revealed that the failure group was associated with old age (P=0.043), low hemoglobin (Hb) (P=0.037), low albumin (0.017), lower Glasgow Coma Scale (GCS) score (P=0.0001), higher Acute Physiology and Chronic Health Evaluation II (APACHE II) score (P=0.001), higher heart rate (P=0.002), lower systolic blood pressure (SBP) (P=0.013), lower diastolic blood pressure (DBP) (P=0.034), and higher white blood cells (WBCs) (P=0.0001).
Multiple regression analysis identified age more than 65 years, respiratory rate 35 or more, pH less than 7.26, and WBCs more than or equal to 20 000 or less than 4000 as significant independent predictors of NIPPV failure in our patients.

Conclusion NIPPV is an effective and safe modality for treating patients with AHRF secondary to AECOPD. Widespread availability and training of medical staff in the use of NIPPV is recommended.

Egypt J Bronchol 2017 11:215–223

Egyptian Journal of Bronchology 2017 11:215–223

Keywords: acute exacerbation of chronic obstructive pulmonary disease, noninvasive positive-pressure ventilation, respiratory failure

Departments of, [a]Chest Diseases, [b]Clinical Pathology, Faculty of Medicine, Minia University, Minia, Egypt

Correspondence to Ali O. Abdel Aziz, MD, Department of Chest Diseases, Faculty of Medicine, Minia University, Minia, 61519, Egypt;
Tel: 086-2333196; fax: +20 (86) 234 2601;
e-mail: info@minia.edu.eg

Received 7 October 2016 **Accepted** 28 November 2016

Introduction

Noninvasive positive-pressure ventilation (NIPPV) represents a significant advancement in the management of acute respiratory failure (ARF) in patients with severe chronic obstructive pulmonary disease (COPD) [1]. It is claimed to be safe and effective and helps in preventing endotracheal intubation in ARF secondary to COPD as compared with causes [2,3]. Several randomized controlled trials show a success rate of 80–85% [4]. It has been shown that NIPPV in addition to conventional treatment of COPD exacerbation significantly reduces mortality and complications as compared with standard medical therapy alone [5]. It can be effectively used both inside and outside the ICU. Ventilators used in NIPPV range from ICU ventilators with full monitoring and alarm systems, to light-weight, free-standing devices with limited alarm systems specifically designed for this purpose [6]. Although NIPPV is well tolerated by most patients, it is not entirely free from serious adverse effects and complications. The safety of NIPPV can be enhanced by a greater awareness of factors predictive of complications and early management of such complications [7].

This prospective study was conducted to assess intubation and mortality in patients with acute hypercapnia respiratory failure (AHRF) secondary to acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and in whom NIPPV was applied, to detect differences, if any, in the clinical variables at admission in the success and failure groups of patients, and compare our results with those from other studies.

Patients and methods

The present study was conducted in the general ward and the ICU of our department from January 2014 to

 DOI: 10.4103/1687-8426.211398

July 2016. It included 119 consecutive patients admitted to the department for AHRF secondary to AECOPD and in whom NIPPV was applied. Thirty-five patients were managed in the ward and the remaining 84 were managed in the ICU. The randomization of the patients was not intended. It was done just before the full establishment of our ICU, when patients were managed in the ward.

The study was approved by the scientific committee of our institution.

Diagnosis of COPD was based on the Global Initiative for Chronic Obstructive Lung Disease strategy [4].

Patients were considered for NIPPV if despite the standard medical treatment (controlled oxygen therapy, nebulized salbutamol and ipratropium bromide, systemic corticosteroids, and antibiotics when indicated) they still fulfilled the criteria for NIPPV [4]: namely, pH less than 7.35 or $PaCO_2$ more than 45 mmHg; PaO_2 less than 60 dyspnea at rest with respiratory rate (RR) more than 25 breaths/min; and use of accessory respiratory muscles or paradoxical abdominal breathing. Exclusion criteria were refusal of NIPPV, facial deformity affecting mask fitting, severe encephalopathy unrelated to hypoxaemia and/or hypercapnia, overt gastrointestinal bleeding, upper airway obstruction, acute ischemic heart disease, and need for urgent intubation due to cardiac or respiratory arrest, prolonged respiratory pauses and psychomotor agitation requiring sedation.

NIPPV was administered by the use of standard critical care ventilators. It was delivered to patients in bed at an angle of 30–45°. An oronasal or full face mask was used. NIPPV was applied for most of the time over 24 h. Patients were instituted on NIPPV through Bilevel Positive Airway Pressure (BIPAP) mode. The setting of the machine was as follows: at the outset the patient was started on an inspiratory positive airway pressure (IPAP) of 8 and Expiratory positive airway pressure (EPAP) of 4 cmH_2O, which was gradually adjusted as tolerated on the basis of alleviation of the patient's dyspnea, decrease in RR, and continuous pulse oximeter readings. Expiratory pressure was increased by 1–2 cmH_2O to achieve an PaO_2 of more than or equal to 60 mmHg or a SaO_2 of 90% or more. Inspiratory pressure was increased at increments of 2–3 cmH_2O ($\leq$20 cmH_2O) to obtain a tidal volume of 6–8 ml/kg and RR of up to 30. FiO_2 was set to achieve an SaO_2 of at least 90%. Once the patient became clinically stable with satisfactory arterial blood gases (ABG), the pressure support was decreased by 2 cmH_2O every 4 h with good tolerance and with close monitoring for any change in oxygen saturation and RR. As soon as we could reduce the IPAP and EPAP levels to 8 and 4 cmH_2O, respectively, with a satisfactory ABG of pH at least 7.35, SaO_2 of at least 90%, FiO_2 up to 40%, and RR less than 30/min, the patients were allowed to breathe spontaneously. The need for intubation was established by the attending physician depending on his clinical judgment.

