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Bi-level Positive Airway Pressure (BiPAP) ventilation vs Continuous Positive Airway Pressure (CPAP) ventilation in acute cardiogenic pulmonary oedema in the emergency department; a study conducted in two hospitals in Sri Lanka

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ABSTRACT

Introduction: Acute pulmonary oedema is a life-threatening condition, and some patients require non-invasive ventilation such as continuous positive airway pressure (CPAP) ventilation and bi-level positive airway pressure (BiPAP) ventilation for improving alveolar ventilation and haemodynamic stability, thus, improving pulmonary oedema. This study aims to determine the efficacy and suitability of the CPAP vs. BiPAP ventilation in patients with acute pulmonary oedema following acute heart failure.

Methods: The study was conducted as a randomized prospective clinical trial at the emergency treatment unit of the National Hospital of Sri Lanka and Base Hospital, Panadura. **Group A** patient received pressure limits of IPAP - 8 - 20 cm H_2O, EPAP- 4-10 cm H_2O and **Group B** received CPAP 10 - 15 cm H_2O and oronasal mask is used. Patients who do not tolerate CPAP were changed to BiPAP.

Results: Our study demonstrated that in addition to the standard medical care, after 2 hours of treatment, both CPAP and BiPAP improve vital parameters, oxygenation / blood gases, and ameliorate respiratory distress, effectively managing acute pulmonary oedema. A few patients (5.8%) stated that Non-Invasive Ventilation (NIV) is quite difficult to tolerate, but more than 60% of patients agreed that NIV was given less discomfort for them. However, patients receiving BiPAP demonstrated higher heart rate (102 ± 9.282) than the CPAP group 84 ± 13.326 at the end of treatment.

Conclusions: At the end of the treatment, both CPAP and BiPAP treatment modalities are capable of improving vital parameters and respiratory distress even though BiPAP group demonstrated higher heart rate at the end of treatment. However, the study does not demonstrate any significant difference of clinical benefit of BiPAP vs CPAP.

Keywords: *Acute pulmonary oedema, BiPAP, CPAP, ventilation.*

Introduction

One of the common causes of acute respiratory failure which leads to emergency care is acute cardiogenic pulmonary oedema (ACPO). Acute cardiogenic pulmonary oedema is defined as "pulmonary oedema due to increased capillary hydrostatic pressure secondary to elevated pulmonary venous pressure." Although the most patients with acute pulmonary oedema improve with oxygen and conventional medical therapy, patients who present with a pH <7.25 or systolic blood pressure >180 mmHg are regarded as having severe form of ACPO or sometimes called as Sympathetic Crashing Acute Pulmonary Oedema (SCAPE), and they require Non-Invasive Ventilation (NIV) (1). Continuous positive airway pressure (CPAP) and Non-Invasive Bi-level Positive Airway Pressure (BiPAP) ventilation have shown to produce a more expeditious positive response by reducing left ventricular (LV) transmural pressure, lower LV afterload hence improving clinical parameters including respiratory acidosis, respiratory rate, heart rate and dyspnoea (2-5).

CPAP delivers the continuous flow of pressurized room air/ oxygen while the BiPAP refers to two-level positive airway pressure including one higher level of pressure for inhalation (IPAP), and a lower pressure for exhalation (EPAP). This helps to improve air swallowing and to enhance the comfort with patients who struggle to acclimatize CPAP. BiPAP ventilation can decrease inspiratory work of breathing more than CPAP can alone by delivering positive airway pressure at two different levels during inspiration and expiration (5).

NIV ameliorates oxygenation, increase cardiac output thereby results in rapid improvement in gas exchange and diminish the effort of breathing hence it reduces the complexity accompanied with stay in the intensive care unit and mitigating the length of hospital stay and hospital mortality (6-8). The provision of NIV prevents the adverse effects associated with endotracheal intubation (ETI) and invasive ventilation which includes upper airway trauma due to instrumentation, infections of the respiratory tract and cardiovascular complications (9-11). Furthermore, it remains uncertain whether BiPAP is advantageous compared with CPAP in acute cardiogenic pulmonary oedema (6, 8, 12-14).

