ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 04, pp.48853-48860, April, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ROLE OF NON INVASIVE PRESSURE VENTILATION IN PATIENTS WITH ACUTE EXACERBATION OF COPD AND TO DETERMINE ITS OUTCOME

***,[1]Dr. K. Ramesh Kumar, [2]Dr. B. Phani Kumar and [3]Dr. Bhardwaj Reddy**

[1]Assoc. Prof. TB & Respiratory Medicine, Govt. General & Chest Hospital, Osmaina Medical College
[2]Asst. Prof. of TB & Respiratory Medicine, Govt. General & Chest Hospital, Osmaina Medical College
[3]Pulmonologist, Rajahmundry

ARTICLE INFO

Article History:
Received 23rd January, 2017
Received in revised form
12th February, 2017
Accepted 18th March, 2017
Published online 20th April, 2017

Key words:

Non invasive ventilation
Copd
IPAP,
EPAP,
RESPIRATORY FAILURE.

ABSTRACT

- The present study was conducted to understand the role of NIPPV in patients with acute exacerbation of COPD who are medically unresponsive. The sample size was 40.
- The mean age of the study population was 60.7± 7.2 yrs.
- Out of the 40 cases included in the study, 36 (90%) were males and 4 (10%) were females, sex ratio 9:1(male:female).
- A history of smoking was obtained in 90% of study population.
- The Borg dyspnoea score improved from 5 at baseline to 1.4 ± 0.07 at discharge. ($p < 0.0001$)
- The mean respiratory rate dropped from 34.8 ± 4.4 before NIV to 13.82 ± 1.96 ($p < 0.0001$) at discharge. Heart rate too decreased from 102.4 ± 10.9 to 77.1 ± 9.65($p < 0.0001$).
- The mean pH changed from 7.29± 0.02 at baseline to 7.4 ±0.03 at discharge ($p < 0.0001$).
- There was also a marked improvement in mean $PaCO_2$ and PaO_2 which changed from, 67.3 ± 5.61, 54.6 ± 8.85 at baseline to 50.02 ± 4.08, 75.1 ± 9.71 at the time of discharge respectively ($p<0.0001$ for both parameters).
- Respiratory rate at baseline was significantly higher in the patients who failed to respond to NIV and there was a significant improvement in the clinical and blood gas parameters within the 1st of NIV in the successful group whereas no such improvement was observed in the failure group.
- In the present study NIPPV was successful in 34 patients (85%) and 6 patients (15%) failed to respond and required intubation. Of them, 2 patients did not consent and left against medical advice. 4 were intubated and all of them eventually expired. No mortality was observed in the patients improved and continued on NIPPV.
- The mean IPAP used in the present study was 16.5 ± 0.9 and mean EPAP used was 5.2±0.52.
- NIPPV was used for an average of 38.5±13 hrs.
- The incidence of complications in the present study was 10% which included aspiration pneumonia (2.5%), irritation of eyes (5%) and dryness of mouth (2.5%).
- The mean duration of hospital stay in the present study was 10.32±3.46 days.

Our results strongly support and encourage the use of NIPPV as a first line ventilatory management in patients with respiratory failure due to acute exacerbations of COPD.

Citation: Dr. K. Ramesh Kumar, Dr. B. Phani Kumar and Dr. Bhardwaj Reddy, 2017. "Role of non invasive pressure ventilation in patients with acute exacerbation of COPD and to determine its outcome", *International Journal of Current Research*, 9, (04), 48853-48860.

INTRODUCTION

COPD is a major health problem and has huge financial impact on society. Sixth leading cause of death in 1990. Morbidity and Mortality increase during acute exacerbation. Patients may have hypoxia and hypercapnia during acute exacerbations. NIV is slandered care hypercania respiratory failure in such cases and in patients with worsening respiratory symptoms (Fishman *et al*., 2003; Kelly *et al*., 2001; Celli *et al*., 2004). NIV by nasal masks was use for neuromuscular diseases (World Health Report, 2000; Laënnec, 1821). The indication for NIV in COPD are respiratory acidosis PH< 7.35, PCO2 >45, severe dyspnea with respiratory muscles, paradoxical respiratory movements with intercostals retractions. NIV is defined as pressure ventilatory assistants to lungs without invasive artificial airway it is easy to administer intermide and good compliance patients. It reduces to work of breathing and does not interfere with patient speech and eating. NIV reduces a need for sedation and avoids intubation of airways prolong intubation can need to airway infections. It is highly cost effective and easy to administer. NIV is the two types a) Negative pressure ventilation b) positive pressure ventilation (Schonhofer *et al*., 1997)

Corresponding author: **Dr. K. Ramesh Kumar,**
Assoc. Prof. TB & Respiratory Medicine, Govt. General & Chest Hospital, Osmaina Medical College

Aim

Role of non Invasive pressure ventilation in patients with acute exacerbation of COPD and to determine its outcome. The study was conducted on 40 patients with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) admitted to GENERAL HOSPITAL in Hyderabad. The inclusion and exclusion criteria used for the study were-

Inclusion criteria

Moderate to severe dyspnoea lasting < 2 weeks plus any two of the following

Respiratory rate >25/min
Signs of increased work of breathing
pH < 7.35 – 7.25

Partial pressure of carbon dioxide ($PaCO_2$) > 45 mmHg after an aggressive and appropriate medical therapy including oxygen supplementation.
Exclusion criteria
Cardiac / respiratory arrest
Hemodynamic instability
Unstable arrhythmias
Encephalopathy, Irritability
Recent Myocardial infarction
Facial surgery/trauma/deformity,