The following variables were recorded at admission:

Age and sex, smoking status and index, associated comorbidities, primary cause of admission, BMI, vital signs, GCS, APACHE II score, chest radiograph, computed tomography pulmonary angiography when there is high probability for pulmonary embolism according to Wells score [8], ECG, echo-cardiography, ABGs analysis at admission, NIPPV initiation and whenever required thereafter, laboratory data [complete blood count, liver function tests, renal function tests, serum C-reactive protein (CRP) concentration, and serum tumor necrosis factor α], duration of NIPPV, condition at ICU discharge, duration of hospitalization, and any complication developing from the use of NIPPV.

Statistical analysis

Numerical data were expressed as mean and SD. Categorical data were expressed as number and percentage. Analyses were carried out with IBM SPSS statistics (version 17; SPSS for Windows; SPPS Inc., Chicago, Illinois, USA).

Statistical significance was set at a *P*-value less than 0.05. Univariate and multivariate analysis and odds ratio were estimated with logistic regression for identifying the risk factors associated with noninvasive ventilation (NIV) outcome, using the clinical variables illustrated in the Patients and methods section.

Results

Patient characteristics

The present study included 119 patients who had a diagnosis of AHRF secondary to AECOPD and who needed NIPPV. The main baseline patient characteristics and underlying conditions are listed in Tables 1 and 2.

Male patients constituted 69.7% of COPD patients and the mean age was 62.2±9.64 years. About 46% of the patients were current smokers, about 30% were lifelong nonsmokers, and the remaining were ex-smokers. The most common presentation was AECOPD (76.5% of

Table 1 Patient characteristics and underlying conditions

Patients	119
Sex (male)	83 (69.7)
Age (years)	62.2±9.64
BMI (kg/m^2)	27.4±5.6
Smoking index (packs/year)	11.2±15.8
Number of comorbidities	
One	19 (16)
Two	43 (36)
Three or more	57 (48)
Comorbidities	
Cor pulmonale	59 (49.6)
AECOPD	91 (76.5)
CHF	22 (18.5)
Anemia	27 (22.7)
DM	22 (18.5)
OSA	20 (16.8)
Bronchiectasis	13 (10.9)
Liver disease	14 (11.8)
Peptic ulcer	5 (4.2)
Renal disease	4 (3.4)
Pneumonia	3 (2.5)
PE	3 (2.5)

Data presented as *n* (%) or mean±SD. Other comorbidities include pneumothorax (2 patients), interstitial lung disease (1 patient), leukemia (1 patient), kyphoscoliosis (1 patient), dementia (1 patient), parkinsonism (1 patient), hemiplegia (1 patient), old pulmonary tuberculosis, and fibrothorax (1 patient). AECOPD, acute exacerbation of chronic obstructive pulmonary disease; CHF, congestive heart failure; DM, diabetes mellitus; OSA, obstructive sleep apnea; PE, pulmonary embolism.

Table 2 Patient characteristics

Laboratory data	
Total leukocyte count (×10^9/l)	11.9±5.2
Hemoglobin (g/dl)	12.7±2.2
Platelets (×10^9/l)	242.6±72.1
Albumin (g/dl)	3.5±0.6
Serum urea (mg/dl)	58.9±29.5
Serum creatinine (mg/dl)	1.1±0.4
ABG data at admission	
pH	7.3±0.05
$PaCO_2$ (mmHg)	67.7±12.4
PaO_2 (mmHg)	55.7±11.2
HCO_3(mmol/l)	30.5±4.5
Vital signs at admission	
Respiratory rate/min	29.03±9.06
Heart rate (beats/min)	93.1±17.9
Systolic blood pressure (mmHg)	117.06±22.05
Diastolic blood pressure (mmHg)	76.5±13.8
Temperature (°C)	37.1±0.99
Prognostic scores	
GCS	14.8±0.9
APACHE II score	7.9±2.6
Length of hospital stay (days)	13.9±11.3
Duration of NIPPV (days)	4.5±3.2
Overall failure rate (need for intubation) [*n* (%)]	7 (5.9)

Data are presented as mean±SD.ABG, arterial blood gas, APACHE II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Scale, NIPPV, noninvasive positive-pressure ventilation.

patients), followed by heart failure (18.5%). The most frequent comorbidities associated with COPD were heart problems (68% of patients), followed by anemia (22.7%).

The overall failure percentage (patients needed intubation) was 5.9%.

Prognostic factors

The overall failure was 5.9% among the studied patients. Failure for patients who were managed in the ward and those who were managed in the ICU was 5.8 and 5.9%, respectively (P=0.8).

The failure group had a higher mean age (P=0.043), longer hospital stay (P=0.002), and higher mortality (P=0.0001). They also had higher mean APACHE II score (P=0.001) and lower mean GCS (P=0.0001) (Tables 3 and 4) as well as higher mean urea (P=0.0001), higher mean creatinine (P=0.001), and higher mean WBCs (P=0.0001). They also had lower mean albumin (P=0.017) and lower mean Hb (P=0.037). They also had higher mean heart rate (P=0.002), higher mean RR (P=0.04), lower mean SBP (P=0.013), and lower mean DBP (P=0.034). Other parameters listed in Tables 5 and 6 are not significant.