Studies have shown that the use of CPAP in acute pulmonary oedema, reduces the intubation rate and that there is a tendency towards decreased mortality (5-11, 15). Studies appraising BiPAP in acute cardiogenic pulmonary oedema have shown that it enhances gas exchange (16) and further lessens the need for invasive ventilation in patients with hypercapnic respiratory failure (15, 16, 17). However, one of the earlier studies demonstrated that BiPAP compared with CPAP might increase the risk for new onset acute myocardial infarction in patients with acute cardiogenic pulmonary oedema (13, 14). Further studies and meta-analyses demonstrated that there was no such safety issue (18, 19).

Though NIV decreases the necessity of endo-tracheal intubation and improves survival, the studies are not strong enough to definitively confirm that CPAP or BiPAP is superior in terms of hospital stay or the survival rate (12-14). Furthermore, Sri Lankan data in the above field are scarce. Therefore, the following study was conducted with the aim of studying common precipitating factors of pulmonary oedema in AHF and to find out the efficacy and suitability of the CPAP vs. BiPAP ventilation in patients by assessing the outcome of patients and rating patients' preference and perception on CPAP and BiPAP.

Methods

The study was conducted at emergency treatment unit of the National Hospital of Sri Lanka and Base Hospital, Panadura, from August 2020 to December 2020.

Patients eligible for this study were required to be diagnosed with pulmonary oedema, presenting with clinical signs and symptoms such as paroxysmal nocturnal dyspnoea or orthopnoea, jugular venous distension, and inspiratory crackles often accompanied by rhonchi. Clinical and biochemical parameters for inclusion are a respiratory rate greater than 25 breaths per minute, SpO_2 less than 90%, PaO_2 / FiO_2 ratio less than 200 mmHg, or SpO_2 / FiO_2 ratio less than 235. Radiological evidence required included a 'B' profile on point-of-care lung ultrasound, and findings of cardiomegaly, upper lobe blood diversion, and 'Bat-Wing' appearance on chest X-ray. Additionally, patients older than 16 years

were included. Exclusion criteria include the need for intubation upon admission, the presence of a silent chest following respiratory failure, and the absence of clinical, electrocardiographical, and ultrasonographical features suggestive of acute heart failure (AHF). In addition patients younger than 16 years, respiratory failures other than following AHF or multiple organ dysfunctions or transferred patients who are already been stabilized were excluded.

This study was done as a preliminary study with the intention of expanding into a much larger comprehensive multi-centre study. A total of 95 patients were assessed for eligibility and 87 patients were recruited after excluding 8 patients. Under BiPAP arm 49 patients and under CPAP arm 38 patients were recruited respectively.

The recruitment procedure was done at on admission to the ETU / PCU. Once the definitive diagnosis was made, the administration of CPAP or BiPAP was selected by randomization.

Randomization

Randomization were carried out by the principal investigator at the ETU (PI). The PI used computer-generated random number software each time a patient gets admitted. Even numbers were considered as group A and odd numbers belong to group B.

Group A patients were administered with BiPAP ventilation, and group B patients received CPAP. Depending on their clinical features and the disease severity, the PI decided on pressure support (PS) and peak end-expiratory pressure (PEEP).

At any time, if the deterioration of a patient's respiratory distress is noted, treatments were given irrespective of their treatment groups.

Intervention

Standard medical therapy with oxygen, vasodilators, diuretics, thromboprophylaxis, and positioning (upright position) are instituted according to the European Society of Cardiology (ESC) guideline on ACPO. Inotropes and or vasopressors are used in selective patients. Routine monitoring of NIV, heart rate and rhythm, SPO_2 and Urine output were carried out and documented in monitoring charts.

