A comparative study between the effect of continuous positive air way pressure ventilation and standard oxygen therapy in acute cardiogenic pulmonary edema patients

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Abstract: Background: Acute cardiogenic pulmonary edema (ACPE) is one of the most common conditions presenting to the emergency department which require rapid assessment and intervention. It is associated with mortality rates of 10-20% (1). Acute cardiogenic pulmonary edema is a common cause of acute respiratory distress among patients presenting to the emergency departments and intensive care units. Hypoxemia, sometimes associated with hypercapnia, is a common feature in the clinical presentation of acute cardiogenic pulmonary edema. The use of noninvasive ventilation (NIV) in the acute care setting in general has been fueled by the desire to avoid the complications associated with intubation and invasive ventilation, (4) including trauma to the larynx, pharynx, and trachea, arrhythmia, hypotension, aspiration of gastric contents, sinusitis, pneumonia, and loss of the ability to eat and communicate verbally (5). **Objectives**: The aim of this study is to determine the clinical outcome with continuous positive pressure ventilation in adults with acute cardiogenic pulmonary edema compared to standard oxygen therapy. **Patient and methods:** This was a prospective, randomized, comparative clinical study to evaluate the clinical outcome with continuous positive pressure ventilation (CPAP) in adults with acute cardiogenic pulmonary edema (ACPE) compared to standard oxygen therapy. After approval of the ethical committee and obtaining a written informed consent from patient guardians, this prospective, randomized, comparative clinical study conducted in Ain Shams University hospitals on (20) adult patients aged more than 20 years, presenting to ICU of Ain Shams University hospitals with acute cardiogenic pulmonary edema. **Results: Comparative** studies between control and CPAP showed that highly significant decrease in average follow up HR and RR and highly significant increase in O_2 saturation; in CPAP group compared to control group; with highly significant statistical difference ($p < 0.001$ respectively). Combined paired and un-paired comparative studies showed that: After analysis of all 20 (control and CPAP) patients according to the 5 serial (baseline and follow up) vital and ABG data; with entering a dichotomous grouping factor (control – CPAP). Factorial ANOVA studies showed that; CPAP group had a higher average decline in HR and RR; and a higher average increase in O_2 saturation compared to control group; during serial 5 (baseline and follow up) vital data measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.001$ respectively). Factorial ANOVA studies showed that; CPAP group had a higher average increase in PaO_2 compared to control group; during serial 5 (baseline and follow up) ABG measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.001$). **Conclusion:** Based on our findings and those previously published, we conclude that CPAP should be considered especially in patients with respiratory failure due to ACPE. Also, $PaCO_2$ levels should be monitored closely in order to assess the response to treatment. Non-Invasive Ventilation has been shown to be effective in acute respiratory failure of various etiologies in different health care systems and ward settings. It should be seen as complementary to invasive ventilation and primarily as a mean of preventing some patients from deteriorating to the point at which intubation is needed.

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Keywords: comparative; study; effect; continuous positive air; pressure; ventilation; standard; oxygen; therapy; acute cardiogenic pulmonary edema patient

1. 1. Introduction

Acute cardiogenic pulmonary edema (ACPE) is one of the most common conditions presenting to the emergency department which require rapid assessment and intervention. It is associated with mortality rates of 10-20% [(1)].

Pulmonary edema is an abnormal accumulation of fluid in the interstitial space surrounding the alveoli with advancement of the fluid accumulated in the alveoli. It results from increased trans-vascular pressure gradient as in cardiogenic pulmonary edema, or increase in the microvascular permeability to solutes as in non-cardiogenic pulmonary edema [(2)].

Acute cardiogenic pulmonary edema is a common cause of acute respiratory distress among patients presenting to the emergency departments and intensive care units. Hypoxemia, sometimes associated with hypercapnia, is a common feature in the clinical presentation of acute cardiogenic pulmonary edema.

Standard medical therapy includes diuretics, vasodilators, and inotropes results in rapid improvement of the respiratory symptoms. In this context, oxygen delivered through a face mask is the basic respiratory support. Although many patients respond rapidly to standard treatment, a significant number progress to severe respiratory distress leading to end tracheal intubation with its associated complications [(3)].

