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The Effect of Non-Invasive Positive Pressure Ventilation (NPPV) via a Face Mask vs. Conventional Mechanical Ventilation (CMV) via Endotracheal Intubation (ETI) in Adult Patients with Acute Respiratory Failure (ARF): A Systematic Review of the Literature

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The Effect of Non-Invasive Positive Pressure Ventilation (NPPV) via a Face Mask vs. Conventional Mechanical Ventilation (CMV) via Endotracheal Intubation (ETI) in Adult Patients with Acute Respiratory Failure (ARF): A Systematic Review of the Literature

Abstract

Background: Traditionally, conventional mechanical ventilation (CMV) and intubation was the preferred route commonly employed by physicians to support patients with acute respiratory failure. However, mechanical ventilation via endotracheal intubation (ETI) may lead to injury of the trachea and may also result in ventilator-associated nosocomial pneumonia. As a consequence, there has been growing interest in NPPV support because of its promising role in avoiding intubation and associated complications.

Purpose: To assess the effectiveness of non-invasive positive pressure ventilation (NPPV) vs. conventional mechanical ventilation (CMV) on the need for intubation, length of hospital ICU stay, mortality rates, and complications on adult patients with acute respiratory failure (ARF).

Study Design: To select for randomized control trials (RCT), randomized prospective studies, only trials done in the ICU, trials that compare NPPV vs. CMV, articles with a Jadad score of two or greater.

Methods: A multi-method approach was used to identify relevant research for this review. A computerized exhaustive literature search using the following search engines: Medline, Ovid, Cinahl, and Cochrane from the years 1990 to 2009. Bibliographies of all selected articles and review articles that included information on NPPV and CMV were reviewed also. Included were English language studies on adult subjects. Once irrelevant studies had been excluded individual review of the titles and abstracts were conducted. Searches were run numerous times with different combinations of key terms to eliminate irrelevant materials that didn't address the clinical question and selected PICO.

Results: The three included studies are all randomized studies comparing the effectiveness of NPPV via a face mask vs. CMV via ETI in hospital ICU setting. These three studies are all in agreement on the effect of NPPV reducing the need for intubation with p-values that are statistically significant. Results of hospital ICU length of stay, mortality rates and complications, there exists apparent inconsistencies among the studies, for example, in the study by Honrubia et al and Conti et al, both indicated findings of non-significant differences between NPPV or CMV in hospital length of ICU stay, mortality, and complications. However, in the study by Antonelli et al, the NPPV group had statistically significant findings of decreased length of ICU stay with $p=0.002$, and fewer complications with $p=0.02$ respectively.

Conclusion: There is promising evidence in the literature supporting the use of NPPV in adult patients with ARF especially those with acute exacerbation of COPD. At present, with the limited studies published in "randomized controlled trials", addressing the clinical question, despite promising data from uncontrolled studies, it is clearly necessary to pursue further information in the form of randomized, controlled trials to definitively assess the effectiveness and safety of noninvasive positive pressure ventilation in the setting of acute respiratory failure due to other causes as well.

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The Effect of Non-Invasive Positive Pressure Ventilation (NPPV) via a Face Mask vs. Conventional Mechanical Ventilation (CMV) via Endotracheal Intubation (ETI) in Adult Patients with Acute Respiratory Failure (ARF): A Systematic Review of the Literature

My T. Ly



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School of Physician Assistant Studies

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Faculty Advisor: Rob Rosenow Pharm D

Clinical Graduate Project Coordinators: Rob Rosenow Pharm D, OD & Annjanette Sommers MS, PAC

Biography

My Ly was born in Qui Nhon, Vietnam. Later, she immigrated with her family to Grand Rapids, Michigan in 1985. She considers herself to be multicultural and is proud to be of Chinese ethnicity. My, completed her undergraduate degree in sociology, specializing in ethnic groups and healthcare in geriatric populations at the University of Michigan in Ann Arbor. Post graduation, she was employed by the university's hospital, working on the Dermatology/Plastic surgery unit. Later, she transferred to the Trauma/Burn unit and worked as an ICU technician for almost four years. She feels privileged to have had a valuable work experience at the University of Michigan Medical Center, Trauma-Burn Unit. From both the trauma and burn populations, she has gained experience in emergency code situations, medical terminologies, medical procedures, and experience with direct patient care from pediatrics to geriatrics. In her healthcare experiences, she has found that her services both great and small have been personally rewarding.