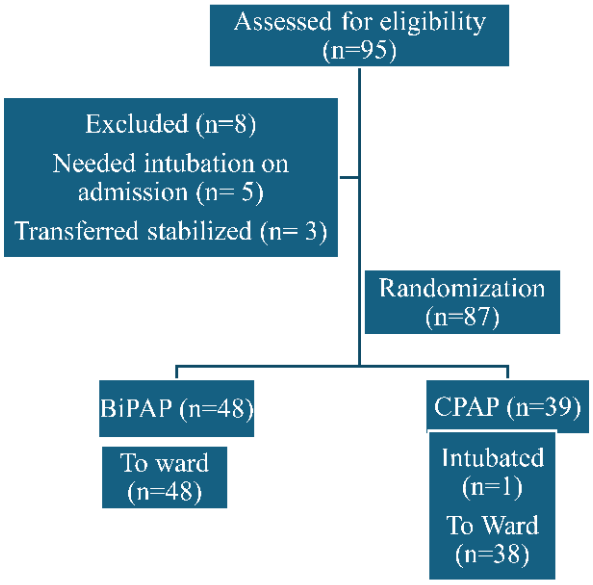

Figure 1: Consort diagram

Once randomization was completed, patients were divided into two groups. Group A received pressure limits set as follows: IPAP between 8 and 20 cm H_2O and EPAP between 4 and 10 cm H_2O, with synchronous pressure support aligned with the patient's inspiratory effort. Group B received a CPAP set between 10 and 15 cm H_2O. An oronasal mask was used for both groups. Patients who could not tolerate CPAP were switched to BiPAP.

Therapy was administered for a duration of two hours, after which outcome variables were measured to assess the efficacy of the intervention. Serial arterial or venous blood gases (ABG/ VBG) were obtained, particularly before the intervention, at the two-hour mark of treatment initiation, or before weaning, whichever occurred first. Weaning was carried out when the respiratory rate was less than 25 breaths per minute and SpO_2 was greater than 95%. During weaning, CPAP/ BiPAP pressures were gradually reduced by 2 cm H_2O at a time.

Outcomes

After 2 hours of CPAP or BiPAP therapy, improvement of respiratory distress (determined by improvement of clinical features) was assessed. According to the response, a Trained/ Senior Medical Officer in the ETU/ Senior Registrar made a further treatment plan (PI).

The following situations were considered as instances of treatment failures

1. Discontinuation of the treatment (Technique) in patients who could not tolerate it for 2 hours or deterioration of either gas exchange or clinical situation/ parameters

   GCS < 13, Respiratory rate > 40 breaths/ minute, PaO_2 < 60 mmHg, $PaCO_2$ increase of 5 mmHg
2. Death

Ethical Consideration

Following recruitment, all patients were given the information sheet in their conversant language and the procedure were explained by the Medical Officer/ Senior Registrar. Once all the problems are clarified, informed written consent was obtained.

Randomization procedure was done strictly by the Trained/ Senior Medical Officer in the ETU/ Senior Registrar and patient's social factors will not be considered under any circumstance. However, during the whole process of clinical trial, all patients were monitored for deterioration. In any deterioration appropriate measurements were taken irrespective of patient's group (i.e. group A or B).

All patients and their bystanders were informed prior to the procedure regarding the study. Any patient who did not show interest on participation, were still treated during the entire period. If any patient who consented to participate in the study, and later wished to withdraw, were still treated as the same way as other patients.

Finally, minimal disturbance to routine activities at ETU/ PCU is ensured during the whole period. Ethical approval for the study was obtained from Ethics Review Committee, National Hospital of Sri Lanka, Colombo.

Results

A total of 95 patients were assessed in the study and 87 were recruited while 8 were excluded. There were 48 patients for BiPAP and 39 patients for CPAP. The mean age of the study sample was as 64.58 (SD ± 11.85) years with a gender distribution of 54% females and 46% of males.

Most common comorbidity among the studied population was hypertension (57 patients - 66.3%) patients followed by ischaemic heart disease (43 - 50.0%), diabetes mellitus (41 - 47.7%) and congestive heart failure (33 - 38.4%) (Table1). Furthermore, acute onset myocardial ischemia was identified as probable precipitating factors in 45 (53.57%) patients. Moreover, infection and poor drug compliance were evident in 14 (16.66%) patients (Table 2).