The use of noninvasive ventilation (NIV) in the acute care setting in general has been fueled by the desire to avoid the complications associated with intubation and invasive ventilation, [(4)] including trauma to the larynx, pharynx, and trachea, arrhythmia, hypotension, aspiration of gastric contents, sinusitis, pneumonia, and loss of the ability to eat and communicate verbally [(5)].

Non-invasive ventilation may improve short-term outcomes in patients with acute cardiogenic pulmonary edema. The majority of studies compare continuous positive airway pressure (CPAP) against standard oxygen therapy and consistently report that non-invasive positive ventilation (NIPV) via CPAP mode more rapidly improves symptoms and short-term physiological parameters including decreasing respiratory acidosis, respiratory rate, work of breathing, heart rate, and sensation of dyspnea [(6)], and also reduces the need for intubation and invasive ventilation [(7)].

A meta-analysis of 15 small-scale trials has suggested that non-invasive ventilation reduces mortality and the need for intubation [(8)].

In spite of the potential advantages of NIPV for the management of ACPE, CPAP through face mask appears to be have some disadvantages like: patient discomfort, skin breakdown, and air leak due to poor fit over the bridge of the nose or mandible. In addition, they interfere with speech, eating and expectoration [(9)].

2. Patients and Methods

This was a prospective, randomized, comparative clinical study to evaluate the clinical outcome with continuous positive pressure ventilation (CPAP) in adults with acute cardiogenic pulmonary edema (ACPE) compared to standard oxygen therapy.

After approval of the ethical committee and obtaining a written informed consent from patient guardians, this prospective, randomized, comparative clinical study conducted in Ain Shams University hospitals on (20) adult patients aged more than 20 years, presenting to ICU of Ain Shams University hospitals with acute cardiogenic pulmonary edema.

Patient selection

• Inclusion Criteria:

• An age of more than 20 years.

•Clinical diagnosis of acute cardiogenic pulmonary edema that typically presented by Dyspnea at rest, orthopnea, tachycardia, tachypnea with respiratory rate more than 30 breaths/min, crackles on pulmonary auscultation, third heart sounds on cardiac auscultation.

• Conscious patients with intact cough reflex and swallowing function.

• Exclusion Criteria:

• Pregnant female with +ve B-HCG test.
• Previous cardiac/respiratory arrest.
• Non-cooperative.
• Mask refusal after explanation of advantages of mask over invasive ventilation.
• Severe hemodynamic instability (systolic blood pressure SBP <80 mm Hg) or severe ventricular arrhythmia.
• Decreased conscious level (Glasgow coma score of 11 or less).
• Need for emergency intubation.
• More than one severe organ dysfunction.
• Copious, unmanageable respiratory secretions.ī
• Sever hypoxemia (Pa02<40 mm Hg, Spo2 <75 %, or PaO2 <60mmHg on FiO2 100%).
• Facial Surgery, trauma, or deformity.
• Upper GI or airway surgery.
• Chest problems (Acute bronchial asthma, lung contusion, pneumonia, pneumothorax).
• Severe upper gastrointestinal tract bleeding.
• Non cardiogenic pulmonary edema (end stage renal failure, acute respiratory distress syndrome (ARDS) and neurogenic pulmonary edema, High altitude pulmonary edema, Pneumonia, Illicit drug use or Inhaled toxins).

Patients with inclusion criteria were randomly divided into TWO Groups:

• Control group:

This group received conventional oxygen therapy with simple oxygen mask (n =10).

• Study group (CPAP group):

This group received CPAP ventilation through a full face CPAP mask (n = 10).

Intervention:

All patients received the standard medical treatment, according to the emergency department protocol, at the Ain Shams University Hospitals, Patients were given standardized pharmacological treatment which includes:

1) Intravenous furosemide 40-120 mg as an initial dose then the dose will be repeated if required to achieve sufficient urinary output.