My Ly had aspirations to become a physician assistant; therefore, she applied and was accepted to Pacific University, physician assistant (PA) program. In May of 2007, she started PA school and in August of 2009, she graduates with honors.

Her hope is to continue serving patients on a more advanced level, particularly, helping those who are less privileged and under served.

Abstract

Background: Traditionally, conventional mechanical ventilation (CMV) and intubation was the preferred route commonly employed by physicians to support patients with acute respiratory failure. However, mechanical ventilation via endotracheal intubation (ETI) may lead to injury of the trachea and may also result in ventilator-associated nosocomial pneumonia. As a consequence, there has been growing interest in NPPV support because of its promising role in avoiding intubation and associated complications.

Purpose: To assess the effectiveness of non-invasive positive pressure ventilation (NPPV) vs. conventional mechanical ventilation (CMV) on the need for intubation, length of hospital ICU stay, mortality rates, and complications on adult patients with acute respiratory failure (ARF).

Study Design: To select for randomize control trials (RCT), randomized prospective studies, only trials done in the ICU, trials that compare NPPV vs. CMV, articles with a Jadad score of two or greater.

- 1) Population: adult patients with acute respiratory failure (ARF) in the Intensive care unit (ICU)
- 2) Intervention: the use of non-invasive positive pressure ventilation (NPPV)
- 3) Comparison: to conventional mechanical ventilation (CMV)
- 4) Outcome: need for intubation, length of ICU stay, mortality rate, and complications

Methods: A multi-method approach was used to identify relevant research for this review. A computerized exhaustive literature search using the following search engines: Medline, Ovid, Cinahl, and Cochrane from the years 1990 to 2009. Bibliographies of all selected articles and review articles that included information on NPPV and CMV were reviewed also. Included were English language studies on adult subjects. Once irrelevant studies had been excluded individual review of the titles and abstracts were conducted. Searches were run numerous times with different combinations of key terms to eliminate irrelevant materials that didn't address the clinical question and selected PICO.

Results: The three included studies are all randomized studies comparing the effectiveness of NPPV via a face mask vs. CMV via ETI in hospital ICU setting. These three studies are all in agreement on the effect of NPPV reducing the need for intubation with p-values that are statistically significant. Results of hospital ICU length of stay, mortality rates and complications, there exists apparent inconsistencies among the studies, for example, in the study by Honrubia et al and Conti et al, both indicated findings of non-significant differences between NPPV or CMV in hospital length of ICU stay, mortality, and complications. However, in the study by Antonelli et al, the NPPV group had statistically significant findings of decreased length of ICU stay with $p=0.002$, and fewer complications with $p=0.02$ respectively.

Conclusion: There is promising evidence in the literature supporting the use of NPPV in adult patients with ARF especially those with acute exacerbation of COPD. At present, with the limited studies published in "randomized controlled trials", addressing the clinical question, despite promising data from uncontrolled studies, it is clearly necessary to pursue further information in the form of randomized, controlled trials to definitively assess the effectiveness and safety of noninvasive positive pressure ventilation in the setting of acute respiratory failure due to other causes as well.

Keywords: The following search terms were used: acute respiratory failure, BiPAP, conventional mechanical ventilation, intubation, noninvasive mechanical ventilation, and randomized control trial.