Written informed consent was obtained from the patient or from his closest relative. Baseline evaluation consisting of patient's clinical history and detailed clinical examination was conducted. Parameters that were recorded include dyspnoea graded by modified Borg dyspnoea score, respiratory rate (RR), heart rate (HR), arterial blood gas analysis. Routine blood investigations were sent. A chest X-ray was taken. All patients were administered NIPPV using the BiPAP ventilatory support system (GE Inc). A well fitting face mask was used for the study. The procedure was explained to the patient. The head end of the bed was elevated to 45º angle. Patients were initiated with an IPAP 10cm H_2O and EPAP of 4–5 cm H_2O. IPAP was gradually increased at a rate of approximately 5 cm H_2O every 10 minutes, with a pressure target of 20 cm H_2O or until a therapeutic response is achieved or patient's tolerability has been reached. Supplemental Oxygen therapy was administered with NIPPV and titrated to achieve an oxygen saturation of 88-92%.After starting treatment each patient was monitored closely for initial one hour. Patient's discomfort and intolerance to mask was looked for. Once initiated continuous application of NIPPV was encouraged, with intermittent discontinuation for eating and drinking. Standard pharmacologic treatment including bronchodilators [inhaled salbutamol, ipratropium bromide and steroids (IV hydrocortisone)] and antibiotics were given along with NIPPV. Blood pressure, respiratory rate, heart rate, dyspnoea using modified Borg scale were recorded at the baseline, 1 hr, 6hrs and daily until discharge. The outcome of NIPPV usage was measured in terms of the number of patients cured by NIPPV and those who failed on NIPPV. The mean duration of NIPPV application, duration of hospital stay and any complications related to the procedure. Statistical analysis was done using standard methods. A p value <0.05 is considered significant and p value < 0.001 is considered extremely significant.

RESULTS (Rocai Wagner, 1994)

Age distribution

Table 1

Age	No of patients(n=40)	Percentage
41-50	6	15
51-60	16	40
61-70	16	40
71-80	2	5

The mean age of the study population is 60.7 ± 7.8 yrs. Majority of them were in the age group of 51-60 yrs and 61-70 yrs each constituting 40%

Sex distribution

Out of the 40 patients included in the study 36 (90%) were males and 4 (10%) were females. Sex ratio (M:F) is 9:1

Table 2

Gender	No of Patients(n=40)	Percentage
Male	36	90
Female	4	10

Smoking History

Table 3

Pack years of smoking	No of patients(n=40)	Percentage
Nil	4	10
≤ 10	9	22.5
11-20	20	50
21-30	5	12.5
>30	2	5

In the present study a history of smoking (either active or ex smokers) was obtained in 36 patients (90%). Most of the patients had an average smoking pack years of 11-20 (50%). Among the males 34 were smokers, 2 were non smokers and among the females 2 were smokers. Most of the patients had an average smoking pack years of about 11-20.Demographic and baseline characteristics of the study population

Table 4

Characteristic of the patient	
Total no of patients (n)	40
Age (yrs)	60.7 ± 7.8*
Sex ratio (M: F)	36:4
Smokers	36(90%)
Dyspnoea score	5
Respiratory rate	34.8 ± 4.4*
Heart rate	102.4 ± 10.9*
pH	7.29 ± 0.02*
$PaCO_2$	67.3 ± 5.61*
PaO_2	54.6 ± 8.85*
Comorbidities	
Diabetes	6 (15%)
Hypertension	8 (20%)
Diabetes + Hypertension	4 (10%)
Cor pulmonale	12 (30%)
Chronic kidney disease	2 (5%)
Ischaemic heart disease	0

RESULTS

Dyspnoea scores reduced remarkable in many patients who are receiving NIV

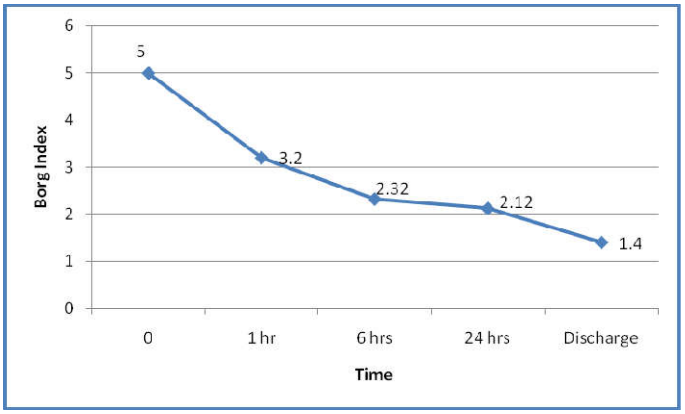
Table 11

	0(n=40)	1 hr(n=40)	6 hrs(n=34)	24 hrs(n=34)	Discharge(n=34)
Dyspnoea score	5	3.2 ± 0.02*	2.32 ± 0.47*	2.12 ± 0.38*	1.4 ± 0.07 *
Heart rate (per min)	102.4 ± 10.9	97.2 ± 9.39*	88.23 ± 8.12*	77.47± 8.62*	77.1 ± 9.65*
Respiratory rate(breaths/min)	34.8 ± 4.4	26.9 ± 5.66*	16.64 ± 1.73*	15.47± 1.2*	13.82 ± 1.96*

