Outcomes in Patients with Congestive Heart Failure Treated with Bi-Level Positive Airway Pressure: Safer Than Previously Thought?

Kalp yetmezliği hastalarında "bi-level positive airway pressure" uygulamasının sonuçları: Düşünüldüğünden daha mı güvenli?

Türkiye Acil Tıp Dergisi - Turk J Emerg Med 2009;9(2):53-58

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SUMMARY

Objective: Previous studies indicate that bi-level positive airway pressure (BiPAP) for congestive heart failure (CHF) may increase the rate of myocardial infarction (AMI). We compare rates of AMI and death in patients receiving medical therapy, BiPAP or intubation for CHF in the emergency department (ED).

Methods: Retrospective chart review of ED patients with CHF over 2 years.

Results: 745 subjects were enrolled. 553 (74.2%) received medical therapy alone; 158 (21.2%) received BiPAP and medical therapy; 34 patients (4.6%) were intubated in the ED. Patients receiving medical therapy alone had an AMI rate of 6.2%, compared with 15.8% of patients on BiPAP, and 32.4% of intubated patients (p<0.0001). Death rate in patients treated with medical therapy alone was 2.4%, compared with 8.2% of patients on BiPAP, and 20.6% of intubated patients (p<0.0001).

Conclusions: ED patients treated with Bi-PAP for CHF have lower rates of AMI than intubated patients. Patients receiving medical therapy only had the lowest rates of AMI and mortality.

Key words: Bi-level positive airway pressure; heart failure; intubation; medical therapy.

ÖZET

Amaç: *Daha önceki çalışmalar konjestif kalp yetmezliğinde 'bi-level positive airway pressure' (BİPAP) kullanımının miyokard infarktüsü (MI) oranını arttırdığını belirtmişlerdir. Biz bu çalışmada, acil serviste kalp yetmezliği nedeniyle medikal tedavi, BİBAP veya entübe edilerek tedavi edilen hastalarda MI ve ölüm oranlarını karşılaştırmayı amaçladık.*

Gereç ve Yöntem: *Acil servise son iki yılda kalp yetmezliği nedeniyle başvuran hastaların dosyaları geriye dönük olarak incelendi.*

Bulgular: *Çalışmaya 745 hasta dahil edildi. Çalışma hastalarının 553'ü (%74.2) sadece medikal tedavi, 158'i (%21.2) BİPAP ve medikal tedavi ,34 (%4.6) hasta ise entübe edilerek tedavi edildi. Sadece medikal tedavi alan hastaların %6.2'si, BİPAP uygulananların %15.8'i ve entübe edilenlerin de %32.4'ünde MI gelişti (p<0.0001). Sadece medikal tedavi alanlarda ölüm oranı %2.4, BİBAP grubunda %8.2 ve entübasyon grubunda %20.6'ydı (p<0.0001).*

Sonuç: *Acil servise kalp yetmezliği nedeniyle başvuran hastalarda BİPAP uygulanlarda ölüm oranı entübe edilen hastalarda gore daha düşüktür. En düşük ölüm oranları medikal tedavi alan gruptadır.*

Anahtar sözcükler: *Bi-level positive airway pressure; kalp yetmezliği; entübasyon; medikal tedavi.*

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Introduction

Congestive heart failure (CHF) is a common cause of acute respiratory compromise in the Emergency Department (ED). Frequently, dramatic clinical improvement can be made by treating these patients with medical therapy alone. Some patients, however, present to the ED in extreme respiratory distress and require emergent ventilatory assistance. Bilevel positive airway pressure (BiPAP) is a non-invasive means of mechanical ventilation that can be used to treat CHF, and to prevent the need for endotracheal intubation.

While BiPAP is a commonly used modality for noninvasive ventilation in the ED, there is little literature studying the safety and efficacy of BiPAP for the treatment of CHF.[1,2] Three randomized, prospective trials have addressed that the rate of AMI in patients treated with BiPAP for CHF, but these studies were limited by size and had conflicting conclusions.[3-5] Should ED patients with severe CHF requiring emergent ventilatory support be intubated, or receive BiPAP? Our study was designed to retrospectively compare the rates of AMI and death in patients receiving medical therapy, BiPAP, or intubation for the treatment of CHF in the ED.