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Table I: Summary Matrix

Table II: Indications and contraindications for NPPV

List of Abbreviations

ARF.....	Acute respiratory failure
BCV.....	Bi-phasic cuirass ventilation
BiPAP.....	Bi-level positive airway pressure
CMV.....	Conventional mechanical ventilation
COPD.....	Chronic obstructive pulmonary disease
CPAP.....	Continuous positive airway pressure
CRF.....	Chronic respiratory failure
EPAP.....	Expiratory positive airway pressure
FiO ₂	Fractional inspired oxygen
ICU.....	Intensive care unit
IPAP.....	Inspiratory positive airway pressure
NPPV.....	Non-invasive positive pressure ventilation
NIMV.....	Non-invasive mechanical ventilation
NIV.....	Non-invasive ventilation
PaCO ₂	Arterial carbon dioxide tension
PaO ₂	Arterial oxygen tension
PEEP.....	Positive end expiratory pressure
PICO.....	Population, Intervention, Comparison, and Outcome
RCT.....	Randomized controlled trial

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Introduction

The purpose of this systematic review is to assess the effectiveness of non-invasive positive pressure ventilation (NPPV) vs. conventional mechanical ventilation (CMV) on the need for intubation, length of hospital ICU stay, and mortality rates on adult patients with acute respiratory failure (ARF). Respiratory failure (RF) is a condition in which the respiratory system fails in one or both of its gas-exchanging functions; oxygenation of mixed venous blood and elimination of carbon dioxide.¹ The respiratory system consists of two parts: (a) the gas-exchanging organ (lung) and (b) the ventilatory pump; chest wall, respiratory muscles, respiratory controllers, and the pathways that connect the central controllers with the respiratory muscles. Failure of the gas-exchanging organ causes type I RF, this is characterized by hypoxemia with normocapnia or hypocapnia. Failure of the pump, causes type II RF (ventilatory failure) the hallmark of which is hypercapnia.² The distinction between type I and II RF must not be viewed as rigid, since (a) type I failure may be complicated by respiratory pump failure and hypercapnia, and (b) type II failure may be complicated by severe hypoxemia due to secondary pulmonary parenchymal processes (eg, pneumonia, atelectasis, pulmonary edema), or vascular disorders like pulmonary embolism.¹ In ARF, regardless of the presence or absence of hypercapnia, treatment of hypoxemia is the first priority especially in patients with type II RF, because hypoxemia kills quickly, while hypercapnia kills more slowly. At the same time, when appropriate, measures to improve alveolar ventilation should be taken.³ Type III, or perioperative RF, is predominantly the result of atelectasis, although fluid overload, bronchospasm, airway secretions, and preexisting lung disease can also contribute. The end result may be hypoxemic respiratory failure with increased shunt, ventilatory failure, or both. Type IV RF is seen in patients who are in shock or in hypoperfusion states, without associated pulmonary problems. In a way it is a subtype of type II RF, resulting from greatly increased work of

breathing in conjunction with reduced perfusion, and therefore oxygen delivery, by the diaphragm and other respiratory muscles.

Respiratory failure is further classified as acute RF (ARF) and chronic RF (CRF). Respiratory failure in its acute form is a direct threat to life, which can develop within minutes or hours, while, in its chronic form it can affect both the quality of life and the expected survival of involved patients. Critical care can be lifesaving for patients with ARF while interventions incorporating medical technology can ameliorate the consequences of CRF and its exacerbations. This review will only be focusing on acute respiratory failure.

Data on the incidence of ARF in the community are hard to come by. The disorder may be caused by a multitude of underlying disease entities, may have widely varying severity, prognosis, varying treatment strategies, and may be treated in a great variety of settings: emergency department, medical unit, and intensive care unit. According to Conti et al⁴ ARF was defined as the presence of all the following criteria: a) respiratory acidosis with pH values lower than 7.32, b) bicarbonate levels higher than 30mEq/L, c) hypoxemia with PaO₂ values lower than 45 while breathing room air, d) respiratory rate higher than 30 breaths/min, and e) history of worsening dyspnea of less than 2 weeks duration.⁴