*p value less than <0.0001 from baseline

In the present study NIPPV was administered to 40 patients. Out of 40, 6 patients deteriorated and required intubation within 6 hrs. 34 patients who remained by the end of 6 hrs continued to receive NIPPV.NIPPV was effective in lessening the dyspnoea score from 5 at baseline to 3.2± 0.02 at 1 hr, to 2.32±0.4 at 6hrs , 2.12±0.38 at 24 hrs and 1.4±0.07 at the time of discharge. (p<0.0001 from base line to all 4 measurements)The respiratory rate decreased from 34.8 ± 4.4 at baseline to 26.9 ± 5.66 at 1 hr, to 16.64±1.73 at 6hrs, 15.4±1.2 at 24 hrs and 13.8 ± 1.9 at the time of discharge. (p<0.0001 from base line to 4 measurements)The heart rate reduced from 102.4±10.9 at baseline to 97.2±9.39 at 1 hr to 88.2±8.1 at 6 hrs to 77.4 ± 8.6 at 24 hrs and 77.1±9.65 at the time of discharge. (p<0.0001 from base line to 4 measurements)

Chart



Graph showing evolution of modified Borg dyspnoea score during hospitalization. High score indicates more dyspnoea. There was significant decrease of dyspnoea throughout hospitalization. (p<0.0001 from baseline to all measurements)
Graph showing change in respiratory rate during hospitalization in the study population. There was significant fall in respiratory rate with NIPPV over time in the study population. (p <0.0001 from baseline to all 4 measuements)
Changes in the ABG parameters before, during and after NIPPV

Table 6

	0hr (n=40)	1hr (n=40)	24hrs (n=34)	Discharge (n=34)
pH	7.29±0.02	7.31±0.02*	7.37±0.02*	7.40±0.03*
$PaCO_2$ mm Hg	67.3±5.61	62.8±5.74 *	51.8±3.7*	50.02±4.08*
PaO_2 mm Hg	54.6±8.85	61.7±7.17*	70.3±9.19*	75.14±9.71*

*p < 0.0001 from baseline

Out of the 40 patients administered NIPPV, 6 patients deteriorated and required intubation and only 34 patients remained by the end of 6 hours. The pH changed from 7.29 ± 0.02 at baseline to 7.31± 0.02, 7.37±0.02 and 7.40±0.03 at 1 hr, 24 hrs and at discharge respectively. (p< 0.0001 from baseline to all 3 measurements)$PaCO_2$ decreased with time significantly from 67.3 ± 5.61 to 62.8 ± 5.74 at 1 hr, 51.8±3.7 at 24 hrs and 50.02 ±4.08 at discharge (p<0.0001 from baseline to all 3 measurements)A rise in PaO_2 was observed from 54.6±8.85 to 61.7±7.17 at 1 hr, to 70.3±9.19 at 24 hrs and to 75.14 ± 9.71 by the time of discharge. (p<0.0001 from baseline to all 3 measurements)Graph showing the change in pH during hospitalization in the study population. pH improved significantly over time in the study population (p<0.0001 from baseline to all 3 measurements) Graph showing changes in $PaCO_2$ and PaO_2 in the study population. There was a significant fall in $PaCO_2$ with NIPPV over time and PaO_2 also improved significantly. (p <0.0001 for both $PaCO_2$ and PaO_2 from baseline to all measurements).

Ventilatory requirements

Table 5

	Mean ± SD (Range)
IPAP	16.5 ± 0.9 (15-20)
EPAP	5.2 ± 0.52 (5-8)
Duration on NIPPV(hrs)	38.5±13.1 (24-80)

The mean IPAP used in the present study was 16.41 ± 0.69
The mean EPAP used was 5.11 ± 0.32. NIPPV was used for an average of 38.5 ± 13.1 hrs.

Complications

In the present study 4 complications occured (10%) and none required discontinuation of ventilation. One is aspiration pneumonia, 2 patients experienced irritation of eyes (5%) and 1 patient experienced dryness of mouth (2.5%). Aspiration pneumonia was treated with antibiotics and it resolved completely.

Duration of hospital stay

Mean duration of hospital stay in our study was 10.32±3.46 days. Majority of patients were discharged within the 2nd week.

Table 7

No of days	No of patients n=34	Percentage
1-7	5	12.5
8-14	22	55
15-21	4	10
22-28	2	5
>28	1	2.5

Graph showing the duration of hospital stay in the study population

Clinical and ABG Status Prior To and 1 Hr After NIPPV

Although the $PaCO_2$ of patients who failed NIPPV was higher than the patients who succeeded this did not reach statistical significance. (70.3 ± 5.7 vs 67.2±5.8, p 0.19 NS) No other differences were observed in baseline characteristics of patients who failed versus those who succeeded. After 1 hr of NIPPV, pH was significantly higher and $PaCO_2$, was significantly lower in the success group as compared to failed group (7.31±0.01vs 7.29±0.01, 61.2±5.2 vs 73.8±4.6, p<0.0001).When compared to baseline values there was a significant improvement in RR (34.2 ±4.4 to 25.02± 3.1, p <0.001), HR (102.6 ±11.2 to 97.8±9.1), pH (7.29±0.02 vs 7.31±0.01, p <0.001), $PaCO_2$ (67.2±5.8 vs 61.2±5.2,p<0.001), PaO_2 (54.6±9.1 to 62.7±6.8, p<0.001) in the success group. There was no change in pH and $PaCO_2$ deteriorated in the failure group.

