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The Use of Non-Invasive Positive Pressure Ventilator (NIPPV) and Conventional Medical Care to Treat Respiratory Failure Arising from Acute Exacerbation of COPD: A Systematic Review

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Abstract

Chronic obstructive pulmonary disease (COPD) is the third leading cause of mortality in the United States, costing the healthcare industry more than $40 billion. This mortality rate, as a result of COPD, increases each year. This paper is a systematic review of the effectiveness of non-invasive positive pressure ventilation (NIPPV) versus invasive mechanical ventilation (IMV) in treating patients admitted in the intensive care unit (ICU) due to exacerbated COPD.

Failure rate, respiratory ICU mortality rate, and length of ICU stay were compared between the two modes of treatments for exacerbated COPD. Four studies met the review inclusion criteria. Based on the four studies included in the review, NIPPV is recommended by the authors since treatment outcomes based on mortality rate, failure rate, and length of stay in the ICU resulted in lower mortality, lower length of stay in the ICU, and a higher success rate as a treatment mode for exacerbated COPD.

Keywords: COPD, NIPPV, Non-Invasive Ventilation, Mechanical Ventilation.

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1 Introduction

Chronic obstructive pulmonary disease (COPD) is also known as chronic obstructive lung disease. COPD is an umbrella term for a number of lung diseases wherein the exchange of respiratory gases is ineffective due to abnormalities in the airways and air sacs. COPD includes emphysema, chronic bronchitis, and chronic asthma. The airways and air sacs of the lungs are destroyed or partially obstructed depending on how serious the disease is or how advanced it is already. As a result of the obstruction or destruction of the airways and air sacs, persons with COPD experience labored breathing. Obstruction comes from the environment like dust and pollution, as well as, from smoking. Quitting from the habit of smoking will alleviate the symptoms even if the lungs are permanently damaged [1].

Inside the lungs are branches that contain tiny air sacs called alveoli where the actual exchange of oxygen and carbon take place. In healthy people, the alveoli are clear and respond well to the inhalation and exhalation pattern. But in people with COPD, the air sacs are weak and floppy, losing their roundness due to the obstruction. The walls inside the sacs have either been inflamed or destroyed [1].

As COPD progresses over a long period of time, the obstruction becomes thicker. The patient's breathing becomes more labored and difficult. A person with chronic bronchitis has airways that are inflamed while the cells are producing mucus. s a result, the patient coughs and breathes with difficulty. In emphysema, the walls between the air sacs are destroyed, causing larger but fewer sacs to form. The damage from COPD could be permanent and may lead to respiratory failure and admission to the ICU in cases where the patients' lives are already at stake.

The conventional treatment upon admission to the ICU for exacerbated COPD involves the use of bronchodilators, oxygenation, and antibiotics to make the person's respiratory process continue. The conventional treatment is to provide patients with continuous oxygenation while treating the root of the exacerbated COPD. In cases where patients do not respond to the first line of intervention, invasive ventilation is administered so that the respiratory functioning is restored. Invasive ventilation (IV) involves tracheal intubation and assisted ventilation, which are associated with high morbidity and difficulty of weaning from ventilation. Aside from this, invasive procedure is associated with many other complications, like pneumonia and damage to local tissues, among others. The complications are usually the reasons why patients stay longer in the ICU. Reference [2] noted the instances when complications from the use of IV resulted to mortality in the ICU.

In light of these complications and adverse conditions, non-invasive positive pressure ventilation (NIPPV) was developed as an alternative treatment for patients with respiratory failure due to exacerbated COPD. NIPPV involves the use of full facial or nasal masks wherein a mixture of air and oxygen are delivered to the patient. In earlier ventilators, negative pressure was delivered from outside the thorax. This procedure was effective for cases such as neuromuscular disorders or chest wall abnormalities but not with COPD. Negative pressure had no benefits for COPD [3].