Univariate analysis for NIPPV failure showed that failure rate was higher for patients older than 65 years (P=0.004), those with pH less than 7.26 at baseline (P=0.015), those with RR at least 35 (P=0.004), those with total leukocyte count 20 000 or more or less than

Table 3 Comparisons between the success and failure groups regarding the demographic characteristics and severity scores

	Success (n=112)	Intubated patients (n=7)	P
Age (years)	61.7±8.5	69.3±20.3	0.043
Male sex [*n* (%)]	79 (70.5)	4 (57.1)	0.357
Mortality [*n* (%)]	0 (0)	6 (85.7)	0.0001
Smoking index (packs/year)	10.8±16.8	18.3±14.9	0.706
BMI (kg/m^2)	27.7±5.7	25.0±3.8	0.216
GCS	14.9±0.6	12.9±2.1	0.0001
APACHE II score	7.7±2.5	11.1±2.7	0.001
Duration of NIPPV (days)	4.5±2.8	4.8±7.6	0.841
Duration before NIPPV (days)	0.9±1.9	2.1±5.7	0.167
Duration of hospitalization (days)	13.4±7.0	24.0±22.1	0.002

The success group was significantly younger, have shorter hospital stay, reduced mortality, and lower APACHE II score. APACHE II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Scale; NIPPV, noninvasive positive-pressure ventilation.

Table 4 Comorbidities in the success and failure groups

	Total (*n*=119) [*n* (%)]	Success (*n*=112) [*n* (%)]	Intubated patients (*n*=7) [*n* (%)]	*P*
Bronchiectasis	13 (10.9)	12 (10.7)	1 (14.3)	0.565
OSA	20 (16.8)	20 (17.9)	0 (0)	0.266
Pneumonia	3 (2.5)	3 (2.7)	0 (0)	0.832
ILD	1 (0.8)	1 (0.9)	0 (0)	0.941
PE	3 (2.5)	2 (1.8)	1 (14)	0.941
CHF	22 (18.5)	20 (17.9)	2 (28.6)	0.383
Cor pulmonale	59 (49.6)	55 (49.1)	4 (57.1)	0.301
Peptic ulcer	5 (4.2)	5 (4.5)	0 (0)	0.735
DM	21 (17.6)	20 (17.9)	1 (14.3)	0.617
renal disease	4 (3.4)	2 (1.8)	2 (28.6)	0.017
liver disease	14 (11.8)	11 (9.8)	3 (42.9)	0.035
Leukemia	1 (0.8)	1 (0.9)	0 (0)	0.941
Kyphoscoliosis	1 (0.8)	1 (0.9)	0 (0)	0.941

No significant differences exist in the associated comorbidities in the success and failure groups except for the presence of chronic liver and renal disease, which was higher in the failure group.CHF, congestive heart failure; DM, diabetes mellitus; ILD, interstitial lung disease; OSA, obstructive sleep apnea; PE, pulmonary embolism.

Table 5 Differences between the success and failure groups regarding the laboratory data

	Success (*n*=112)	Intubated patients (*n*=7)	*P*
RBS (mg/dl)	176.7±70.9	141.0±43.1	0.192
AST (U/l)	39.4±133.7	51.6±40.5	0.811
ALT (U/l)	50.4±183.5	82.0±82.2	0.653
Albumin (g/dl)	3.7±0.5	3.2±0.8	0.017
Total bilirubin (U/l)	0.9±0.5	1.1±0.5	0.442
Direct bilirubin (U/l)	0.4±0.3	0.5±0.2	0.406
Urea (mg/dl)	55.9±29.5	90.0±51.1	0.0001
Creatinine (mg/dl)	0.9±0.4	1.5±0.7	0.001
RBCs ($\times 10^9$/l)	5.3±0.8	5.0±0.3	0.261
WBCs ($\times 10^9$/l)	10.9±5.2	21.8±7.7	0.0001
Platelets ($\times 10^9$/l)	244.6±72.1	206.0±86.4	0.177
Hb (g/dl)	13.3±2.2	11.6± 2.2	0.037
HCT	47.9±6.6	45.1±6.9	0.266
TNFα	20.3±10.4	17.9±10.7	0.300
CRP positive (%)	42.9	50.9	0.500

Serum urea, creatinine, and WBCs were significantly higher in the failure group, whereas serum albumin and Hb were significantly lower. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; Hb, hemoglobin; HCT, hematocrit; RBS, random blood sugar; TNFα, tumor necrosis factor α; WBC, white blood cells.

4000 (*P*=0.0001), those with Hb less than 11 (*P*=0.04), and those who had chronic liver (*P*=0.035) or renal (*P*=0.017) disease. Other parameters listed in Table 7 are not significant.

Multiple regression analysis in Table 8 identified that age older than 65 years (*P*=0.01), RR 35 or more (*P*=0.007), pH less than 7.26 (*P*=0.022), and WBCs at least 20 000 or less than 4000×10^9 (*P*=0.001) were significant independent factors related to failure of NIPPV in patients with acute hypercapnia respiratory failure (AHRS) secondary to AECOPD.

The most common complications encountered in our patient group were air leak (29% of patients), followed by mask-related discomfort (24%) and mask-related ulcer (9.2%). Other encountered complications are listed in Table 9.