2) Continuous intravenous nitroglycerin initial dose of 0.5 to 1 mcg/kg/min then the dose increased in increments of 0.5 to 1 mcg/kg/min every three to five minutes as required and tolerated (dose range 1 to 20 mcg/kg/min) if systolic blood pressure was above 100 mm Hg.

3) Morphine sulphate 3 mg iv once.

4) Weight-adjusted doses of subcutaneous or intravenous heparin and oral 300 mg aspirin if the ECG was suggestive of ischemia.

Ventilatory support based on randomization include patients assigned to the conventional Oxygen therapy group receiving oxygen by a simple oxygen mask 15 L/Min (controlled group). In the CPAP group, patients were ventilated using the CPAP mask was delivered through a ResMed Mirage Quattro Full Face CPAP Mask by a Newport™ e360 Ventilator, T model, U.S, manufactured by (Newport Medical Instrument, Inc., Costa Mesa, CA 92626).

Pressure support started at 10 cmH_2O. Pressure support increased 5 cmH_2O every ten minutes as clinically indicated with a maximal pressure target of 20 cmH_2O or either a therapeutic response was achieved or patient tolerability was reached to obtain a respiratory rate <20/min and rest the respiratory muscles. Slight PEEP (4-7 cm H_2O) was used to increase PaO_2, O_2 saturation and to prevent atelectasis. All patients was given CPAP for 24 h and CPAP mask was removed for 20 min every 2 hours to facilitate eating, drinking and verbally communications. Clinical stability was defined as an improvement in oxygenation (paO_2 >60 mm Hg or oxygen saturation >90% SaO_2), a respiratory rate of <25 breaths\min with the presence of a normal breathing pattern and a heart rate <110 beats/min.

• ***Data collected:***

Heart rate (HR), ECG and respiratory rate (RR) was monitored continuously. Arterial blood gas (ABG) sampling was obtained through a 18-gauge plastic cannula placed in the radial artery and blood pressure was measured invasively. Pulse oximeter was used to monitor arterial oxygen using Space Labe monitor.

Respiratory Rate (RR), heart rate (HR), blood pressure (BP), SPO_2 and arterial blood gases ($PaCO_2$, PaO_2, and pH) was recorded at different time points (0, 1hr, 6hrs, 12hrs, 24hrs).

- ***Study Endpoint:***

When the patient need endotracheal intubation, or progress to hemodynamic instability, cardiogenic shock. Intubation was performed after 1 h of study if there is persistent hypoxemia, agitation or worsened neurological status, inability to tolerate the mask or aspiration of gastric content. Study ends after 24 hours.

Outcome Measures:

The primary outcome measures were physiological parameters concerning blood gases (PaCO2, PaO2, SaO2, pH, and HCO3), and physiological parameters (HR, RR, SBP, and DBP). These parameters were collected at different time points (0, 1hr, 6hrs, 12hrs, 24hrs). Secondary outcomes were rate of endotracheal intubation, and the rate of death that reported at the time of discharge. Therapist recorded the adverse events of NIV (mucosal pain, nasal bridge erythema, or ulcerations, eye irritation, vomiting & gastric distension) during applications.

3. Results

Descriptive data:

The demographic and clinical variables in 20 ACPE patients who were included in the study are shown in the following tables & figures:

Comparative studies:

The 20 ACPE patients were classified according type of intervention into 2 groups:

- **Patients used standard oxygen therapy (control group) (10 patients)**
- **Patients used CPAP (10 patients)**

Comparative studies are shown in the following tables and figures;

Socio-demographic and clinical data:

Table (1): Comparison between control group and CPAP group as regards age of patients using Student's t test:

Variable	Control group (N= 10)	CPAP group (N= 10)	t test
	Mean ± SD	Mean ± SD	p value
Age (years)	57.7 ± 10.01	61 ± 13.54	= 0.543

Comparative study between the 2 groups revealed non-significant difference as regards age of the patients (p > 0.05).