NIPPV has been increasingly used in the respiratory ICU as a first-line of treatment or an adjunct in managing patients with exacerbated COPD. The recent increase in the use of NIPPV for cases involving the failure of respiratory functions was due to how patients are able to tolerate nasal masks. The main advantages of NIPPV are, however, related to the prevention of morbidity and the lower cost of treatment. Although NIPPV has become increasingly popular in the recent past, it cannot be administered to all patients who suffer

from respiratory failure. There are certain conditions wherein IV is still used. Some situations wherein NIPPV is not ideal are for those patients who are not cooperative, massively obese, and with high aspiration risk, among others [4]. Uncooperative patients cannot survive on NIPPV because they may likely take off the mask. There are also those who experience adverse reactions to their facial tissues in reaction to the wearing of masks.

Many studies have shown the benefits of NIPPV in acute exacerbation of COPD. These include lowering the intubation rate by 66%, lower mortality rate (average is 9%), and significant decreases in ICU stay and hospital stay. NIPPV also preserves some functions like feeding, speech, coughing, and swallowing. Despite its advantages and benefits, NIPPV cannot be used at random. Some studies showed that patients who are very ill need intubation immediately upon admission [4].

The purpose of this study was to determine, through a systematic review of the literature, if NIPPV is a safe and effective mode of treating acute respiratory failure arising from acute exacerbation of COPD and if NIPPV is more effective than mechanical ventilation and can reduce the need for invasive tracheostomy in patients suffering from acute exacerbation of COPD. The determination of whether NIPPV is a safe and effective mode of treating acute respiratory failure arising from acute exacerbation of COPD was assessed in specific areas, such as mortality rate, failure rate, ICU length of stay, and the presence of complications. It was hypothesized that NIPPV was safe and more effective than invasive treatment.

1.1 Study Design

The study design was a systematic review of the literature. The reasons for performing such a systematic review were twofold: (1) to search all the available literature and reduce the chances of any bias, and (2) to perform in-depth assessment of the studies to analyze the quality.

1.2 Literature Search Methods

Four databases were searched for information on NIPPV and invasive mechanical ventilation and their application in acute exacerbation of COPD. These were Pubmed, Cochrane, CINAHL and OVID. Journal articles that concentrated on using NIPPV and invasive mechanical ventilation in cases of respiratory failure from acute exacerbation of COPD were reviewed and analyzed for the aforementioned issues. The common search terms that were utilized in the study included “COPD”, “NIPPV”, “Non-Invasive Ventilation” and “Ventilation” in combination.

1.3 Study Criteria

The criteria of the study was very critical for ensuring that the quality of the literature review was high and the expected results obtained were valid and reliable for the given population. As much as possible, homogeneity of the study was maintained by choosing articles with research of similar settings, design, intervention, and characteristics of the subjects.

To ensure quality of the studies, the PEDro rating scale was utilized. The studies that have utilized NIPPV and/or mechanical ventilation in humans only were taken into account. All non-English studies were included as long as they were able to provide an English abstract to enable search and provision of primary information. The types of articles that were included
were clinical trials, randomized controlled trials (RCT's) and meta-analyses. Articles involving all age groups were included.
All studies that were analyzed during the systematic review compared the effectiveness, safety and the application of NIPPV and invasive mechanical ventilation in the treatment of acute respiratory failure following acute exacerbation of COPD. Several aspects of the participants (as the health outcomes) were analyzed by the researchers: mortality rate, failure rate, and ICU length of stay. Mortality rate refers to the number of deaths per treatment mode. Failure rate refers to the number of patients who had to transfer to another mode of treatment. ICU length of stay is the number of days that a patient spent in the ICU.

1.4 Data Analysis

A systematic review of literature was used to gather relevant data concerning the efficacy of NIPPV compared to invasive mechanical ventilation. All studies concentrated on the use of NIPPV and/or invasive mechanical ventilation.To give the readers better perception of how NIPPV is compared to mechanical ventilation, tables were used since visuals were helpful to determine which treatment or treatments work better for patients suffering from exacerbated COPD. Conclusions were inferred from the data gathered. The inferences drawn explained why one intervention is better, according to the literature reviewed, than another when it comes to exacerbated COPD treatment.