Materials and Methods

This study was a retrospective chart review at an adult, urban university affiliated ED with an annual volume of 75,000. The study was first approved by the hospital's institutional review board (IRB). Patients were identified by ED admission ICD-9 codes for CHF as a primary or secondary diagnosis in the ED from January 2001 to December 2003. Charts were then randomly selected for review during a one-month data collection period. Patients were excluded from our study if they were <18 years old, had a diagnosis other than CHF or did not receive medical therapy as defined below. Patients were also excluded if they did not have 3 compete sets of cardiac enzymes drawn, unless those initially drawn were positive.

Data abstraction was performed by two unblinded physicians. Demographic data was collected on each of the patients. The ED chart, hospital chart, and discharge dictations were then reviewed to obtain information regarding the patient's history of coronary artery disease (defined as history of a myocardial infarction, coronary artery stent, angina, positive stress test or angiogram, or coronary artery bypass surgery), hypertension, or diabetes mellitus. The hospital discharge dictations were used to determine the patient's length of stay (LOS).

Medical therapy was defined as patients receiving oxygen, aspirin, diuretics, and nitrates in either the prehospital setting or in the ED. Both the ED chart and EMS log sheets, if available, were reviewed to obtain this information. The ED chart and hospital charts were then reviewed to determine if the patients were treated with BiPAP or intubation in the ED. Patients were included in the BiPAP group if they received BiPAP in the ED and continued therapy for at least 30 minutes. Patients who were intubated at any time in the ED were included in the intubation group, including those who started on BiPAP but were then intubated.

The criteria used to determine an AMI in study subjects was a typical rapid rise and fall of CK-MB biochemical markers of myocardial necrosis.[6,7] CK-MB biomarkers were drawn initially in the ED and at 8-hour intervals during the first 24 hours. Cardiac troponin biochemical markers were not used to define an AMI in this study because these levels fall more gradually in the serum. An elevated cardiac troponin drawn in the ED may indicate a subacute infarction, unrelated to ED intervention for CHF. In, addition, modest elevations of cardiac troponins can be nonspecific, and cardiac troponins were not uniformly sent on all patients with acute CHF at the time of the study. Patients who had a positive CK-MB level by the second set drawn (even if a third set was not drawn) were considered positive for AMI.

Statistical analysis was performed using chi square testing to determine the difference among rates of AMI and death between the standard therapy, BiPAP, and intubated groups. Chi square and Bartlett's test for equal variances were used in the analysis to determine differences in age, sex, race, length of stay, or comorbid illnesses among the three groups. All statistics were performed using Stata v. 8 (Stata Corp., College Station, TX).

Results

During the study period, 2737 patients were given a diagnosis of CHF; 838 charts were then randomly selected for review. Of these, 745 met study inclusion criteria and were enrolled in the study. 93 were excluded due to incomplete data. Average patient age was 74.8 years (range 28-101). Among study subjects 53% were female; 83% were white,

Table 1. *Rates of myocardial infarction and death in patients treated with standard therapy alone, BiPAP and standard therapy, and intubation and standard therapy respectively (p<0.05).*

	MI	Death
Medical Therapy	6.2	2.4
Bi-level positive airway pressure	15.8	8.2
Intubation	32.4	20.6

MI: Myocardial infarction.

7% black, and 7% Hispanic.