Table (2): Comparison between control group and CPAP group as regards some demographic and clinical variables using Chi square test:

Variable		Control group (N= 10)	CPAP group (N= 10)	p value
Gender	Female (N=10)	4 (40%)	6 (60%)	= 0.6703
	Male (N=10)	6 (60%)	4 (60%)	
HF	HF (N=13)	7 (70%)	6 (60%)	= 0.8959
	Not (N=7)	3 (30%)	4 (40%)	
Arrhythmia	Arrhythmia (N=7)	3 (30%)	4 (40%)	= 0.8959
	Not (N=13)	7 (70%)	6 (60%)	
AMI	AMI (N=8)	3 (30%)	5 (50%)	= 0.6592
	Not (N=12)	7 (70%)	5 (50%)	
HTN	HTN (N=9)	4 (40%)	5 (50%)	= 0.9039
	Not (N=11)	6 (60%)	5 (50%)	
Non-restricted dietary salt	Non-restricted (N=8)	4 (40%)	4 (40%)	= 1.0000
	Restricted (N=12)	6 (60%)	6 (60%)	

Comparative study between the 2 groups revealed non-significant difference as regards gender, HF, arrhythmia, AMI, HTN and non-restricted dietary salt ($p > 0.05$).

Follow up data:

Table (3): Comparison between control group and CPAP group as regards average follow up vital data using Student's t test:

Variable	Control group (N= 10)	CPAP group (N= 10)	t test
	Mean ± SD	Mean ± SD	p value
SBP (mmHg)	136.12 ± 27.66	149.17 ± 24.28	= 0.277
DBP (mmHg)	85.07 ± 11.64	90.82 ± 10.77	= 0.267
MAP (mmHg)	110.6 ± 19.43	120 ± 17.34	= 0.269
HR (N/min)	97.17 ± 0.81	88.07 ± 0.67	< 0.001**
RR (N/min)	28.85 ± 0.8	25.87 ± 1	< 0.001**
O_2 saturation (%)	90.52 ± 0.8	93.7 ± 0.65	< 0.001**

Comparative study between the 2 groups revealed; highly significant decrease in average follow up HR and RR and highly significant increase in O2 saturation; in CPAP group compared to control group; with highly significant statistical difference ($p < 0.001$ respectively).

Comparative study between the 2 groups revealed non-significant difference as regards average follow up SBP, DBP and MAP ($p > 0.05$).

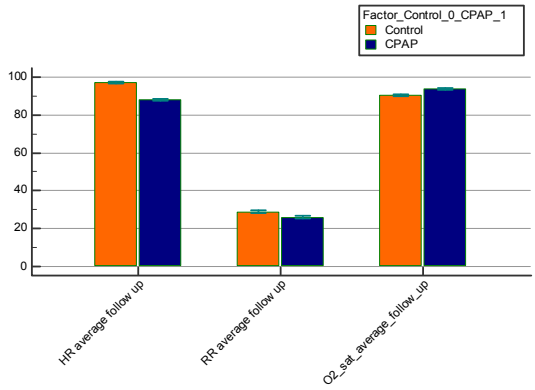

Figure (1): Multiple comparison graph between control group and CPAP group as regards average follow up HR, RR and O_2 saturation.

Table (4): Comparison between control group and CPAP group as regards average follow up ABG data using Student's t test:

Variable	Control group (N= 10)	CPAP group (N= 10)	t test
	Mean ± SD	Mean ± SD	p value
pH	7.39 ± 0.06	7.37 ± 0.07	= 0.454
$PaCo_2$ (mmHg)	39.3 ± 6.29	41.5 ± 9.29	= 0.543
PaO_2 (mmHg)	64.62 ± 0.99	81.05 ± 1.04	< 0.001**
HCO_3 (mEq/L)	25.25 ± 2.67	26.55 ± 3.79	= 0.388

Comparative study between the 2 groups revealed; highly significant increase in average follow up PaO2; in CPAP group compared to control group; with highly significant statistical difference ($p < 0.001$).

Comparative study between the 2 groups revealed non-significant difference as regards pH, PaCo2 and HCO3 ($p > 0.05$).