2 Main Results

2.1 Study Selection

The search of electronic databases yielded a total of 78 studies (see Figure 1). After removing 19 duplicates, there were 59 studies left. Of the 59 studies, 39 were not selected because they did not meet the inclusion criteria. The remaining 20 studies were assessed by reading the full-text, which resulted in four studies remaining for inclusion in the systematic review. Although the other studies used either mechanical ventilation (MV) or NIPPV, they were not applied to exacerbated COPD cases.
The four studies included in the review were located in different countries as summarized in Table 1. Reference [5] conducted their study in Italy with 98 patients; reference [6] was in Croatia with 156 patients; reference [7] was in Singapore with 102 patients; and reference [8] was done in India with 42 patients. Of the four studies, only reference [7] randomly assigned patients to either NIPPV or invasive mechanical ventilation while the others decided on either one of the treatments depending on the needs of the patients. For instance, reference [5] established predefined criteria for receiving treatment while reference [8] used NIPPV as a first-line of treatment. In terms of quality assessment, each criterion met under the PEDro scale received one point.

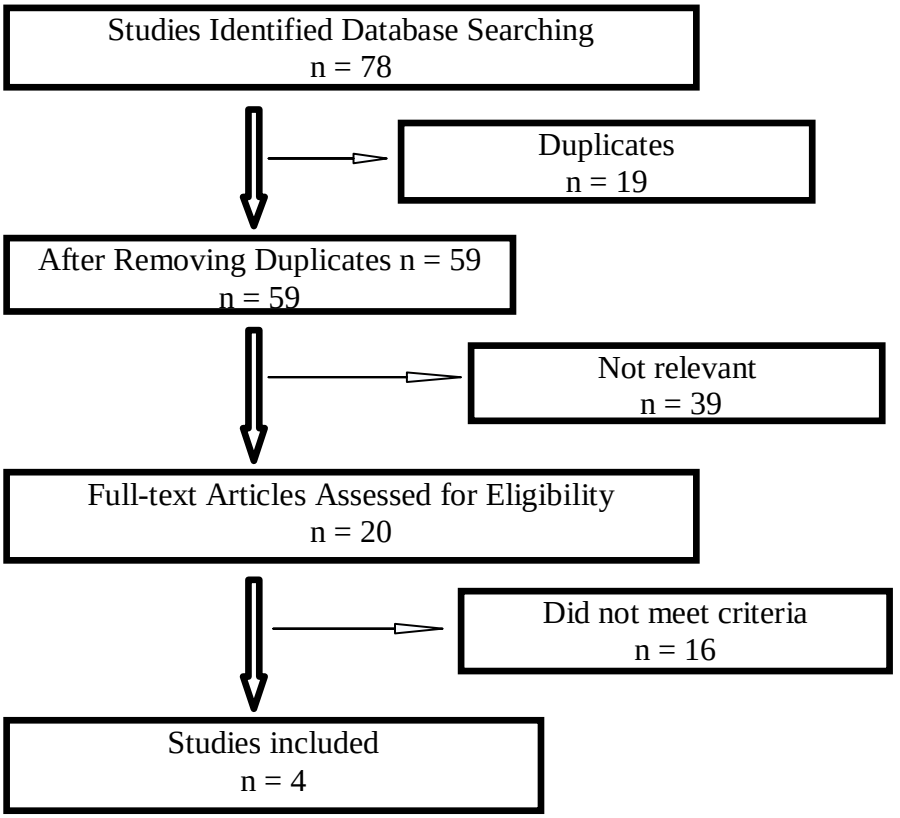

Figure 1: Study Selection Process

There were a total of 11 criteria wherein a score of 6-11 was considered acceptable. Of the four, reference [6] received 9 points, the highest PEDro score for quality assessment among the studies in this systematic review. The other three studies all received six points since they lacked the blinding aspect.