Table 8

	Successful group(n=34)			Failure group(n=6)		
	0 hr	1 hr	p value	0hr	1hr	p value
Age	60.8±8			61.1±5.48		0.94
RR	34.2±4.4*	25.02±3.1†	<0.001	38.3±2.4*	36.6±4.7†	0.44
pH	7.29±0.02	7.31±0.01†	<0.001	7.29±0.01	7.29±0.01†	1.0
$PaCO_2$	67.2±5.8	61.2±5.2 †	<0.001	70.3±5.7	73.8±4.6†	0.26
PaO_2	54.6±9.1	62.7±6.8ψ	<0.001	54.3±7.24	56.3±5.8ψ	0.44

- Success defined by avoidance of ETI
*p value significant (<0.05) between failed and successful groups at baseline
† p value significant (<0.001) between failed and successful groups at 1 hr
Ψ p value < 0.05 between failed and successful groups at 1 hr
In the present study NIPPV was successful in 34 (85%) and failed in 6 (15%) patients. RR at baseline was significantly higher in the patients who failed NIPPV (p value 0.03).

Outcome

In the present study the success rate with NIPPV was 85%, with 34 patients weaned off successfully and discharged. Of the six patients who failed NIPPV, 2 patients did not consent and left against medical advice. The other 4 were intubated and mechanically ventilated.

All these 4 patients eventually expired

– 2 due to ventilator associated pneumonia, 1 from gram negative sepsis and multi organ dysfunction syndrome, 1 from acute cerebrovascular accident. No mortality was observed in the patients improved and continued on NIPPV

Table 8

	Successful	Failure
Number	34	6
Percentage	85	15

DISCUSSION

A significant number of acute exacerbations of COPD are associated with hypercapnic respiratory failure. Ventilatory management in such patients include both NIPPV and invasive mechanical ventilation. Numerous studies have been conducted at many centers in the past and highlighted the benefits of NIPPV usage in acute exacerbation of COPD in terms of reduced need of endotracheal intubation and invasive mechanical ventilation, shorter length of hospital stay and decreased mortality. Metaanalysis (Smith and Shneerson, 1996; Plant *et al*., 2000) of these trials have also confirmed the benefits of NIPPV in AECOPD. The results of previous studies and a rapidly reversible nature of most episodes of acute decompensation suggests that patients with acute exacerbations of COPD should benefit from NIPPV. The present study was undertaken to understand the role of NIPPV in patients with acute respiratory failure due to acute exacerbations of COPD and to determine the outcome of such patients attending to our hospital. The current study group comprised of 40 patients with a mean age of 60.7± 7.2 yrs. Majority of patients were males (90%) with a sex ratio (M:F) of 9:1. All patients were administered BIPAP with a mean IPAP of 16.5 ± 0.9 and a mean EPAP of 5.2 ±0.52 in addition to standard medical treatment.

Outcome

NIPPV was successful in 85% of patients in our study cohort . In the study of Verma *et al*. (Kramer *et al*., 1995) in an ICU in northern India, NIPPV was successful in 90% of the study population while Umberto Meduri *et al*. (Brochard *et al*., 1995) reported it to be only 66% in a similar group of hypercapnic patients. The reported success rates in the patients treated with NIV in previous controlled studies were as follows:

Brochard *et al*. (1996) – 74%
Plant *et al*. (2000)- 85% (100/118)
Celikel *et al*. (1998) - 93.4 % (14/15)
Avdeev *et al*. (1998) – 88%
The results obtained in our study are comparable to the above mentioned studies.

Response to NIPPV

In our study a significant improvement was observed in the clinical and the blood gas parameters within 1 hr of application of NIPPV. The dyspnoea score has improved from 5 at baseline to 3.2± 0.02(p<0.0001) at 1 hr. The RR has fallen from a baseline of 34.8 ± 4.4 to 26.9± 5.66 (p<0.0001). There was a significant improvement in the average $PaCO_2$ levels within 1 hr from 67.3± 5.61 to 62.8 ± 5.74. This change was also reflected in pH with improvements from 7.29 ± 0.02 to 7.31 ± 0.02. The PaO_2 has also changed from 54.6 ± 8.85 to 61.7±7.17. Mc Laughlin *et al*. (1998) also noted a similar significant improvement in P_H which changed from 7.29 to 7.3 and $PaCO_2$ which changed from 70.1 to 63.7 mmHg within the 1st hour of application of NIPPV (p<0.0001). Brochard *et al*. (1995) found that in the NIV group RR has fallen from 35±7 to 25±8, phimproved from 7.27±0.1 to 7.31±0.09 (p<0.001) in 1 hr whereas $PaCO_2$ improved significantly at 3 hrs. Plant *et al*. (2000) in their study noted that NIV led to a significant improvement in pH in 1st hr whereas $PaCO_2$,RR changed significantly at 4 hrs. In our study further significant