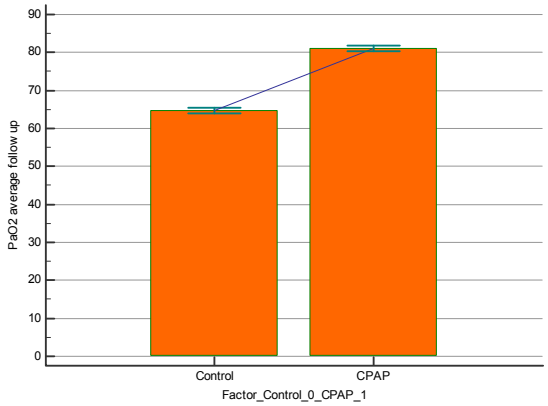

Figure (2): Comparison between control group and CPAP group as regards average follow up PaO_2.

Combined paired and un-paired comparative studies:

We further analyzed and compared all 20 (control and CPAP) patients according to the 5 serial (baseline and follow up) vital and ABG data; with entering a dichotomous grouping factor (control – CPAP).

Data are shown in the following tables and figures:

Table (5): Comparison between control group (10) and CPAP group (10) as regards serial (baseline and follow up) vital data measurements using factorial ANOVA test (2-Factor study):

Investigations	Repeated 5 measures ANOVA (2-F: between control and CPAP groups)	
	F value	p value
SBP (mmHg)	1.19	0.289
DBP (mmHg)	1.51	0.235
MAP (mmHg)	1.31	0.268
HR (N/min)	310.87	<0.001**
RR (N/min)	49.77	<0.001**
O_2 saturation (%)	120.66	<0.001**

ANOVA: analysis of variance, 2-F: 2-factor study.

Factorial ANOVA studies showed that; CPAP group had a higher average decline in HR and RR; and a higher average increase in O2 saturation compared to control group; during serial 5 (baseline and follow up) vital data measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.001$ respectively).

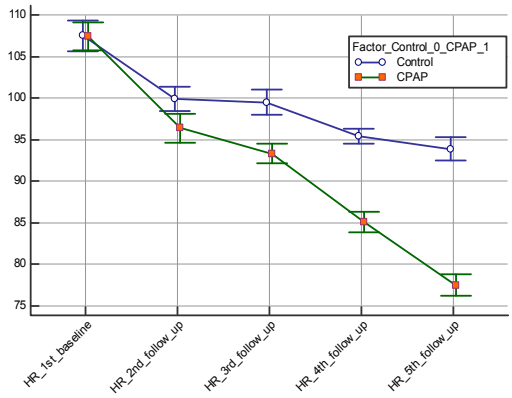

Figure (3): Comparison between control group and CPAP group as regards serial (baseline and follow up) HR measurements.

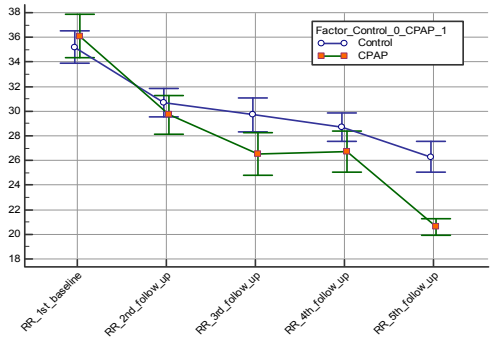

Figure (4): Comparison between control group and CPAP group as regards serial (baseline and follow up) RR measurements.

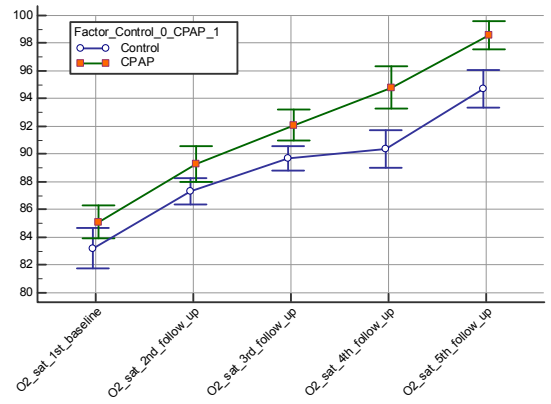

Figure (5): Comparison between control group and CPAP group as regards serial (baseline and follow up) O_2 saturation measurements.