A total of 553 patients (74.2%) were given medical therapy (aspirin, oxygen, nitrates and furosemide) without ventilatory assistance. One hundred fifty-eight patients (21.2%) received BiPAP in addition to medical therapy. Thirty four patients (4.6%) were intubated in the ED. Eight of these patients had initially received BiPAP but deteriorated in the ED and required intubation. Patients receiving medical therapy alone had an AMI rate of 6.2% (95%CI 4.2%-8.5%), compared with 15.8% (95%CI 10.5%-22.5%) of patients on BiPAP (p<.0001) and 32.4% (95% CI 17.4%-50.5%) of patients who were intubated (p<.0001). The difference in the rate of AMI for patients treated with BiPAP versus intubation reached significance (p=0.025). Death rate in patients treated with medical therapy alone was 2.4% (95% CI 1.3%-4.0%), compared with 8.2% (95% CI 4.5%-13.7%) of the BiPAP group (p<0.001) and 20.6% (95% CI 8.7%-37.9%) of the intubated patients (p<.0001) (Table 1). The difference in the death rate for patients treated with BiPAP versus intubation was also significant (p=0.032). Three of eight patients (37.5%) who initially received BiPAP and later required intubation in the ED died after hospital admission. There were no significantly different outcomes with medical therapy, BiPAP and intubation with respect to age, gender, race, history of diabetes, coronary artery disease, or prior history of CHF. There was a significant difference in outcomes in patients with a history of hypertension. In patients receiving medical therapy 80% had a history of hypertension, versus 85% in those receiving BiPAP and 94% who were intubated (p=.046). Average LOS for each group was also significantly different. Patients receiving medical therapy had an average LOS of 5.3 days (range 5-44 days), compared with 6.6 days for BiPAP patients (range 1-38 days) and intubated patients 7.9 days (range 1-22 days) (p=.02) (Table 2).

Table 2. *Table showing baseline demographics and characteristics of patients.*

	Medical Therapy	BiPAP	Intubation	p
No. of Patients	554	171	34	
Age (yr.)	74.7±13.5	74.9±10.6	74.4±11.2	NS
Gender				NS
Male	258 (46.6%)	77 (45.0%)	20 (58.8%)	
Female	296 (53.4%)	94 (55.0%)	14 (41.2%)	
Race				NS
Caucasian	465 (84.7%)	133 (79.6%)	25 (75.8%)	
Black	36 (6.6%)	15 (9.0%)	4 (12.1%)	
Hispanic	35 (6.3%)	11 (6.6%)	4 (12.1%)	
Other	13 (2.4%)	8 (4.8%)	0 (0.0%)	
Risk Factors				NS
HTN	443 (80.0)	144 (84.2%)	32 (94.1%)	NS
CAD	393 (70.9%)	119 (69.6%)	24 (70.6)	NS
DM	253 (45.7%)	79 (46.2%)	20 (58.8%)	NS
CHF	158 (28.5%)	42 (24.6%)	11 (32.4%)	NS
LOS (days)	5.34±4.62	6.56±5.59	7.88±6.03	0.02

*p is significant (p<0.05).

BiPAP: Bi-level positive airway pressure; HTN: Hypertension; CAD: Coronary artery disease; DM: Diabetes mellitus; CHF: Congestion heart failure; LOS: Length of stay.

Discussion

In acute, severe CHF, patients generally fall into two categories: those who are treated with medical therapy alone, and those who require additional mechanical ventilatory support. The majority of patients who present to the ED with CHF will respond quickly to a medical therapy. It is not uncommon though, for a patient to present in extremis such that ventilatory support is needed as a life-saving measure. In these cases, there are currently two choices, either noninvasive ventilation or endotracheal intubation. Endotracheal intubation can provide life-saving respiratory support for severe cases of CHF or for patients unable to tolerate noninvasive ventilation (NIVV), but it is not without risk. Studies have shown frequent complications including esophageal intubation, pneumothorax, pulmonary aspiration,[8,9] and other complications as a result of repeated intubation attempts such as hypoxemia, airway trauma, bradycardia, and cardiac arrest.[10]

NIVV has become an increasingly popular method of treating acute, severe CHF in the ED. The first type of NIVV was CPAP, which delivers a constant positive airway pressure during a patient initiated inspiration. CPAP was initially studied most extensively in the treatment of patients with COPD; only a few trials exist which examine its use in patients with CHF. Bersten et al. showed that patients with severe cardiogenic pulmonary edema who were treated with CPAP had a decreased need for intubation than patients treated with oxygen alone.[11] Lin and Chiang published two papers which described an improvement in cardiovascular and pulmonary function, a decreased need for intubation, but no significant change in mortality in patients treated with CPAP for CHF.[12,13] These studies contributed to the popularity of using NIVV for the treatment of CHF.