Traditionally, conventional mechanical ventilation (CMV) and intubation was the preferred route commonly employed by physicians to support patients with acute respiratory failure. However, endotracheal intubation (ETI) via mechanical ventilation may lead to injury of the pharynx, larynx, and trachea.⁵ Mechanical ventilation via an endotracheal tube may also result in ventilator-associated nosocomial pneumonia.⁵ Other complications include: barotrauma, upper-airway injury, and prolonged ICU and hospital stay. As a consequence, there has been growing interest in non-invasive ventilatory support because of its promising role in avoiding intubation and associated complications.⁶ According to Poponick et al, “over the past decade non-invasive positive pressure ventilation (NPPV) has gained in

popularity".⁷ This term refers to positive pressure ventilation delivered through a noninvasive interface such as a nasal mask, facemask, or nasal plugs, rather than an invasive interface with an endotracheal tube, or tracheostomy.

The use of NPPV to treat patients with ARF may be lifesaving, as it decreases the load on respiratory muscles, changes the pattern of breathing, and results in oxygen treatment without further increasing arterial carbon dioxide tension (PaCO_2), and reverses hypercapnia within 1–4 hours. The application of NPPV to appropriate patients with type 2 RF can avert intubation and has been shown by prior studies to improve survival mainly because of decreased rates of nosocomial infection. Non-invasive positive pressure ventilation should not replace invasive mechanical ventilation in severely compromised patients, but as a measure that if used in a timely fashion can prevent further deterioration of the patient and can avoid intubation altogether.

The use of NPPV is recommended for relaxed, non-combative patients and doesn't generally require sedation. Some complications include gastric distention, aspiration pneumonia, hypotension, and pneumothorax.⁸ For these reasons, NPPV shouldn't be used on patients who have facial traumas or have undergone recent facial surgery, who have excessive secretions for risk of aspiration, are experiencing gastrointestinal bleeding or don't have the ability to protect their own airways. Other complications of NPPV are typically minor and include injury to tissues where the mask makes contact with the skin of the face. This risk is especially true for older patients who typically have friable skin. Indications and contraindications for the application of NPPV in patients with ARF appear in (Table II).

BiPAP can be administered both with nasal and full-face masks. The nasal mask is usually well tolerated because it causes less claustrophobia and discomfort. It allows eating, drinking and expectorating. Conversely, a facial mask is preferable in severe respiratory failure, because dyspneic patients breathe through the mouth in order to bypass resistance in the nasal passages, and mouth

opening during nasal mask ventilation results in air leakage and decreased effectiveness.⁹ Masks are firmly secured with elastic straps to the face in order to avoid air leaks and consequent malfunction.

Tracing back into history, the concept of non-invasive mechanical ventilation first evolved with negative-pressure ventilation. Woillez, in 1876 developed the first workable iron lung. Then, in 1889, Alexander Graham Bell designed and built a prototype of iron lung. On October 12, 1928, Drinker was first to use a non-invasive negative-pressure ventilation machine on a child with respiratory failure resulting in success and popularized the iron lung. The iron lung was in high demands during the polio epidemics of the 1930s, 1940s, and 1950s and was the first non-invasive mechanical ventilator of its time. Then the biphasic cuirass ventilation (BCV) was developed as a refinement of the iron lung ventilator. With time, more refinements from the original iron lung concept took place; during the 1940s to 1960s the intermittent positive pressure breathing (IPPB) machines were developed and used. The newer bi-level positive airway pressure (BiPAP) machine is a descendant of the IPPB and is a form of NPPV now used on patients with ARF.

There are multiple reasons why BiPAP might improve breathing and should be used. It would improve alveolar ventilation and gas exchange, counteract intrinsic positive end expiratory pressure (PEEP), decrease pre-load and after-load, improve lung compliance, and decrease the work of breathing.¹⁰ BiPAP delivers inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) at a different level (IPAP>EPAP) to result in bi-level positive airway pressure ventilation.¹⁰ In another words, BiPAP delivers continuous positive airway pressure (CPAP), but also senses when an inspiratory effort is being made and delivers a higher pressure during inspiration. When flow stops, the pressure returns to the CPAP level. The positive pressure wave during inspirations unloads the diaphragm, which aids in decreasing the work of breathing.