improvement was obtained at 24 hrs and it maintained upto the time of discharge. The pH, $PaCO_2$ and PaO_2 changed from baseline of 7.29± 0.02 , 67.3 ± 5.61, 54.6 ± 8.85 to 7.4 ±0.03, 50.02 ± 4.08,75.1 ± 9.71 at the time of discharge respectively. The above results are very close to the results obtained in the Verma *et al*. (1995) study where also the pH, $PaCO_2$, PaO_2 from baseline of 7.33 ± 0.08, 66.4 ±16.24,53.4 ± 18 to 7.42 ± 0.06, 56±12, 71± 24.1 at the time of discharge. The results in the present study indicate that NIV not only relieves respiratory distress and rests fatigued respiratory muscles but also can significantly improve hypercapnia and acidosis in patients with respiratory failure in acute exacerbation of COPD and thus alleviate the need for endotracheal intubation. In the present study it was observed that RR at baseline was significantly higher in the patients who failed NIPPV (34.2±4.4 vs 38.3±2.4, p <0.05). Although the $PaCO_2$ of patients who failed NIPPV was higher than the patients who succeeded this did not reach statistical significance. After 1 hr of NIPPV, pH was significantly higher and $PaCO_2$ was significantly lower in the success group as compared to failed group pH. (7.31±0.01vs7.29±0.01, 61.2±5.2 vs 73.8±4.6, p<0.0001). When compared to baseline values there was a significant increase in pH and fall in $PaCO_2$in the success group ,whereas there was no change in pH,$PaCO_2$ deteriorated in the failure group. These findings suggests that respiratory rate at admission and an improvement in gas exchange parameters within the 1st hour of NIPPV could possibly be used to predict response to NIPPV. However other determinants of success (like level of consciousness, comorbidities, BMI etc) NIPPV were not evaluated in the present study. Garpested *et al*. (1994) have shown that an improvement in pH and $PaCO_2$ within 1 hr to be associated with success of NIPPV.

Duration of NIPPV

In our study NIPPV was used for a mean duration of 38.5 ±13 hrs. In the study of Umberto Meduri *et al*. (1995), it was 23±17 hrs. Avdeev *et al*. (1998)reported it to be 29± 25hrs in their study.

Complications

Only 4 (10%) complications occurred in the current study which were dryness of mouth and irritation of eyes which is very similar to the complication rate in Umberto Meduri *et al*. (1995) (12%). This low rate of infectious complications in patients receiving NIPPV has been confirmed in randomized studies by Brochard *et al*. (1995) and Bott *et al*. (1993).

Duration of hospital stay

The mean duration of hospital stay in our study was 10.32 ±3.46 days. The shorter duration of hospitalisation with the use of NIPPV is also cost effective. The limitation in the present study is the small sample size. The results in the present study support the use of NIPPV in patients with acute exacerbations of COPD.

Conclusion (1987)

The results in the present study showed that NIPPV is a promising therapeutic modality for management of selected patients with exacerbations of COPD who have respiratory acidosis even after standard medical therapy. Its timely institution leads to a rapid and profound improvement in subjective symptoms and blood gas variables helps into avoiding intubation and invasive ventilation. With its associated complications. The protocol is simple to implement and to monitor. In the present study patients dysponea improved well in first six hours, a significant improvement in clinical and blood gas parameters within the 24hrs. Early response to NIPPV indicated a favourable response. However further studies are required to establish this and to evaluate other potential predictors of success for better outcomes with NIPPV.

REFERENCES (Longobardo *et al*., 2002)

Abbey DE, Burchette RJ, Knutsen SF, McDonnell WF, Lebowitz MD, Enright PL. 1998. Long-term particulate and other air pollutants and lung function in nonsmokers. *Am J Respir Crit Care Med*., 158:289-98.

Amato MBP, Barbas CSV, Medeiros DM, *et al*. 1998. Effect of a protective-ventilation strategy on mortality in acute respiratory distress syndrome. *N Engl J Med.,* 338:347–54.

Angus *et al*. 1996. Compared effects of NIPPV with those of doxapram over 4 hrs in patients with AECOPD and found that NIPPV was more effective. (Thorax 51:1048-50)

Appendini *et al*. 1994. Found although PEEPI may be 10-15cm H2O in patients with severe acute COPD, levels of EPAP of >5cm H2O are rarely tolerated and also found greater reduction in work of breathing with the addition of PEEP in acute COPD. (*Am J Respir Crit Care Med*., 149-1069-76)

Appendini L, Patessio A, Zanaboni S, *et al.* 1994. Physiologic effects of positive end-expiratory pressure and mask pressure support during exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*., 149:1069–76.

Avdeev *et al*. in a randomized controlled study also noted that there was a significant rise of pH and fall of $PaCO_2$ after 1 h of ventilation with NIPPV. The need in intubation (12 Vs 28%), hospital stay (26 ± 7 vs. 34±10 days) and mortality rate (31 vs. 8%) were lower in the NPPV group as compared to the reference group. (Anesteziol Reanimatol 1998; May-Jun; (3):45-51.

Bahadori K, FitzGerald JM. 2007. Risk factors of hospitalization and readmission of patients with COPD exacerbation-systematic review. *Int J Chron Obstruct Pulmon Dis*., 2:241-51

Barbe *et al*. 1996. Showed lack of difference between NIPPV and SMT groups. Arterial oxygenation, respiratory acidosis and airflow obstruction improved significantly similarly in the two groups. (*Eur Respir* J., 9:12, 40-45)

Barker DJ,Godfrey KM, Fall C, Osmond C, Winter PD, Shaheen SO. 1991. Relation of birthweight and childhood respiratory infection to lung function and ans death from chronic obstructive airways disease. *BMJ*, 303:671-5.

Barnes PJ, Shapiro SD, Pauwels RA. 2003. Chronic obstructive pulmonary disease: molecular and cellular mechanisms.*Eur Respir J*., 22:672-88.