Table 1: General Characteristics of Studies

Studies	Population	Country	Setting	PEDro Score
Reference [5]	98	Italy	RICU	6
Reference [6]	156	Croatia	RICU	9
Reference [7]	102	Singapore	RICU	6
Reference [8]	42	India	RICU	6

Note: RICU = Respiratory ICU. PEDro scores range from 1-11. Acceptable scores

2.2 Study Characteristics

Table 2 outlines the characteristics of the studies included in the present review. They were published between 2004 and 2009. The number of subjects for all studies ranged from 42 to 216. All studies, except reference [7] showed statistically significant differences (p = 0.01 - 0.03) in the failure rate, which is between the NIPPV and MV treatments.

Table 2: Study Characteristics

Studies	INT	n	FR	RICUM	LRICU	Complications	p-values (failure rate)
Reference [5]	NIPPV	79	25.3	10.1	7-13	Intolerance to mask ventilation	0.01
	MV	19	26.0	26.0	10-20	Upper airway obstruction Large air leaks	
Reference [6]	NIPPV	78	39.0	5.1	1-5	Facial damage Nasal damage Gastric distension Aspiration risk	0.01
	MV	78	51.0	6.4	1-9	Difficulty in weaning Pneumonia Tracheal injury	
Reference [7]	NIPPV	44	14.2	0	1-2	None	0.20
	MV	58	15.5	0	1-8	None	
Reference [8]	NIPPV	39	4.4	0	1-2	None	0.03
	MV	3	100.0	100	1-4	Airway Trauma Pneumonia	

*Note: Values for FR and RICUM are in %; INT = Intervention; n = number of samples; FR = failure rate; RICUM = respiratory ICU mortality rate; LRICU = length of stay in RICU

The mortality rate for those who had been admitted to the respiratory intensive care unit was higher among all studies for patients receiving the traditional treatment for exacerbated COPD, with reference [8] showing a 100% mortality rate. Wow! The high percentage was the result of only three patients receiving MV treatments and all three died in the ICU. The higher mortality rates for MV were likely associated with several complications associated with the treatment, like upper airway obstruction, tracheal injury, and ventilator-associated pneumonia. NIPPV was also associated with several types of complications but they were less serious compared to MV.

All studies showed that the length of stay in the ICU for patients who suffered from respiratory failure due to exacerbated COPD was lowered when the first line of treatment was NIPPV (2-13 days) compared to MV (4-15 days).

Reference [5] investigated the role of NIPPV on treating exacerbated COPD during an 18-month period in a specialized respiratory intensive care unit in a university-affiliated hospital. There were 258 patients included in the study. The researchers had predefined criteria on when to use non-invasive ventilation and the invasive treatment. The emphasis of the study was to find out if NIPPV was enough for saving patients' lives during

episodes of exacerbated COPD at the ICU. Of the 258 patients, not everyone qualified because their illnesses were not COPD. Ninety-eight were analyzed (79 NIPPV and 19 invasive treatments).

The rate of mortality and the length of stay in the respiratory ICU unit were substantially lower for NIPPV at 10.1% (mortality) and 7-13 days (length of stay) compared with invasive treatment of 26.0% (mortality) and 10-20 days (length of stay). However, reference [5] failed to report the failure rate for invasive treatment. This is partly because the researchers wanted to establish if NIPPV could be used as a first line of treatment. Those patients who did not respond to NIPPV (25.3%) were transferred to invasive treatment. Both treatments showed adverse reactions but the use of NIPPV reported a minor discomfort to the use of masks. On the other hand, invasive treatment was associated with two serious complications: upper airway obstruction and large air leaks. These results are summarized in Table 2. Further, the p value ($p = .01$) showed that the failure rate between NIPPV and invasive treatment was statistically significant, which meant that NIPPV had been more successful in treating patients.

Reference [6] compared the efficacy of NIPPV and the invasive method in a randomized trial of 156 patients for a period of 36 months in a multidisciplinary intensive care unit. The researchers were able to confirm the efficacy of NIPPV over the intensive method, particularly for the early stages of COPD, but did not conclude that NIPPV was superior when the illness is already exacerbated. The patients were in different stages of need: some were already in the ICU; others were in a coma; and there were those who were in shock. The patients' responses to treatments were measured after one hour, four hours, 24 hours, and 48 hours after they were admitted. They were also evaluated based on outcomes.