Methods

Search strategy

A multi-method approach was used to identify relevant research for this review. A computerized exhaustive literature search using the following search engines: Medline, Ovid, Cinahl, and Cochrane from the years 1990 to 2009. The following search terms were used: acute respiratory failure, BiPAP, conventional mechanical ventilation, intubation, noninvasive mechanical ventilation, and randomized control trial. Bibliographies of all selected articles and review articles that included information on NPPV and CMV were reviewed also. Included were English language studies on adult subjects. Once irrelevant studies had been excluded individual review of the titles and abstracts were conducted. Searches were run numerous times with different combinations of key terms to eliminate irrelevant materials that didn't address the clinical question and selected PICO.

Study selection

Specific inclusions were 1) Population: adult patients with acute respiratory failure (ARF) in the Intensive care unit (ICU); 2) Intervention: the use of non-invasive positive pressure ventilation (NPPV); 3) Comparison: to conventional mechanical ventilation (CMV); 4) Outcome: need for intubation, length of ICUs stay, mortality rate, and complications. Additional inclusions were to select for randomize control trials (RCT), randomized prospective studies, only trials done in the ICU, trials that compare NPPV vs. CMV, articles with a Jadad score of two or greater.

The following criteria were used to identify articles for exclusion: pediatric patient, animal studies, non-English articles, retrospective studies, sample surveys, observational study, CPAP only studies, studies which included patients who failed intubation and were then placed on BiPAP, studies of patients using NPPV as a weaning modality, studies which did not implement both NPPV and CMV. From a narrowed down pool of 25 articles, after applying the exclusion criteria, three articles met the criteria and addressed the clinical question.

Assessment of quality/Validity

The selected randomized studies were independently reviewed using the Jadad score: A numerical score between 0-5 is assigned as rough measures of study design/reporting quality (0 being weakest and 5 being strongest).¹¹ This number is based on a well-established, validated scale developed by Jadad et al.¹¹ The selected studies earned Jadad score of 2 or greater. A critical appraisal form for articles focusing on therapy was also used to assess the quality and validity of each individual study. The appraisal form was retrieved through Pacific University's blackboard, student resources link.

Results

Study description

The three included studies are all randomized studies comparing the effectiveness of NPPV via a face mask vs. CMV via ETI in hospital ICU setting. These trials were conducted not in the USA, but in countries like Spain, Rome, and Italy. Publications are in English from credited sources like CHEST, Intensive Care Med, and The New England Journal of Medicine. One study was conducted as a randomized multi-center control trial at the ICU of seven different hospitals; the other two studies were conducted at a single center, University hospital, ICU. One study looked at adults with ARF from multiple factors; the second study looked mainly at chronic obstructive pulmonary disease (COPD) patients; and the third study looked at patients with hypoxemic acute respiratory failure.

Outcomes

Honrubia et al¹² conducted a multi-center randomized controlled trial from seven hospital ICUs, screening for patients with ARF from various causes who meet the criteria for mechanical ventilation. Between November 1999 and September 2001, 64 patients were recruited; 31 were assigned to non-invasive mechanical ventilation, and 33 were assigned to CMV.¹² The noninvasive group received ventilation through a face mask in pressure support mode plus, positive end-expiratory pressure ie. BiPAP; the conventional group received ventilation through a tracheal tube.¹²

Honrubia et al¹² reported, in the non-invasive group, 58% of patients were intubated, vs. 100% in the conventional group (RRR, 43%; $p < 0.001$). In the ICU death occurred in 23% and 39% ($p = 0.09$) respectively and complications occurred in 52% and 70% ($p = 0.07$) in the noninvasive and conventional groups. There were no differences in length of hospital stay. The study found a non-significant trend of reduction in ICU and hospital mortality, together with fewer complications during the ICU stay.¹²

Conti et al⁴ conducted a randomized prospective study comparing NPPV with CMV via ETI in a group of patients with COPD who failed standard medical treatment in the emergency ward and met predetermined criteria for ventilatory support. The study was conducted at a university hospital 13-bed general ICU. Between October 1996 and January 1999, all non-intubated COPD patients with ARF caused by acute exacerbation admitted to La Sapienza University Hospital emergency ward, were screened for the study. Patients who meet predetermined criteria for ventilatory support were admitted to the ICU to receive mechanical ventilation. After ICU admission, 49 patients were randomly assigned, 23 patients were randomized to NPPV and 26 to conventional ventilation.