Discussion

In the present study, we prospectively determined the characteristics, effectiveness, safety, and complications associated with the use of NIPPV in patients with AHRF secondary to AECOPD.

The success rate in the present study was about 94%, which is comparable to that reported in two previous studies [9,10] and higher than the rates (50–80%) reported by some other studies [11–15]. Even in a group of COPD patients with severe respiratory acidosis with a mean arterial pH of 7.22, Carrillo *et al.* [16] found that NIPPV was highly effective, with a success rate of 89%.

The variability in the success rate among different studies could be attributed in part to the differences in patient characteristics and severity of illness. Table 10 shows the comparison of the main points in our study with some of these previous studies.

In the present study the failure percentage of NIPPV among patients who were managed in the ward and those who were managed in the ICU was comparable (*P*=0.8). This comes in line with other studies that reported the safety and efficacy of NIPPV in non-ICU wards [6,10,17,18].

The present study found that NIPPV is associated with lower mortality (*P*=0.0001) and significantly shorter hospital stay (*P*=0.002). These results are in agreement with those of previous studies [2,3,10,16]. The mortality in the failure group in our study was significantly high (85.7%). The high mortality can be attributed to the more severe nature of the disease in this group, as evidenced by the higher RR, lower blood pressure, and higher WBCs, which could denote sepsis. However, it is worth mentioning that this group of patients was managed first by NIPPV and hence whether the high mortality in this group is related to the severity of the underlying disease or to the delay in the initiation of invasive ventilation must be considered.

The main cause of acute deterioration and hence hospital admission in our patients was AECOPD,

Table 6 Comparisons between the success and failure groups regarding baseline vital signs and arterial blood gas

Baseline data	Total (*n*=119)	Success (*n*=112)	Intubated patients (*n*=7)	*P*
RR/min	29.03±9.06	27.6±9.1	37.1±7.0	0.04
HR/min	93.1±17.9	91.9±17.6	112.9±12.6	0.002
SBP (mmHg)	117.06±22.05	118.4±21.1	97.1±29.3	0.013
DBP (mmHg)	76.5±13.8	77.2±13.3	65.7±20.7	0.034
Temperature (°C)	37.1±0.99	37.1±1.0	36.6±0.4	0.200
pH	7.3±0.05	7.3±0.1	7.3±0.1	0.225
$PaCO_2$ (mmHg)	67.7±12.4	67.1±12.4	69.4±14.2	0.712
PaO_2 (mmHg)	55.7±11.2	56.1±11.3	53±9.6	0.167
HCO_3 (mmol/l)	30.5±4.5	30.6±4.9	29.1±2.5	0.451
PaO_2/FiO_2	185.7±38.2	186.8±39.1	168.1±16.4	0.214

Heart rate and respiratory rate were significantly higher, whereas SBP and DBP were significantly lower in the failure group.DBP, diastolic blood pressure; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure.

Table 7 Univariate analysis of the different parameters in the success and failure groups

	Success (*n*=112)	Failure (*n*=7)	Relative risk	95% CI	*P*-value
Age>65 years	31 (27.7)	6 (85.7)	1.7	1.8–1.5	0.004
Male sex	79 (70.5)	4 (57.1)	0.6	0.1–2.6	0.357
Current Smoking	34 (30.4)	2 (28.6)	0.9	0.2–4.9	0.643
Mortality	0 (0)	6 (85.7)	0.9	0.2–4.9	0.0001
pH<7.26 at baseline	27 (24.1)	5 (71.4)	0.36	0.12–1.21	0.015
$PaCO_2$≥50 at baseline	110 (98.2)	7 (100)	1.1	1.0–1.1	0.885
PaO_2/FiO_2<146 baseline	20 (17.9)	0 (0)	0.9	0.9–0.9	0.296
RR≥35 baseline	19 (17)	5 (71.42)	12.34	2.2–6.8	0.004
TLC≥20 000 and <4000	9 (8.03)	5 (71.4)	0.28	0.07–1.07	0.0001
LTOT	59 (52.7)	5 (71.4)	0.45	0.34–0.61	0.287
Duration of MV<10 days	9 (8.03)	2 (28.6)	0.32	0.11–0.98	0.126
Frequent exacerbation≥2	94 (83.9)	6 (85.7)	0.39	0.14–1.14	0.690
Liver disease	12 (10.7)	2 (28.6)	2.5	0.86–7.56	0.06
Renal disease	2 (1.8)	2 (28.6)	0.95	0.25–3.75	0.017
Serum albumin<3	9 (8.03)	2 (28.6)	4.5	0.78–27.0	0.13
Hemoglobin<11	4 (3.6)	2 (28.6)	10.8	1.5–73.6	0.04

CI, confidence interval; LTOT, long term oxygen therapy; MV, mechanical ventilation; RR, respiratory rate; TLC, total leucocyte count.

Table 8 Multivariate analysis of the different parameters in the success and failure groups

	Success (*n*=112)	Failure (*n*=7)	Relative risk	95% CI	*P*-value
Age>65 years	31 (27.7)	6 (85.7)	0.29	0.09–0.89	0.01
pH<7.26 basal	27 (24.1)	5 (71.4)	0.36	0.12–1.21	0.022
RR≥35 basal	19 (17)	5 (71.42)	0.34	0.11–1.07	0.007
TLC≥20 000 and $<4000\times10^9$ basal	9 (8.03)	5 (71.4)	0.28	0.07–1.07	0.001
Liver disease	12 (10.7)	2 (28.6)	2.5	0.86–7.56	0.053
Renal disease	2 (1.8)	2 (28.6)	0.95	0.25–3.75	0.06

CI, confidence interval; RR, respiratory rate; TLC, total leukocyte count.