Bartolome R Cell. 2000. The importance of spirometry in COPD and Asthma. *Chest*, 117:15S-19S.

Bhowmik A, Seemungal T A R, Sapsford R J. *et al*. 2000. Relation of sputum inflammatory markers to symptoms and lung function changes in COPD exacerbations. *Thorax*, 55114–120.120.

Bott *et al*. 1993.1993. in a randomized controlled study showed that in the COPD patients with acute respiratory

failure subjected to NIPPV there was a significant fall in $PaCO_2$ and improved dyspnoea score within 1 hr whereas no such improvement occurred in the control group and also demonstrated a survival benefit with NIPPV. (*Lancet*, 341:1555-15)

Brochard *et al*1995. in a prospective randomised study reported that most of the excess mortality and complications were attributed to intubation. NIV may be superior to invasive mechanical ventilation in highly selected group. Mild COPD are not benefitted from NIV in the study. Brochard also found that not only vital signs, blood gases values and encephalopathy scores improved more rapidly in NIV group than controls but also that intubation rates decreased from 74% to 26% ,complication rates (pneumothorax and ET tube complications), hospital stay (35 to 17 days) and mortality rates (from 31 to 9%) fell significantly. (*N Engl J Med*., 333:817-22)

Brochard *et al*. 1990. showed that pressure support ventilation with face mask significantly reduced the need for intubation , duration of mechanical ventilation or length of ICU stay. (*N Engl J Med*., 329:1523-30)

Brochard L, Mancebo i, Sibbald Wi, *et al*. 1995. Non-invasive ventillation for acute exacerbations of chronic obstructive pulmonary disease. *N. Eng. J. Med*., 333:817-22.

Buist AS, McBurnie MA, Vollmer WM, *et al*. 2007. International variation in the prevalence of COPD (the BOLD Study):a population-based prevalence study. *Lancet*, 370:741-50.

Burge S. and Wedzicha JA. 2003. COPD exacerbations: definitions and classifications. *Eur Respir J Suppl*., 41:46s-53s.

Calverley P M A. 2003. Respiratory failure in chronic obstructive pulmonary disease. *Eur Respir J*., 2226–30s.30s

Celikel *et al*. 1998. in a prospective study , showed that there was more rapid improvement in various physiological parameters in the NIPPV group but no difference in intubation rate or survival rate. (*Chest*, 114:1636-42)

Celikel T, Sungur M, Ceyhan B, *et al*. 1998. Comparison of non-invasive positive pressure ventilation in acute respiratory failure. *Chest*, 114:1636–42.

Celli BR, Cote CG, Marin JM, *et al*. 2004. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*., 350:1005-12.

Celli BR. and Barnes PJ. 2007. Exacerbations of chronic obstructive pulmonary disease. *Eur RespirJ*., 29:1224-38.

Centers for Disease Control and Prevention. Recommended adult immunization schedule. United States, 2010. MMWR Morb Mortal Wkly Rep 2011;60:1-4.

Colleen Sanders. The radiographic diagnosis of emphysema. *Radiologic Clinics of North America*, 1991; 29(5):1019-1039

Connors AF, Jr., Dawson NV, Thomas C, *et al*. 1996. Outcomes following acute exacerbation of severe chronic obstructive lung disease *Am J Respir Crit Care Med*., 154:959-67.

Denis E, O'Donnell. 2000. Assessment of bronchodilator efficiency in symptomatic COPD, is spirometry useful. *Chest*, 117:42S-47S.

Department of Health. Comprehensive critical care. London: Department of Health, 2000.

Doll R. and Peto R. 1976. Mortality in relation to smoking: 10 years observation on British doctors. *BMJ*, 2:1525.

Edwin K Silverman, Frank E Speizer. 1996. Risk factors for the development of chronic obstructive pulmonary disease. *Medical Clinics of North America*, 80(3):501-22.

Elliot MW. and Simonds AK.1995. Found that in patients with stable neuro muscular disease, the addition of PEEP to Pressure support increased over night oxygenation. (*Eur Respir J*., 8:436-40)

Elliott MW. and Simmonds AK. Nocturnal assisted ventilation using bilevel positive airway

Ellis E, Bye P, Brudere JW, *et al*. 1987. Treatment of respiratory failure during sleep in patients with neuromuscular disease: positive pressure ventilation through a nose mask. *Am Rev Respir Dis*., 135:523–4.

Ezzati M. 2005. Indoor air pollution and health in developing countries. *Lancet*, 366:104-6.

Fabbri LM, Calverley PM, Izquierdo-Alonso JL, *et al*. 2009. Roflumilast in moderate-to-severe chronic obstructive pulmonary disease treated with long acting bronchodilators: Two randomised clinical trials. *Lancet*, 374:695-703.

Ferguson T. and Gilmartin M. 1995. CO_2 rebreathing during BiPAP ventilatory assistance. *Am J Crit Care Med*., 151:1126–35.

Fishman A, Martinez F, Naunheim K, *et al*. 2003. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med.,* 348:2059-73.

Forster RE.1964. Rate of gas uptake by red cells. Hand book of physiology, Washington DC American physiological society, 839.

Girault C, Richard JC, Chevron V, *et al*. 1997. Comparative physiologic effects of noninvasive assist-control and pressure support ventilation in acute hypercapnic respiratory failure. *Chest*, 111:1639–48.

Global Initiative for Chronic Obstructive Lung Disease – Global Strategy for Diagnosis,Management, and Prevention of Chronic Obstructive Pulmonary disease. http.//www.goldcopd.com (accessed. 06-06-2011).