Table (6): Comparison between control group (10) and CPAP group (10) as regards serial (baseline and follow up) ABG measurements using factorial ANOVA test (2-Factor study):

Investigations	Repeated 5 measures ANOVA (2-F: between control and CPAP groups)	
	F value	p value
pH	0.81	0.379
$PaCo_2$ (mmHg)	0.46	0.504
PaO_2 (mmHg)	817.19	<0.001**
HCO_3 (mEq/L)	0.71	0.411

ANOVA: analysis of variance, 2-F: 2-factor study.

Factorial ANOVA studies showed that; CPAP group had a higher average increase in PaO_2 compared to control group; during serial 5 (baseline and follow up) ABG measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.001$).

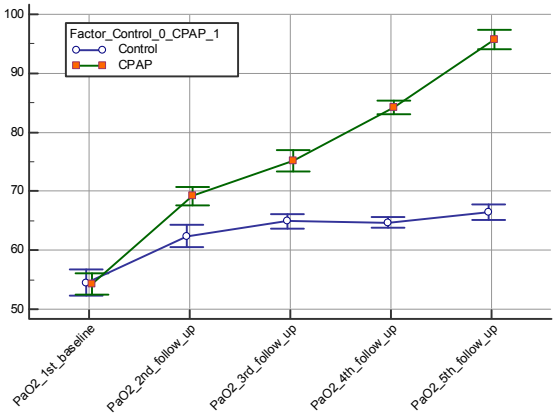

Figure (6): Comparison between control group and CPAP group as regards serial (baseline and follow up) PaO_2 measurements.

4. Discussion

Acute cardiogenic pulmonary edema usually presents with the sudden onset of acute hypoxemic respiratory failure that requires rapid assessment and treatment. Although this may be secondary to sudden decompensation of chronic heart failure, myocardial ischemia is also common. Typically, patients are hypoxemic with increased work of breathing, acidemic because of both respiratory and metabolic factors, and hypertensive and tachycardic. Diastolic dysfunction is the major contributor to raised hydrostatic pressure and pulmonary edema [(10)]. Despite standard medical therapy with oxygen, nitrates, and diuretics, ventilator assistance may be needed.

Noninvasive ventilation is widely used in cardiogenic pulmonary edema [(11)], usually resulting in rapid relief of dyspnea.

Almost six decades ago, Poulton and Oxon [(12)] described the use of CPAP delivered by the ‘‘pulmonary plus pressure machine’’ through a facemask to patients with ‘‘cardiac asthma’’. Several studies have shown that CPAP is effective in patients with ACPE as it rapidly improves gas exchange and cardiac hemodynamics, and can decrease intubation rates and inhospital mortality.

Compared with those treated conventionally, While the term noninvasive ventilation covers numerous methods of ventilator assistance without endotracheal intubation, it is most commonly applied as positive airway pressure using a mask as the interface. The simplest and most commonly used technique in cardiogenic pulmonary edema is continuous positive airway pressure (CPAP). There has been growing interest, however, in the use of modes where inspiratory effort is supported by a greater level of positive pressure (pressure support) interposed on top of positive end-expiratory pressure (PEEP), also termed bilevel positive airway pressure. Raised intrathoracic pressure increases functional residual capacity and oxygenation, improves lung mechanics, and reduces work of breathing [(13)].

There may also be beneficial cardiovascular effects resulting in reduced afterload and preload; clinical studies, necessarily performed some hours after onset, show reduced transmural ventricular filling pressures. As mask CPAP leads to more rapid physiologic improvement, consistently reduced intubation rate, and a tendency to reduced mortality [(14)], there are qualified recommendations for its use in cardiogenic pulmonary edema. Nava and colleagues [(15)] prospectively randomized 130 patients with cardiogenic pulmonary edema, receiving standard medical therapy, to either oxygen at ambient pressure or oxygen with mask pressure support plus PEEP. Consistent with previous studies, this led to a more rapid improvement in physiologic variables, such as

oxygenation, arterial carbon dioxide tension, respiratory rate, dyspnea, blood pressure, and heart rate.