Table 9 Complications of NIMV in the studied group

Complications	Incidence [*n*/*N* (%)]
Air leak	35/119 (29)
Mask-related discomfort	29/119 (24)
Mask-related ulcer	11/119 (9.2)
NIPPV failure	7/119 (5.9)
Abdominal distension	4 (3.4)
Mask intolerance	3 (2.5)
Pneumonia	1/119 (0.8)

The most common complications encountered in our patient group were air leak, followed by mask-related discomfort and mask-related ulcer.NIPPV, noninvasive positive-pressure ventilation.

which was present in 76.5%, followed by cardiac failure, in 18.5%. This finding is in agreement with reports from other studies [10,16,19].

The mean age of COPD patients treated with NIPPV varies across studies. The mean age of our patients was 61.3±14.5 years. The failure group was older compared with the success group (P=0.043). Multivariate analysis demonstrated that age more than 65 years was an independent factor for NIPPV failure. These results are in agreement with previous studies [14,20,21].

Table 10 Comparison of studies on the use of noninvasive positive-pressure ventilation in acute hypercapnia respiratory failure due to acute exacerbation of chronic obstructive pulmonary disease

References (success rate)	Site	Patients (*N*)	Mean age	Initial pH, RR	Interface	Initial setting
This study (94%)	ICU and ward	119	62.2±9.64	7.3±0.05	Oronasal (main) full face	IPAP: 8–20
				29.03±9.06		EPAP: 4^1–2
						Initial most of the day
Nicolini *et al.* [10] (93.4%)	Ward	1809	79.5±7.1	7.22±0.05	Not mentioned	Initial IPAP: 10 ^by 2 to 3
				30±3		Initial EPAP: 4 cm ^by 1 to 2
						Target TV: 6–8 ml/kg
						Initial 20 h/day
Plant *et al.* [6] (84.7%)	Ward	118	69±7	7	Full face or nasal	IPAP: 10–20, EPAP: 5 for median of 8 h
				32		
Nava *et al.* [9] (92.7%)	ICU	43	81.3±3.5	–	Full face	Mean IPAP: 16.3±2.2
						Mean EPAP: 4.1±1.1 cmH_2O
						Target TV: 6–8 ml/12.7±2.3 h/day
Carrillo *et al.* [16] (89%)	ICU	543	71.6±10	7.22±0.08	Face (main), nasal (few)	IPAP: 12–25
				31±68		EPAP: 5 for initial EPAP: 5, ^by 1–2
Soo Hoo *et al.* [11] (50%)	Ward	12	–	–	Nasal	–
Iqbal *et al.* [12] (90%)	ICU and ward	50	64.98±10.3	7.28±4.39	NM	IPAP: 9–15
				24.16±3.47		EPAP: 4 initially most of the time
Soliman *et al.* [13] (78.8%)	ICU	27	58.3±8.8	7.26±0.04	Full face mask	Initial IPAP: 8
						Initial EPAP: 4 ^gradually as tolerated
Ibrahim and Jaber [14][a] (78% for all 75% for COPD)	ICU	52	72.4±14.7	7.36±0.1	Full face	IPAP 10–25 initial
						EPAP: 5 ^ by 2
						Target TV: 5–7 ml/kg
Ahmad *et al.* [15][b] (77.36%)	–	53	55.75	7.23	Full face	EPAP: 5
				0.063		IPAP: 10 initially and then adjusted as per requirement

The exclusion criteria for most of the above-mentioned studies are mainly as per the GOLD guidelines.[a]Ibrahim and Jaber [14] studied 52 patients with acute respiratory failure: only 8 patients had acute respiratory failure due to COPD; the remaining cases were due to pneumonia, pulmonary edema, and other causes.[b]Ahmad *et al.* [15] studied 53 patients with acute hypercapnia respiratory failure of different etiologies. COPD, chronic obstructive pulmonary disease; NM, not mentioned; RR, respiratory rate; TV, tidal volume. ^ = increased by.

On the other hand, Soo Hoo *et al.* [11] found that there were no differences in age in those patients successfully treated and those patients who failed NIPPV.

The prevalence of comorbidities in our patient cohort is strikingly high, with 100% of our patients having at least one comorbidity, 84% having two or more disorders, and 48% having three or more disorders. Our data are in line with recent studies focusing on the prevalence of comorbidities in COPD [22–24].

The present study found that the presence of one or more comorbidities had no significant effect on the effectiveness of NIPPV. This result is in agreement with that reported in some previous studies [25,26]. However, some other studies found a significant impact of the number of comorbidities on failure of NIPPV and mortality [13,27].

COPD can progressively affect the functions of other organs (e.g. heart, vasculature, muscles, kidney, liver, gastroenteric apparatus, and brain); it is frequently associated with various disorders [28].

In the present study, as well as in most of the previous studies [24,29], cardiovascular problems were the most commonly associated comorbidities (68%). At the individual level, comorbid ischemic cardiovascular disease among stable COPD patients is associated with a poorer health-related quality of life and more severe dyspnea [30].