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of COPD. NHLBI/WHO Workshop Report, Executive Summary 2004; p. 1-21.

Gravil JH, Al-Rawas OA, Cotton MM, Flanigan U, Irwin A, Stevenson RD. 1998. Home treatment of exacerbations of chronic obstructive pulmonary disease by an acute respiratory assessment service. *Lancet*, 351:1853-5.

Hogg JC. 2004. Pathophysiology of airflow limitation in chronic obstructive pulmonary disease. *Lancet*,364:709-21.

International Consensus Conferences in Intensive Care Medicine: noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med.,* 2001;163(1):283-91.

John J Reilly, Jr., Edwin K Silverman. 2005. Chronic obstructive pulmonary disease. Chapter 242. In: Dennis L Kasper, Eugene Braunwald, editors. Harrison's Principles of Internal Medicine, 16th edition. New York: McGraw-Hill, p. 1547-48.

Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. 2009. Development and first validation of the COPD Assessment Test. *Eur Respir J*., 34:648-54.

Julie E Takasug, David J Godwin. 1998. Radiology of chronic obstructive pulmonary disease. *Radiologic Clinics of North America*., 36(1):29-5

Keenan SP *et al*2003. in a meta analysis compared the results of some of these studies and came to similar conclusion

about need for intubation and mortality, (*Ann Intern Med.,* 138:861-70)

Kelly AM, McAlpine R, Kyle E. 2001. How accurate are pulse oximeters in patients with acute exacerbations of chronic obstructive airways disease? *Respiratory Medicine*, 95:336-40.

Kerby G, Mayer L, Pingleton SK. 1987. Nocturnal positive pressure ventilation via nasal mask. *Am Rev Respir Dis*., 135:738–40.

Klocke RA. 1987. Carbon dioxide transport, in Farhi LE, Tenney SM (eds), Hand book of Physiology. Section 3: The respiratory system vol 4, Bethesda MD,*American Physiological Society*, p173.

Kramer *et al*1995. in a randomized prospective trial of NIV in acute respiratory failure noted a reduction in intubation rate in COPD patients (67% to 9%) but no difference in mortality (*Am J Respir Crit Care Med*., 151:1799-806)

Kramer N, Meyer Ti. Mcharg J, *et al*. 1995. Randomized prospective trial of noninvasive positive pressure ventilation in acute respiratory failure. *Am. J. Respir. Crit. Med*., 333:1799-806.

Laënnec RTH. 1821. In: A treatise on the diseases of the chest (English translation from the French) Forbes J, editor. London: T and G Underwood.

Leung P, Jubran A, Tobin MJ. 1997. Comparison of assisted ventilator modes on triggering, patient comfort and dyspnoea. *Am J Respir Crit Care Med*., 155:1940–8.

Lightowler JV *et al*. 2003. in a metaanalysis of eight randomized controlled trials showed NIPPV with usual medical care significantly reduces mortality, endotracheal intubation, treatment failure, complications, length of hospital stay, and improves blood gas tensions and also recommended that NPPV should be considered early in the course of respiratory failure and before severe acidosis ensues, to avoid endotracheal intubation and treatment failure, (*BMJ*, 326:185)

Lofaso F, Brochard L,Hang T, *et al*. 1996. Home versus intensive care pressure support devices. Experimental and clinical comparison. *Am J Respir Crit Care Med*., 153:1591–9.

Longobardo G, Evangelisti CJ, Chernaick NS. 200. Effects of neural drive on breathing in the awake state in humans. *Respir Physiol*., 129; 317-333.

Martin *et al*. 2000. in a prospective comparative study, showed a significant reduction in intubation rate with NIV but there was no difference in mortality. (*Am J Respir CritCare Med*., 161:807-13)

Martinez FJ, de Oca MM, Whyte RI, Stetz J, Gay SE, Celli BR. 1997. Lung-volume reduction improves dyspnea, dynamic hyperinflation, and respiratory muscle function. *Am J Respir Crit Care Med*., 155:1984-90

Mathers CD. and Loncar D. 2006. Projections of global mortalityand burden of disease from 2002 to 2030. PLoS Me, 3:e442.

NEW Rijcken B Schouten JP, Weiss ST, Speizer FE, vander Lende R. 1987. The relationship of nonspecific bronchial responsiveness to respiratory symptoms in a randompopulation sample. *Am Rev Respir Dis*., 136:62-8.

NIPPV Non-Invasive Ventilation in Acute Respiratory Failure British Thoracic Society Standards of Care Committee - Thorax 2002; 57:192-211

Noninvasive ventilation Sangeetha Mehta and Nicholas S Hill *Am J Respir Crit Care Med*., 2001: Vol 163 pp540-577

Oroczo-Levi M, Garcia-Aymerich J, Villar J, Ramirez-Sarmiento A, Anto JM, Gea J. 2006. Wood smoke exposure and risk of chronic obstructive pulmonary disease. *Eur Respir J*., 27:542-6.

Pellegrino R, Viegi G, Brusasco V, *et al*. 2005. Interpretative strategies for lung function tests. *Eur Respir J*., 26:948-68.

Phyllis K Stein, Patricia Nelson. 1998. Heart rate variability reflects severity of COPD in Piz a1-antitrypsin deficiency. *Chest*, 113:327-333.