The invention of BiPAP added another dimension to the use of NIVV. BiPAP allowed for positive airway pressure during both inspiration and expiration and was a true form of mechanical ventilation. Again, the initial studies using BiPAP were mainly in patients receiving therapy for COPD. In a randomized, prospective study published in 1997, Mehta et al. compared the use of CPAP to BiPAP in patients with acute CHF. After enrolling only 27 patients, the study was terminated due to a significantly higher rate of AMI in the patients treated with BiPAP (71% v. 31%).[3] The results of this study prompted Levitt to prematurely end his randomized, prospective trial comparing the use of BiPAP to high flow oxygen by mask. His results showed that there was no significant difference in the rate of AMI between the two groups.[4] Both studies were limited by a small sample size, but raised an important question as to the safety of the use of BiPAP in patients with CHF.

Since the time of Mehta and Levitt's studies, there has been little literature on the subject of the use of BiPAP in CHF. Sharon et al. published the results of a study comparing BiPAP versus intravenous isosorbide dinitrate in the treatment of acute, severe CHF.[5] They also terminated their study after enrolling 40 consecutive patients due to an increase in adverse outcomes in the BiPAP group, including increased rate of AMI, need for intubation, and death. In Sharon's study 11 (55%) patients treated with BiPAP had AMIs, versus 2 (10%) patients treated with intravenous isosorbide dinitrate (p=0.006). This study was again limited by a small sample size, but the results of

Table 3. *Table showing MI and death rates in studies involving BiPAP.*

Study Group	Study Design and Comparison	BİPAP	MI	Death
Mehta et al.	N = 27; Randomized trial; BiPAP vs CPAP	14	10 (71%) (95% CI 46-94%)	1 (7.1%)
Sharon et al.	N = 40; Randomized trial; BiPAP vs high-dose ISDN	20	11 (55%) (95% CI 31.5-76.9)	2 (10.0%)
Levitt	N = 38; Randomized, convenience sample; BiPAP vs high flow oxygen mask	21	4 (19%) (95% CI 2.2-35.8%)	3 (14.3%)
Rotter et al.	N = 759; Retrospective chart review of CHF patients receiving BiPAP	158	25 (15.8%) (95% CI 10.5-22.5%)	13 (8.2%)

BiPAP: Bi-level positive airway pressure; MI: Myocardial infarction; CPAP: Continuous positive airway pressure; ISDN: Intravenous isosorbide-dinitrate.

this and the previous study by Mehta have led many to speculate that until more research is done, patients with acute CHF should not be treated with BiPAP (Table 3).[14]

To our knowledge, this is the first retrospective study examining AMI and death rates in patients presenting in CHF treated with BiPAP. Compared to intubation, patients treated with BiPAP did have a statistically significant difference in the rate of AMI. Although our study is limited by the small number of patients in the intubated group, the data thus far shows a decreased rate of AMI in the BiPAP group compared to patients that were intubated (15.82% v. 32.35% p=0.023). In addition, there was a significant reduction in the rate of death in the patients treated with BiPAP compared to intubation (8.23% v. 20.59% p= 0.001).

Although our data cannot be directly compared with data from previous studies with different designs, the results of this study also show a large discrepancy in the previously reported data on AMI rates in patients receiving BiPAP therapy for CHF. Mehta et al.'s study showed an AMI rate of 71%, and Sharon's study showed an AMI rate of 55 %.[3,5] These high rates of AMI would lead many to conclude that BiPAP may not be safe to use in patients with CHF. Our study showed a dramatically lower rate of AMI in patients treated with BiPAP for CHF (15.82%). This more closely approximates the results of the study by Levitt et al.[4] Of note, the Mehta and Sharon studies had higher baseline rates of mortality and AMI in their control groups. This makes meaningful analysis and comparisons between these studies and our study difficult. Our study was also unable to assess the safety and efficacy of BiPAP in CHF. Due to the paucity of literature on this subject, there is a significant need for further research in this area.