This was a prospective, randomized, comparative clinical study to evaluate the clinical outcome with continuous positive pressure ventilation (CPAP) in adults with acute cardiogenic pulmonary edema (ACPE) compared to standard oxygen therapy.

Comparative studies between control and CPAP showed that:

Comparative study between the 2 groups revealed; highly significant decrease in average follow up HR and RR and highly significant increase in O_2 saturation; in CPAP group compared to control group; with highly significant statistical difference ($p < 0.001$ respectively).

Rasanen et al [16] randomised 40 patients with ACPE to either facemask CPAP (10 cm H2O) or standard medical therapy, and showed improvement in gas exchange, decrease in respiratory work.

Comparative study between the 2 groups revealed non-significant difference as regards average follow up SBP, DBP and MAP ($p > 0.05$).

Comparative study between the 2 groups revealed; highly significant increase in average follow up PaO_2; in CPAP group compared to control group; with highly significant statistical difference ($p < 0.001$).

Comparative study between the 2 groups revealed non-significant difference as regards pH, $PaCo_2$ and HCO_3 ($p > 0.05$).

Paired comparative studies regarding control group showed that:

After analysis of all 10 control patients according to the 5 serial (baseline and follow up) vital and ABG data, we found that:

Comparative study between baseline and follow up vital data measurements revealed; highly significant decrease in follow up SBP, DBP, MAP, HR and RR measurements (especially at 24-hours); with highly significant statistical difference ($p = 0.0025$, $p = 0.0001$, $p = 0.001$, $p < 0.0001$, $p < 0.0001$ respectively).

Comparative study between baseline and follow up vital data measurements also revealed; highly significant increase in follow up O_2 saturation measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.0001$).

Comparative study between baseline and follow up ABG measurements revealed; highly significant increase in follow up PaO_2 measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.0001$).

Comparative study between baseline and follow up ABG measurements also revealed; non-significant difference as regards pH and $PaCo_2$ ($p > 0.05$).

Paired comparative studies regarding CPAP group showed that:

After analysis of all 10 CPAP patients according to the 5 serial (baseline and follow up) vital and ABG data, we found that:

Comparative study between baseline and follow up vital data measurements revealed; highly significant decrease in follow up SBP, DBP, MAP, HR and RR measurements (especially at 24-hours); with highly significant statistical difference ($p = 0.0003$, $p < 0.0001$, $p = 0.0001$, $p < 0.0001$, $p < 0.0001$ respectively).

The CPAP-treated patients in the trial by ***Kelly et al*** [17] had more significant symptom and physiologic improvement in the first hour.

Comparative study between baseline and follow up vital data measurements also revealed; highly significant increase in follow up O_2 saturation measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.0001$).

Comparative study between baseline and follow up ABG measurements revealed; highly significant increase in follow up PaO_2 measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.0001$).

Comparative study between baseline and follow up ABG measurements also revealed; highly significant decrease in follow up HCO_3 measurements (especially at 24-hours); with highly significant statistical difference ($p = 0.01$).

Bersten et al [18] compared the efficacy of CPAP (10 cmH_2O) with that of conventional treatment in 39 patients with ACPE and found a significant and rapid improvement in arterial oxygen tension and a significant decrease in arterial carbon dioxide tension in patients treated with CPAP.

Unlike in our study comparative study between baseline and follow up ABG measurements also revealed; non-significant difference as regards pH and $PaCo_2$ ($p > 0.05$).

Combined paired and un-paired comparative studies:

After analysis of all 20 (control and CPAP) patients according to the 5 serial (baseline and follow up) vital and ABG data; with entering a dichotomous grouping factor (control – CPAP).

Factorial ANOVA studies showed that; CPAP group had a higher average decline in HR and RR; and a higher average increase in O_2 saturation compared to control group; during serial 5 (baseline and follow up) vital data measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.001$ respectively).