The results of this study showed that NIPPV was associated with better outcomes than MV. Both groups had equal number of patients ($n = 78$). In terms of failure rate, NIPPV registered a failure rate of 30% ($n = 30$) compared to the invasive method at 40% ($n = 51$). Those patients who did not respond to NIPPV and were transferred to invasive treatment were those who suffered from respiratory arrest, lost their consciousness, or those that required sedation due to severe agitation of psychomotor functions. The success of a treatment mode is considered if the patient exercises normal respiration for at least 48 hours after the treatment was withdrawn.

The number of days that patients stayed in the ICU also varied with NIPPV-supported patients spending up to five days in the unit compared to the use of invasive treatment where patients stayed up to nine days. NIPPV resulted in less adverse effects compared with the adverse effects in the invasive treatment. The p value ($p = .01$) in the failure rate was considered statistically significant. NIPPV was considered more effective.

Reference [8] conducted their study on the use of NIPPV and invasive treatment on 248 patients during an 18-month period. The study was not purely on COPD but included other ailments. There were 39 cases for NIPPV and 3 for invasive treatment, which were given after the patients suffered from acute respiratory failure. The baseline characteristics of the patients were established, including the partial pressure of oxygen in the arterial blood and the partial pressure of carbon dioxide in the arterial blood. There were 18 patients with co-morbid illnesses along with COPD.

NIPPV was successful in 71.4% of the subjects with a failure rate of 4.4% using a .05 confidence level. Unfortunately, those three patients who were transferred to the invasive method all died. There was no discussion in the paper whether or not those patients would

have survived if they were immediately given endotracheal intubation and invasive ventilation rather than wait for them to suffer from respiratory failure before a transfer to the invasive treatment. The number of days in the ICU for both treatments in the reference [8] study was the lowest among the four studies included in the review. Those given NIPPV stayed up to two days in the ICU before their conditions stabilized, making it safe to transfer them to the recovery units. Patients given invasive treatment stayed up to four days in the ICU before expiring. In terms of complications, the NIPPV mode of treatment showed no adverse effects while the invasive treatment resulted to airway trauma and pneumonia, ultimately leading to death. The p-value ($p = .03$) for failure was statistically significant.

Reference [7] studied 102 admissions to the intensive care unit due to exacerbated COPD over a four-year period. There were 44 patients who were administered with NIPPV while there 58 who were given invasive treatment. This study, however, was more focused on the factors that caused NIPPV to fail on four patients. These factors were identified as serum total protein and surrogate markers for nutrition, which were also associated with hospital mortality.

Mortality in Table 2 was listed as 0 because it referred to deaths that occurred in the ICU while the patient was getting treatment for exacerbated COPD using either the non-invasive or invasive mode of treatment. There were, however, hospital deaths (18%) for 18 patients due to other factors. These deaths may not be considered as treatment-related because they occurred after the patients were weaned and taken out of the intensive care unit.

There were patients (16%) who were successfully weaned from the invasive method and transferred to NIPPV. However, there were nine cases that required re-intubation after weaning. The failure rate of NIPPV was 14.2% compared to the invasive method at 15.5%. This rate was not statistically significant based on the p-value ($p = .20$). On the number of days stayed in the ICU, NIPPV-treated patients spent up to two days in intensive care compared to the four days stay of patients who received invasive treatment.

The patients who received NIPPV also did not suffer from any complications. Those who needed intubation were not considered as part of the adverse reactions since the re-intubations occurred after they were weaned from their ventilators.

3 Discussion

In this systematic review, as shown in the outcomes of the four studies based on mortality, failure rate, length of stay in the ICU, and complications that NIPPV has many advantages and benefits to patients suffering from respiratory failure due to the exacerbation of chronic obstructive pulmonary disease. The overall success of NIPPV over the rate of failure suggests this mode as one of the first-lines of treatment in treating respiratory failure in patients with exacerbated COPD.