In the present study, anemia was present in 22.7% of the patients, which is higher than the reported frequency of anemia in patients with COPD in previous studies [31]. The higher prevalence of anemia in our group can be explained by the fact that our patients were in a very

severe stage of COPD. Blood Hb was significantly lower in the failure group (P=0.037), and Hb level less than 11 g/dl was associated with failure of NIPPV on univariate analysis (P=0.04). Cohort studies suggest that the survival rate in COPD patients with anemia is lower than that in those with a normal level or who had polycythemia [32].

Diabetes mellitus was present in 17.6% of our patient group. This result is in agreement with the reported higher prevalence of diabetes among patients with COPD than that in the general population [33].

In our study, about 17% of our patients had either proved obstructive sleep apnea (OSA) or symptoms that gave a suspicion of a concomitant OSA, based on the Berlin Questionnaire [34]. This is higher than the reported frequency (8–14%) in population-based studies [35]. However, it is worth noting that all our patients had a very severe COPD, which may be reflected in the higher prevalence of associated comorbidities including OSA. Also, the high prevalence of the associated comorbidity, especially cardiac problems, could be the cause for the higher prevalence of OSA in our patient cohort [36].

The present study found that the failure group had significantly higher mean baseline GCS score (P=0.0001). Although a similar result was reported by a previous study [37], another study [38] reported no significant difference in GCS score between the success and failure groups. It is important to mention that there is a risk for interobserver variation when measuring the score [39].

The present study found that APACHE II scores were significantly higher in the failure group (P=0.001), which was unsurprising as this index incorporates several variables that independently predicted outcome. Previous studies reported that APACHE II score was an independent predictor of NIPPV failure [1].

The present study found that BMI had no significant effect on the effectiveness of NIPPV. This result is in agreement with that reported in previous studies [40]. However, some other studies found a significant impact of higher BMI on NIPPV failure and mortality [13,26]. Interestingly, on the other hand Carrillo *et al.* [16] reported that obesity in patients with COPD was associated with less occurrence of late NIV failure and hospital readmission at 1 year.

In the present study, serum albumin was significantly lower in the failure group (P=0.017). This matches with other studies, which showed a negative predictive value of low serum albumin in COPD patients with severe exacerbation [26,41].

In the present study, WBC (P=0.0001), urea (P=0.0001), and creatinine (P=0.001) were statistically higher in the failure group. Multivariate analysis demonstrated that WBC at least 20 000 and less than 4000×10^9 were independent factors for NIPPV failure (P=0.001). These results are in agreement with those of previous studies [20,21].

In our study when comparing the success and the failure group no significant statistical difference was found in the levels of inflammatory markers. In contrast to our result Bastiansen [38] reported that NIPPV failure was associated with higher levels of CRP. However, it is to be noted that in our study CRP was measured by the conventional method, which is less sensitive than measuring high-sensitive CRP.

The present study found that the failure group had significantly higher mean baseline RR (P=0.04). Multivariate analysis demonstrated that baseline RR 35 or more was an independent factor related to NIPPV failure (P=0.004), which is in accordance with other studies [1,13].

In our study, heart rate was significantly higher in the failure group (P=0.002) and both SBP and DBP were significantly lower (P=0.013 and 0.034, respectively). In agreement with this Moretti *et al.* [21] found that hemodynamic variables are one of the predictors of failure of NIPPV.

Although NIPPV is generally perceived as being more comfortable for patients compared with intermittent mandatory ventilation (IMV), intolerance may affect as many as 30–50% of patients, and despite the best efforts of skilled caregivers, discomfort remains responsible for 12–33% of NIV failures [42].

The present study found that air leak was the most frequent complication (seen in 29% of patients), followed by mask-related discomfort (24%) and mask-related ulcer (9.2%). Most of these were due to ill-fitting masks, and with the use of appropriately sized mask it was minimized. Also, the machine used was able to compensate for the leaks. Similar results were reported by other studies [16,19].

Severe complications occur less frequently, including failure of NIPPV (5.9%) and pneumonia (0.8%). The reported incidence of aspiration pneumonia is less than 5% [7,16].

This study is limited by the lack of a control arm without the intervention (NIPPV). We felt that withholding NIPPV would be inappropriate, given the evidence of benefit in other studies. The small number of patients in the failure group could affect the reliability of the statistical significance and the lack of local guidelines for when we should consider NIPPV and intubate.

Conclusion

The success rate of NIPPV in patients with AHRF secondary to AECOPD was high, as reported by most of the other studies. The safety of NIPPV in those patients was good as the majority of complications in our as well as other studies are minor complications and mostly manageable. Thus, widespread availability and training of medical staff on its proper use is recommended.

The comparable success percentage in patients who were managed in the ward and those who were managed in the ICU in our as well as in other studies makes it of particular interest in countries like Egypt with limited health resources and shortage of nursing staff. This will help save a lot of resources as well as create space in the ICU for more critical cases.

In our study as well as in other studies the nonresponders had higher mortality and morbidity. This could be in part related to the delay in the initiation of invasive ventilation. Thus, to optimize outcomes, it is essential to identify patients who are less likely to respond and establish when appropriate early invasive ventilation should be instituted for those patients.

In our study, old age and disease severity at presentation, evidenced by RR at least 35 and pH less than 7.26, and markedly elevated or low WBCs were significant independent factors for failure of NIPPV. However, because of the small number of patients in the failure group these factors need to be validated in larger multicenter studies.