Lin et al [19] in another study randomised 100 patients with ACPE, and showed favouable effects of

incremental CPAP (2.5–12.5 cm H2O) on O_2 saturation, respiratory rates.

Factorial ANOVA studies showed that; CPAP group had a higher average increase in PaO_2 compared to control group; during serial 5 (baseline and follow up) ABG measurements (especially at 24-hours); with highly significant statistical difference ($p < 0.001$).

L'Her et al [20] randomised 89 elderly patients with ACPE to standard medical therapy or CPAP (7.5 cm H2O) plus standard medical therapy, and confirmed that CPAP decreased intubation rates, and promoted early clinical improvement in patients attending emergency departments for severe pulmonary oedema.

CPAP acts both on gas exchange and left ventricular performance. The effect on oxygenation may result from the generated PEEP. PEEP may improve arterial oxygenation by several mechanisms, particularly by a reduction in intrapulmonary shunt. In the present study, when adding CPAP in CPAP group, patients exhibited significantly less symptoms of respiratory fatigue, which may relate to a reduction in the work of breathing and alveolar hypoventilation. These results are consistent with the literature showing a reduction in the work of breathing, an increase in pulmonary compliance and a decrease in airway resistances [21]. Positive pressure ventilation also supports left ventricular contraction, by minimizing the negative swings in intrathoracic pressure seen during inspiration and thus, by decreasing aortic impedance and left ventricular transmural pressure [22]. Indeed, it has been shown that CPAP increases stroke volume, cardiac index and oxygen delivery, improve hemodynamics and decreases myocardial oxygen consumption during severe ACPE as compared with medical treatment [23].

This study confirms previous reports using non-Invasive ventilation in the treatment of ACPE [24, 25].

There are some clinical evidence, since respiratory failure in ACPE is not directly related to hypoxemia and cannot be reversed with oxygen therapy alone. Therefore the primary goal of CPAP in ACPE is to support the respiratory muscle activity and decrease respiratory rate that will improve the efficacy of the patient's effort and allows a reduction in the respiratory work [26], resulting in increased tidal volume and reduced respiratory rate.

Basant et al [27] confirm the result of our study and reported that the effects of CPAP and Bi-PAP were superior to the oxygen therapy group regarding improvement of blood gases (PaO2, PaCO2 and SaO2) and physiological parameters (HR, RR, SBP, and DBP).

However, ***Gray et al*** [28] did not report significant differences between NIV compared to standard oxygen therapy regarding to RR, SBP, and DBP. This may be due to differences in the values of applied pressure and in patient characteristics.

Our results showed no significant difference in the proportion of patients who underwent endotracheal intubation after the end of study and the rate of death till the discharge among groups as we reported only 2 patient in the control group and no patient in CPAP group who needed endotracheal intubation and only one patient in the control group with no patient in the CPAP group who died after the end of the study. These results were similar to previous studies [27, 28].

This study shows that the application of CPAP was successful in improving oxygenation and respiratory distress in patients with ACPE. This result with agreement of [29, 30, 31].

CPAP is an effective front-line treatment to correct hypoxemia in acute respiratory failure and it is still the treatment of choice in cardiogenic pulmonary edema [32].

Limitation of the study:

The limitations of this study were; the physicians who decided when it started endotracheal intubation or to cease NIV were not blinded. This increase the possibility of a bias, however, blinding in our study was not feasible; Further NIV studies should consider blinding physician to the mode of CPAP used. Moreover, small sample size, and long-term results are not available, so additional large international Multicenter study comparing three treatment arms is required to investigate long-term improvement.

Conclusion

Based on our findings and those previously published, we conclude that CPAP should be considered especially in patients with respiratory failure due to ACPE. Also, $PaCO_2$ levels should be monitored closely in order to assess the response to treatment.

Non-Invasive Ventilation has been shown to be effective in acute respiratory failure of various etiologies in different health care systems and ward settings. It should be seen as complementary to invasive ventilation and primarily as a mean of preventing some patients from deteriorating to the point at which intubation is needed.

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