The data from this study showed a statistically significant increase in both the rate of AMI and death in both BiPAP and intubation groups compared to medical therapy alone. A possible explanation for this difference is that patients who received ventilatory support for their CHF had a greater severity of illness than the patients treated with medical therapy alone, and were more likely to rule in for AMI or die. Future prospective studies may determine if differences in outcomes are related to severity of illness or other factors.

This study was limited by its design, in that it was a retrospective chart review. Patients were located by ICD-9 codes for a primary or secondary diagnosis of CHF. By using this method of locating patients retrospectively, patients were not studied consecutively. Another limitation of this study is that due to its retrospective nature, there was no standardization of therapy. While we did require that patients receive aspirin, oxygen, nitrates, and diuretics, the specific agents and dosages were not standardized. Medical intervention and the decision for treatment within each group (standard medical therapy, BiPAP, or intubation) were study limitations as all decisions were based upon clinical presentation and clinician judgment. Disease severity was not measured. However, it is highly likely that patients that received BiPAP presented with more severe CHF than patients that received medical therapy alone. Likewise, patients that were intubated most likely had more severe CHF than those patients that received BiPAP. Therefore, it is possible that differences in outcomes could be due to differences in initial acuity levels between the treatment groups. Finally, this study may be limited by the small number of subjects in the intubated group.

In patients receiving BiPAP therapy for CHF, both AMI rates and death rates were significantly lower than in patients who were intubated. A large ED based prospective study to confirm the findings of this retrospective analysis is needed.

References

1. Summers RL, Patch J, Kolb JC. Effect of the initiation of noninvasive bilevel positive airway pressure on haemodynamic stability. *Eur J Emerg Med* 2002;9:37-41.
2. Yosefy C, Hay E, Ben-Barak A, Derazon H, Magen E, Reisin L, et al. BiPAP ventilation as assistance for patients presenting with respiratory distress in the department of emergency medicine. *Am J Respir Med* 2003;2:343-7.
3. Mehta S, Jay GD, Woolard RH, Hipona RA, Connolly EM, Cimini DM, et al. Randomized, prospective trial of bilevel versus continuous positive airway pressure in acute pulmonary edema. *Crit Care Med* 1997;25:620-8.
4. Levitt MA. A prospective, randomized trial of BiPAP in severe acute congestive heart failure. *J Emerg Med* 2001;21:363-9.
5. Sharon A, Shpirer I, Kaluski E, Moshkovitz Y, Milovanov O, Polak R, et al. High-dose intravenous isosorbide-dinitrate is safer and better than Bi-PAP ventilation combined with conventional treatment for severe pulmonary edema. *J Am Coll Cardiol* 2000;36:832-7.
6. WHO MONICA Project. MONICA Manual, rev ed. Geneva: Cardiovascular Diseases Unit, WHO; 1990.
7. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined-a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959-69.

8. Pingleton SK. Complications of acute respiratory failure. *Am Rev Respir Dis* 1998;137:1463-93.
9. Schwartz DE, Matthay MA, Cohen NH. Death and other complications of emergency airway management in critically ill adults. A prospective investigation of 297 tracheal intubations. *Anesthesiology* 1995;82:367-76.
10. Mort TC. Emergency tracheal intubation: complications associated with repeated laryngoscopic attempts. *Anesth Analg* 2004;99:607-13.
11. Bersten AD, Holt AW, Vedig AE, Skowronski GA, Baggoley CJ. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. *N Engl J Med* 1991;325:1825-30.
12. Lin M, Chiang HT. The efficacy of early continuous positive airway pressure therapy in patients with acute cardiogenic pulmonary edema. *J Formos Med Assoc* 1991;90:736-43.
13. Lin M, Yang YF, Chiang HT, Chang MS, Chiang BN, Cheitlin MD. Reappraisal of continuous positive airway pressure therapy in acute cardiogenic pulmonary edema. Short-term results and long-term follow-up. *Chest* 1995;107:1379-86.
14. Velez LI, Benitez FL, Nazeer SR. Noninvasive ventilation in the emergency department. *Emergency Medicine Reports* 2004;25:1-10.