Acknowledgements

Our department had been in a latent phase since its establishment in the late 1980s, until 2010. Since 2010, thanks to the willingness of good people in the department, marked progress has been achieved. Our ICU has been established, bronchoscopy units have been introduced, and last but not the least the sleep study laboratory has been established.

Ali O. Abdel Aziz, Islam M. Abdel El Bary, Mohamd A. Magdy, Ashraf Osman contributed to study concept and design. Islam M. Abdel El Bary contributed to acquisition of data. Ali O. Abdel Aziz, Mohammad T. Abdel Fattah carried out analysis and interpretation of data. Ali O. Abdel Aziz carried out drafting of the manuscript. Ashraf Osman carried out Laboratory work up. Mohammad T. Abdel Fattah, Ali O. Abdel Aziz carried out statistical analysis. All the authors contributed to critical revision of the manuscript for important intellectual content.

The authors thank all members in the department, from staff doctors and resident doctors to nursing staff. They also thank Dr Nezar Rifaat for great effort in the establishment of the ICU and in the progress of the department.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Chakrabarti, Angus RM, Agarwal S, Lane S, Calverley PM. Hyperglycaemia as a predictor of outcome during non-invasive ventilation in decompensated COPD. *Thorax* 2009; **64**:857–862.

2 Keenan SP, Slnuff T, Cook DJ, Hill NS. Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation? A systematic review of the literature. *Ann Intern Med* 2003; **138**:861–870.

3 Lightowler JV, Wedzicha JA, Elliot MW, Ram FS. Non-invasive positive pressure ventilation to treat respiratory failure resulting from exacerbations of chronic obstructive pulmonary disease: Cochrane systematic review and meta-analysis. *BMJ* 2003; **326**:185.

4 Global Initiative for Chronic Obstructive Lung Disease (GOLD). *Global strategy for the diagnosis, management, and prevention of COPD* 2014. Available from http://www.goldcopd.org/.

5 Hill NS, Brennan, Garpestad E, Nava S. Noninvasive ventilation in acute respiratory failure. *Crit Care Med* 2007; **35**:2402–2407.

6 Plant PK, Elliott MW. Chronic obstructive pulmonary disease • 9: management of ventilatory failure in COPD. *Thorax* 2003; **58**:537–542.

7 Carron M, Freo1 U, BaHammam AS, Dellweg D, Guarracino F, Cosentini R, *et al.* Complications of non-invasive ventilation techniques: a comprehensive qualitative review of randomized trials. *Br J Anaesth* 2013; **110**:896–914.

8 Wells PS, Anderson DR, Rodger M, Ginsberg JS, Kearon C, Gent M, *et al.* Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost* 2000; **83**:416–420.

9 Nava S, Grassi M, Fanfulla F, Domenighetti G, Carlucci, Perren, *et al.* Non-invasive ventilation in elderly patients with acute hypercapnic respiratory failure: a randomised controlled trial. *Age Ageing* 2011; **40**:444–450.

10 Nicolini, Ferrera L, Santo M, Ferrari-Bravo M, Del Forno M, Sclifo F. Noninvasive ventilation for hypercapnic exacerbation of chronic obstructive pulmonary disease: factors related to noninvasive ventilation failure. *Pol Arch Med Wewn* 2014; **124**:525–531.

11 Soo Hoo GW, Santiago S, Williams AJ. Nasal mechanical ventilation for hypercapnic respiratory failure in chronic obstructive pulmonary disease: determinants of success and failure. *Crit Care Med* 1994; **22**:1253–1261.

12 Iqbal Z, Ziaullah, Basit, Yousaf Khan M, Javaid. Changes in ABGs and respiratory rate before and after NIPPV in AE of COPD. *Pak J Chest Med* 2008; **14**:3–8.

13 Soliman MA, El-Shazly MI, Soliman YMA, Mostafa AI. Effectiveness of non invasive positive pressure ventilation in chronic obstructive pulmonary disease patients. *Egypt J Chest Dis Tuberc* 2014; **63**:309–312.

14 Ibrahim BJ, Jaber DK. The effectiveness of non-invasive ventilation in management of respiratory failure in Palestine a prospective observational study. *Egypt J Crit Care Med* 2014; **2**:29–36.

15 Ahmad H, Ashraf S, Farooqi RJ, Zaman M. Efficacy OF BIPAP in patients admitted with hypercapnic respiratory failure; an experience at a tertiary care hospital. *Pak J Chest Med* 2014; **20**:89–94.

16 Carrillo, Ferrer M, Gonzalez-Diaz G, Lopez-Martinez, Llamas N, Alcazar M, *et al.* Noninvasive ventilation in acute hypercapnic respiratory failure caused by obesity hypoventilation syndrome and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2012; **186**:1279–1285.

17 Crummy F, Buchan C, Miller, Toghill, Naughton MT. The use of noninvasive mechanical ventilation in COPD with severe hypercapnic acidosis. *Respir Med* 2007; **101**:53–61.

18 Cabrini L, Antonelli M, Savoia G, Landriscina M. Non-invasive ventilation outside of the intensive care unit: an Italian survey. *Minerva Anesthesiol* 2011; **77**:313–322.

19 Vanani V, Patel M. A study of patients with type II respiratory failure put on non-invasive positive pressure ventilation. *Ann Trop Med Public Health* 2013; **6**:369–377.