NIPPV has been suggested by many other studies as the better choice during admission to the ICU or the respiratory ward in some hospitals because of how more patients are able to tolerate it better than IV given that they are only required to use face masks. Of the four studies, only reference [5] showed that NIPPV had a higher failure rate compared to invasive treatment (25.2 vs 23.4). In this study, the lower NIPPV success rate may have been due to some patients who were not able to tolerate mask ventilation. The three other cases were consistent in showing that NIPPV was the better mode of treatment because

there was lower number of deaths, lower failure rate, lesser number of days in the ICU, and less serious complications.

Although NIPPV has been shown to be beneficial to patients with exacerbated COPD, there is no guarantee that this mode of treatment is going to work for every person with respiratory failure. Reference [9] outlines several conditions that should be met in order for NIPPV to become successful. This includes having the patient's pH level > 7.25. It is important that those who are in the respiratory ICU are able to quickly assess the patient's condition so that the appropriate treatment is given. Three of the studies in this review, references [5, 7 and 8], have determined the right modes of treatment for the patients using certain metrics, including pH level, respiratory rate and the Glasgow Coma Score.

References [5 and 8] did not randomize the treatment modes but instead used the normal assessment procedures, which resulted to the differences in the number of patients using NIPPV and the invasive form of treatment. This assessment method maximized the benefits for each patient because the mode of delivery for ventilation was chosen based on needs.

In reference [6] case, the researchers had used a randomized trial method for selecting which patients were to undergo NIPPV or IV. Not surprisingly, this study showed the highest failure rate (39%) of NIPPV compared to the other studies since patient characteristics were not the basis for the kind of mode of treatment (as shown in table 2). A patient with a low pH level could have found himself/herself under the NIPPV group even if other medical practitioners would have placed him/her under endotracheal intubation. At the same time, a patient who would have been fine with NIPPV could have found himself/herself intubated even when there was no need to do so. As a result, reference [6] showed the most number of complications compared to the three other reviewed studies including aspiration risk (which is rare in others) and tracheal injury. The randomized trial methodology that reference [6] used for comparing NIPPV and IV may have put patients' lives at further risk because it could have caused the death of patients who needed intubation. The researchers reported a mean pH of <7.30, a range that could go below the safe level for NIPPV. The researchers further stated that the intubation need of non-invasive mechanical ventilator dependent patients were recorded, which suggested that they were aware of the risk they were putting the patients in by doing the randomized trial. However, reference [10] also conducted a randomized trial and found that NIPPV and IV were equivalent in terms of efficacy in improving gas exchange during the patient's stay in the ICU. In reference [2] systematic review, the trials were randomized but the comparison was made on NIPPV and the conventional treatment, removing any problems that would arise with the need for IV.

It is notable that in all four studies, the lengths of stay in the ICU were all significantly decreased. In reference [5] the difference between NIPPV and IV was short but the non-invasive delivery still made patients come out of the ICU faster than those who were in IV. The only reported complication in this study was that of the patients' intolerance compared with the more serious upper airway obstruction and large air leaks for IV. As discussed above, reference [6] had the most number of complications for both modes of treatment. In NIPPV, complications included facial and nasal damage, gastric distension, and aspiration risk; the complications for IV included difficulty in weaning, pneumonia, and tracheal injury. It was not clear in the study if the patients were suffering from more serious conditions, which could also account for the higher failure rates.

Among all of the studies, reference [8] study was singular in the sense that the researchers used NIPPV as the first line of treatment rather than assess the needs of the patients before deciding if invasive or non-invasive mode of treatment was more appropriate. The only mortality rates for COPD in this study were those who were transferred to invasive ventilation after NIPPV did not work. It could be argued that the deaths (n = 3; 100%) of all of those who were transferred to intubation was the result of administering NIPPV when the patients' conditions were more serious than the others. They failed to respond to NIPPV within one hour while normally, patients with acidosis would show improvements within one hour. But these patients' pH remained low after given NIPPV for one hour.

4 Conclusion

NIPPV in all four studies appeared to be the more superior mode of treatment for respiratory failure as a result of exacerbated COPD. NIPPV can reduce mortality rate, failure rate, and length of ICU stay provided that the patients' conditions were not on a level that required intubation.

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