Conti et al⁴ reported that both NPPV and conventional ventilation significantly improved gas exchanges. The two groups were similar in length of ICU stay, in number of days on mechanical ventilation, in overall complications, in ICU mortality, and in hospital mortality. In the NPPV group 11 patients, 48%, avoided intubation, survived, and had a shorter duration of ICU stay than intubated patients. One year following hospital discharge the NPPV group had fewer patients readmitted to the hospital 65% vs. 100% of the conventional group.

Antonelli et al¹³ conducted a prospective randomized trial of 64 patients with hypoxemic acute respiratory failure who meet entry criteria and required mechanical ventilation. The trial is of noninvasive positive-pressure ventilation as compared with endotracheal intubation with conventional mechanical ventilation. Antonelli et al¹³ reported results within the first hour of ventilation, 20 of 32 patients, (62%) of the noninvasive-ventilation group and 15 of 32 patients, (47%) of the conventional

ventilation group had an improved ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen ($\text{PaO}_2:\text{FiO}_2$) ($P=0.21$). Ten patients in the non-invasive ventilation group subsequently required endotracheal intubation. Twenty-three patients in the non-invasive ventilation group, (72%) vs. 17 patients in the conventional ventilation group, (53%) survived their stay in the intensive care unit (odds ratio, 0.4; 95 percent confidence interval, 0.1 to 1.4; $P=0.19$); 22 patients in the non-invasive ventilation group and 16 patients in the conventional ventilation group were discharged from the hospital. More patients in the conventional ventilation group had serious complications than in the noninvasive group (66% vs. 38%, $P=0.02$) and had pneumonia or sinusitis related to the endotracheal tube (31% vs. 3%, $P=0.003$). Among the survivors, patients in the noninvasive ventilation group had shorter periods of ventilation ($P=0.006$) and shorter stays in the intensive care unit ($P=0.002$).

Discussion

This systematic review of the effectiveness of non-invasive positive pressure ventilation vs. conventional mechanical ventilation in patients with acute respiratory failure, suggests that NPPV does have beneficial effects on the survival and decreases the need for endotracheal intubation in the studied population. From those articles reviewed, there are strong indications that patients with acute exacerbation of COPD had the most benefit from NPPV, compared to other causes of ARF. Non-invasive positive pressure ventilation should not replace invasive mechanical ventilation in severely compromised patients, but as a measure that if used in a timely fashion can prevent further deterioration of the patient and can avoid intubation altogether.

These three studies are all in agreement on the effect of NPPV reducing the need for intubation with p-values that are statistically significant. In the study by Honrubia et al, 13 patients out of 31 (42%) in the NPPV group avoided intubation, in the study by Conti et al, 11 of 23 (48%) avoided intubation, and Antonelli et al reported 22 of 32 (69%) successfully avoided intubation. With these studies

averaging around 50% of the participants who were able to avoid intubation and survived their hospital stay is a promising fact.

It is also important to note in a long term study report by Conti et al⁴ on patients with COPD, NPPV is comparable to CMV in terms of survival if NPPV is used after the failure of medical treatment. However, in situations where NPPV fails this does not result in a worse outcome. One year following hospital discharge the NPPV group had fewer patients readmitted to the hospital 65% vs. 100% of the conventional group.

Regarding results of hospital ICU length of stay, mortality rates and complications, there exists apparent inconsistencies among the studies, for example, in the study by Honrubia et al¹² and Conti et al⁴, both indicated findings of non-significant differences between NPPV or CMV in hospital length of ICU stay, mortality, and complications. However, in the study by Antonelli et al¹³ the NPPV group had statistically significant findings of decreased length of ICU stay with $p=0.002$, and fewer complications with $p=0.02$ respectively.