20 Salahuddin N, Irfan M, Khan S, Naeem M, Haque AS, Husain SJ, *et al.* Variables predictive of outcome in patients with acute hypercapneic respiratory failure treated with noninvasive ventilation. *J Pak Med Assoc* 2010; **60**:13–17.

21 Moretti M, Cilione C, Tampieri, Fracchia C, Marchioni, Nava S. Incidence and cause of non-invasive mechanical ventilation failure after initial success. *Thorax* 2000; **55**:819–825.

22 Dal Negro RW, Bonadiman L, Tognella S, Bricolo F, Turco P. Extent and prevalence of cognitive dysfunction in chronic obstructive pulmonary disease, in chronic non-obstructive bronchitis, and in asymptomatic smokers, compared to normal reference values. *Int J Chron Obstruct Pulmon Dis* 2014; **9**:675–683.

23 Weinreich UM, Thomsen LP, Bielaska, Jensen VH, Vuust M, Rees SE. The effect of comorbidities on COPD assessment: a pilot study. *Int J Chron Obstruct Pulmon Dis* 2015; **10**:429–438.

24 Fumagalli G, Fabiani F, Forte S, Napolitano M, Balzano G, Bonini M, *et al.* INDACO project: COPD and link between comorbidities, lung function and inhalation therapy. *Multidiscip Respir Med* 2015; **10**:4.

25 Senef MG, Wagner DP, Wagner RP, Zimmerman JE, Knaus WA. Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease. *J Am Med Assoc* 1995; **27**:1852–1857.

26 Pacilli AMG, Valentini I, Carbonara P, Marchetti, Nava S. Determinants of noninvasive ventilation outcomes during an episode of acute hypercapnic respiratory failure in chronic obstructive pulmonary disease: the effects of comorbidities and causes of respiratory failure. *Biomed Res Int* 2014; **2014**:976783.

27 Nevins ML, Epstein SK. Predictors of outcome for patients with COPD requiring invasive mechanical ventilation. *Chest* 2001; **119**:180–189.

28 Sundh, Johansson G, Larsson K, Linden, Lofhal CG, Janson C, *et al.* Comorbidity and health-related quality of life in patients with severe chronic obstructive pulmonary disease attending Swedish secondary care units. *Int J Chron Obstruct Pulmon Dis* 2015; **10**:173–183.

29 Mannino DM, Thorn D, Swensen, Holguin F. Prevalence and outcomes of diabetes, hypertension and cardiovascular disease in COPD. *Eur Respir J* 2008; **32**:962–969.

30 Patel AR, Donaldson GC, Mackay AJ, Wedzicha JA, Hurst JR. The impact of ischemic heart disease on symptoms, health status, and exacerbations in patients with COPD. *Chest* 2012; **141**:851–857.

31 Cote C, Zilberberg MD, Mody SH, Dordelly LJ, Celli. Haemoglobin level and its clinical impact in a cohort of patients with COPD. *Eur Respir J* 2007; **29**:923–929.

32 Kollert F, Tippelt, Müller C, Jörres RA, Porzelius C, Pfeifer M, Budweiser S. Hemoglobin levels above anemia thresholds are maximally predictive for long-term survival in COPD with chronic respiratory failure. *Respir Care* 2013; **58**:1204–1212.

33 Song Y, Klevak, Manson JE, Buring JE, Liu S. Asthma, chronic obstructive pulmonary disease, and type 2 diabetes in the Women's Health Study. *Diabetes Res Clin Pract* 2010; **90**:365–371.

34 Goodwin JL, Kaemingk KL, Mulvaney SA, Morgan WJ, Quan SF. Clinical screening of school children for polysomnography to detect sleep-disordered breathing – the Tucson Children's Assessment of Sleep Apnea study (TuCASA). *J Clin Sleep Med* 2005; **1**:247–254.

35 Krachman S, Minai OA, Scharf SM. Sleep abnormalities and treatment in emphysema. *Proc Am Thorac Soc* 2008; **5**:536–542.

36 Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman, *et al.* Practice parameters for the indications of polysomnography and related procedures: an update for 2005. *Sleep* 2005; **28**:499–521.

37 Schettino G, Altobelli N, Kacmarek RM. Noninvasive positive-pressure ventilation in acute respiratory failure outside clinical trials: experience at the Massachusetts General Hospital. *Crit Care Med* 2008; **36**: 441–447.

38 Bastiansen. Predicting failure of non-invasive ventilation in a mixed population. *J Anesth Clin Res* 2014; **5**:378.

39 Gill M, Martens K, Lynch EL, Salih, Green SM. Interrater reliability of 3 simplified neurologic scales applied to adults presenting to the emergency department with altered levels of consciousness. *Ann Emerg Med* 2007; **49**:403–407.

40 Sakr Y, Madl C, Filipescu D, Moreno R, Groeneveld, Artigas, *et al.* Obesity is associated with increased morbidity but not mortality in critically ill patients. *Intensive Care Med* 2008; **3**:1999–2009.

41 Mahfouz TA, Hassan K, Abdul-galil D. Early mortality predictors in COPD patients admitted to ICU with severe exacerbation. *Egypt J Chest* 2005; **54**:119–123.

42 Glossop AJ, Shepherd N, Bryden DC, Mills GH. Non-invasive ventilation for weaning, avoiding reintubation after extubation and in the postoperative period: a meta-analysis. *Br J Anaesth* 2012; **109**:305–314.