Plant PK, Owen JL, Elliot MW. 2000. Early use of non-invasive ventillation for acute exacerbations of chronic obstructive pulmonary diseaseon general respiratory wards: a multicentre randomisedcontrolled trial. *Lancet*., 355:1931-5.

Plant PK, Owen JL, Elliott MW.2000. In a multicentric randomized controlled trial of NIV in acute exacerbation of COPD in general wards showed that "Treatment failure", a surrogate for the need for intubation, defined by prior criteria reduced from 27% to 15% by NIV ($p<0.05$) and in-hospital mortality also reduced from 20% to 10% ($p<0.05$) . The authors also confirmed the earlier finding of more rapid improvement of arterial pH, respiratory rate and shortness of breath in NIV group compared to control group. (*Lancet*, 355:1931-35)

Plant PK, Owen JL, Elliott MW. 2000. One year period prevalence study of respiratory acidosis in acute exacerbations of COPD: implications for the provision of non-invasive ventilation and oxygen administration. *Thorax*, 55:550–4.

Rahman I. 2005. Oxidative stress in the pathogenesis of chronic obstructive pulmonary disease mechanisms. Cellular and molecular mechanisms *Cell Biochem Biophys*., 43:167-88

Rizvi *et al*. in a prospective nonrandomized study noted that the respiratory rate decreased from 33.2±5.3/min to 22.0±3.5 ($p<0.001$), heart rate also decreased from 113.2±7.6/min to 90.2±11.9 ($p<0.001$). A rise in pH was observed from 7.2±0.09 to 7.4±0.06 ($p>0.41$ NS), PaCO2 decreased from 76.5±15.5 to 51 .3±1 0.5 ($p<0.001$). PaO2 also increased from 52.1±14.3 to 62.9±11.5 ($p<0.01$). The mean hospital stay was shorter i.e., 10.6±5.6 days and the hospital mortality rate 11.1% and came to a conclusion that BiPAP is useful in patients with acute exacerbations of COPD.

Rocai Wagner PD. 1994. Principles and information content of the multiple inert gas elimination technique. *Thorax*, 49:815

Rodriguez-Roisin R. 2000. Toward a consensus definition for COPD exacerbations. *Chest*, 117:398S-401S.

Roughton FJW. and Forster RE. 1957. Relative importance of diffusion and chemical reaction rates determining rate of exchange of gases in the human lung with special reference to true diffusing capacity of pulmonary membrane and volume of blood in the lung capillaries. *J Appl Physiol*., 11:290-302.

Saetta M, Turato G, Maestrelli P, Mapp CE, Fabbri LM. 2001. Cellular and structural bases of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*., 163:1304–1309.

Schonhofer B, Sonneborn M, Haidl P, *et al*. 1997. Comparison of two different modes of noninvasive mechanical ventilation in chronic respiratory failure: volume versus pressure controlled devices. *Eur Respir J*., 10:184–91.

Sethi S, Maloney J, Grove L, Wrona C, Berenson CS. 2006. Airway inflammation and bronchial bacterial colonization in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*., 173:991–998.

Simonds AK. Equipment In: Simonds AK, ed. 1996. Non-invasive respiratory support. London: Chapman and Hall, 16–37.

Smith IE. and Shneerson JM. 1996. A Laboratory comparison of four positive pressure ventilators used in the home. *Eur Respir J*., 9:2410–5.

Soo hoo *et al*, 1994. in a prospective study, found that NIV is successful in 50% cases and those successful patients were able to adopt more rapidly to nasal mask and ventilator, with greater and more rapid reduction in $PaCO_2$, correction of pH and reduction in respiratory rate, (*Crit Care Med*., 22:1253-61)

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

Statement ATS. 2010. Standard for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*., 152:S78-S120.

Stoller JK, Panos RJ, Krachman S, Doherty DE, 2010. Oxygen therapy for patients with COPD: current evidence and the long-term oxygen treatment trial. *Chest*, 138:179-87

Trupin L Earnest G San Pedro M *et al.* 2003. The occupational burden of chronic obstructive pulmonary disease, *Eur RespirJ*., 22:462-9

Vitacca M, Rubini F, Foglio K, *et al*. 1993. Non-invasive modalities of positive pressure ventilation improve the outcome of acute exacerbations in COLD patients. *Intensive Care Med*., 19:450–5.

Wagner PD Laravaso RB, ULI, RR, West JB, 1974. Continuous distribution of V/Q ratios in normal subjects braeathing air and 100% O_2. *J Clin Invest*, 54:54-68

West JB, Dollery CT, Naimark A. 1964. Distribution of blood flow in isolated lung: Relation to vascular and alveolar pressures. *J Appl Physiol*., 19:713-724

William Macnee. 2000. Chronic bronchitis and emphysema. Chapter 23. In: Anthony Seaton, Douglas Seaton, editors. Crofton and Douglas's respiratory disease, 5th edition. Thomson Press India, 1:616-679.

Wood *et al*. showed a non significant trend towards a worsened survival and increased mortality in those given NIPPV and reported that it might be due to failure to move to ETI in a timely fashion.

Woodhead M, Blasi F, Ewig S, *et al*. 2005. Guidelines for the management of adult lower respiratory tract infections. *Eur Respir J*., 26:1138-80.

World Health Report. Geneva: World Health Organization Available from URL: http://www.who.int/whr/2000/ engstatistics.htm; 2000.

Younes M. 1992. Proportional assist ventilation: a new approach to ventilatory support. *Am Rev Respir Dis*., 145:114–20.

****