Strength of study

The strength of a quantitative systematic review includes a comprehensive search strategy, objective study selection criteria, and validity assessment of the primary studies.¹⁴ An extensive search using computerized databases, bibliographies of selected and review articles, was conducted to avoid publication and language bias, making it less likely to affect the results. All studies examined in this systematic review, had similar exclusion criteria for contraindications to NPPV, such as: respiratory arrest, hemodynamic instability, facial deformities, high risks for aspiration, septic shock, and/or deep coma. However, there was some variability within the inclusion criteria among studies, but not within the individual study.

To maintain a non-biased assessment of the quality/validity of individualized selected study with focus on the clinical question and PICO. The first article reviewed is by Honrubia et al¹² a RCT with 64

subjects. This study implemented a computer-based, pseudorandom number generator to randomize the selected subjects. Allocations were issued using opaque, sealed, and numbered envelopes.¹²

Factors which gave this study strength are: at the start, patients were divided into two similar sample size groups, the consent form given and signed, inclusion and exclusion criteria were well described, indications of the types of mechanical ventilation and settings were addressed, and CMV patients were informed about sedation and a record made. Also, follow up was conducted, the study included clear easy to follow tables and figures, and study limitations were mentioned and explained.¹² Overall, this study received high marks for the Jadad score of three, as well as the clinical appraisal form for quality and validity. Points for blinding were not given because it was not applicable.

In the study by Conti and colleagues, a randomized prospective study, was conducted of 49 patients after a pool of 94 patients was assessed. Patients were randomized into two groups; the assignment was made with sealed envelopes. At the start of the study, the two sample groups were close in size. Factors which increased strength in this study were its one year follow up reporting long term benefits with the usage of NPPV in COPD patients. This study, also, defined ARF with its inclusion criteria and included a long list of exclusion criteria applied to recruit the selected patients. The study also mentioned that a consent form was given and signed, indicated the ventilator interventions and settings used, and addressed, complications from patients within the study groups. Sedation was implemented on patients in the CMV group with information given as to the type of drug used, dose, route, and management. Overall, this study also received high marks on the Jadad score of three. No points were given for blinding. The clinical appraisal form was used to assess for quality and validity.

In the study by Antonelli and colleagues, 64 ARF patients were randomized into two groups of either NPPV or CMV. Factors which gave this study strength were: the mentioning of consent form being given and signed, clear inclusion and exclusion criteria, and the indication of the types of mechanical ventilation and settings used to provide similar ventilatory support among the two groups.

The starting sample sizes were equal with similar conditions causing ARF. The study did mention that sedation was used in the CMV coupled group with the type of drug, dose, route, and management. Justifications of the causes of complications and events leading to death were shown in a table form. Overall, this study received average marks for the Jadad score of two, no points for blinding, and the clinical appraisal form was used for assessment of quality and validity.

Limitation of study

Honrubia et al¹² recognized that the limitation of their study was the small sample size. They believed it would decrease the ability to detect differences in mortality and complications. One of the setbacks they experienced was that the study was stopped before achieving the planned sample size due to decreased enrollment.

According to Keenan et al¹⁴ there exists a body of literature reporting the experience of experts in NPPV, consisting of carefully conducted, prospective, but uncontrolled, case series. The results reported by these authors suggest that noninvasive positive pressure ventilation may be useful for patients presenting with respiratory failure from quite a diverse range of etiologies. However, only a few of those studies were about both NPPV and CMV. The same problems were seen during this recent literature search for studies comparing NPPV vs. CMV. There exist, very limited data on RCT for this subject.

In the study by Antonelli et al¹³ factors which made this study weak are: the lack of detail about follow up, it lacked a limitation section to their study, and the process of randomizing patients into the two groups was not described even though they claimed to have done so. Another non-significant weakness of this study was it was not a controlled trial.

There appears to be a lacking of a universal name and abbreviation for “non-invasive positive pressure ventilation”, the term used in this systematic review. Many researchers use a different name and abbreviation in their studies for non-invasive positive pressure ventilation. For example; non-invasive mechanical ventilation (NIMV); Bi-level positive airway pressure (BiPAP); and non-invasive positive

pressure ventilation (NIPPV) vs. NPPV without the “I”. This difference might be due to geographical locations and/or to the time in which the studies were conducted. These terms all appear to refer to the same concept. To make things even more confusing, BiPAP and CPAP are both types of non-invasive ventilator (NIV). However, NIV is not the same as NPPV because of the lack of bi-level pressure, like in BiPAP. Therefore, CPAP was not included in this systematic review because; the clinical focus was on NPPV. This makes it hard for readers to follow along, but not knowing the difference could result in inappropriate data selections and altered review results.

Conclusion

There is promising evidence in the literature supporting the use of NPPV in adult patients with ARF especially those with acute exacerbation of COPD. Non-invasive positive pressure ventilation reduces the need for intubation in patients with ARF from different causes. Regarding results of hospital ICU length of stay, mortality rates and complications, there are apparent inconsistencies among the studies. At present, with the limited studies published in “randomized controlled trials”, addressing the clinical question, despite promising data from uncontrolled studies, it is clearly necessary to pursue further information in the form of randomized, controlled trials to definitively assess the effectiveness and safety of noninvasive positive pressure ventilation in the setting of acute respiratory failure due to other causes as well.

Table I. Summary Matrix of selected studies

Author/ Title	Yr. published	Patients/ Population	Intervention	Comparison	Outcome(s)	Study type	Validity (Jadad score)	Journal
Honrubia et al Noninvasive vs Conventional Mechanical Ventilation in Acute Respiratory Failure: A Multicenter, Randomized Controlled Trial	Dec. 2005	Sixty-four adult patients with Acute respiratory failure (ARF)	Non-invasive mechanical ventilation (NIMV) via face mask	Conventional mechanical ventilation (CMV) via endotracheal tube	Reduction in the need for intubation and therapeutic intervention in patients with ARF from different causes.	Multicenter Randomized controlled trial (RCT)	3	CHEST
Antonelli et al A Comparison of Non- invasive Positive Pressure Ventilation (NPPV) and Conventional Mechanical Ventilation in Patients with ARF	Aug. 1998	Sixty-four adult patients with hypoxemic ARF who required mechanical ventilation	NPPV via face mask	CMV + endotracheal intubation (ETI)	Decreasing complications, and ICU length of stay.	Prospective randomized trial (PRT)	2	New England Journal of Med
Conti et al Non-invasive vs. conventional mechanical ventilation in patients with chronic obstructive pulmonary disease (COPD) after failure of medical treatment in the ward: a randomized trial	Aug. 2002	Forty-nine adult patients with COPD who failed standard medical treatment in the emergency department and were admitted to the intensive care unit (ICU)	NPPV via face mask	CMV via (ETI)	Gas exchange, length of ICU stay, days on mechanical ventilation, complications, and mortality rate	Randomized prospective study (RPS)	3	Intensive Care Med

Table II. Indications and contraindications for the application of NPPV in patients with ARF

Indications	Contraindications
Respiratory acidosis with pH < 7.32	Cardiac/Respiratory arrest
Bicarbonate levels > 30mEq/L	Severe encephalopathy
Hypoxemia with PaO ₂ < 45 while breathing room air	Severe hemodynamic instability
Respiratory rate > 30 breaths/min	Gastrointestinal bleeding/recent surgery
Increase dyspnea, medium severity < 2 weeks	Acute coronary syndrome (unstable angina, MI)
PaCO ₂ < 45mmHg	Impaired consciousness/ coma
PaO ₂ /FiO ₂ < 200	Facial trauma/ deformity
Alert with GCS > 13	Recent upper airway surgery/ airway stenosis
Patent upper airway	High risk for aspiration/inability to clear secretions

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