Table 1: Prevalence of comorbidities in the patient group

Comorbidities	Frequency (%)
Hypertension	57 (66.3)
Congestive heart failure	33 (38.4)
Ischaemic heart disease	43 (50.0)
Diabetes Mellitus	41 (47.7)
Chronic obstructive pulmonary disease	14 (16.3)
Valvular heart disease	4 (4.7)
Atrial fibrillation	3 (3.5)
Chronic kidney disease	13 (15.1)
Congenital heart disease	2 (2.3)

Table 2: Probable precipitating factor for pulmonary oedema

Probable precipitating factors	Frequency (%)
Acute onset myocardial ischaemia	45 (53.57)
Infection	14 (16.66)
Acute kidney injury	3 (3.57)
Acute lung injury	6 (7.14)
Poor drug compliance	14 (16.66)
Other	11 (13.09)

Heart Rate at 2 hours or end of treatment in the BiPAP group was 102 ± 92.819 bpm and 84 ± 13.326 bpm in CPAP group. Blood pressure (SBP/DBP)

at 2 hours or end of treatment was 140 ± 21.780 / 83 ± 11.450 mmHg in BiPAP group and 135 ± 30.042 / 86 ± 14.190 mmHg in CPAP group.

Respiratory rate (RR) at 2 hours or end of treatment was 26 ± 32.448 and 20 ± 4.10 in BiPAP group and CPAP group respectively. $PaCO_2$, at 2 hours or end of treatment was 45 ± 9.241 in BiPAP and 40 ± 7.412 in CPAP. Lactate, at 2 hours or end of treatment was 1 ± 2.385 and 2 ± 2.851 and HCO_3, at 2 hours or end of treatment was 24 ± 5.7, 22 ± 3.745 in BiPAP and CPAP respectively which shows improvement from baseline.

Table 3: Vital parameters by BiPAP and CPAP

BiPAP (N=48)				**CPAP (N=39)**		
Variable	**On admission**	**At 2 hours or end of treatment**	***p* value**	**On admission**	**At 2 hours or end of treatment**	***p* value**
HR (bpm)	112 ± 21.704	102 ± 92.819	<0.001	106 ± 21.044	84 ± 13.326	<0.001
SBP (mmHg)	173 ± 36.855	140 ± 21.780	<0.001	161 ± 43.907	135 ± 30.042	<0.001
DBP (mmHg)	100 ± 24.038	83 ± 11.450	<0.001	100 ± 26.696	86 ± 14.190	<0.001
RR (/min)	32 ± 6.601	26 ± 32.448	<0.001	32 ± 6.085	20 ± 4.108	<0.001
UOP (ml)	320 ± 188.65	210 ± 337.77	0.317	225 ± 317.49	325 ± 247.48	0.425

HR: Heart Rate. SBP: Systolic blood pressure. DBP: Diastolic Blood Pressure
RR: Respiratory rate. UOP: Urine output (for 2hrs on end of treatment)

Table 4: Blood Gas by BiPAP and CPAP

BiPAP (N=48)				**CPAP (N=39)**		
Variable	**On admission**	**At 2 hours or end of treatment**	***p* value**	**On admission**	**At 2 hours or end of treatment**	***p* value**
PaO_2 / FiO_2	36 ± 5.91	128 ± 33.997	<0.001	38 ± 4.836	126 ± 35.10	<0.001
SPO_2 / FiO_2	84 ± 6.162	300 ± 70.371	<0.001	85 ± 7.41	275 ± 78.635	<0.001
PaO_2 (mmHg)	37 ± 12.394	48 ± 21.703	<0.001	33 ± 17.291	43 ± 6.046	<0.001
$PaCO_2$ (mmHg)	62 ± 14.354	45 ± 9.241	<0.001	42 ± 20.8	40 ± 7.412	0.001
Lactate (mmol/l)	3 ± 3.393	1 ± 2.385	<0.001	3 ± 3.136	2 ± 2.851	0.001
HCO_3 (mEq/l)	21 ± 8.583	24 ± 5.7	0.006	16 ± 7.711	22 ± 3.745	<0.001
Base Excess - ECF (mEq/l)	-4 ± 10.09	0.24 ± 7.60	0.034	-6 ± 7.30	-3 ± 2.585	0.003

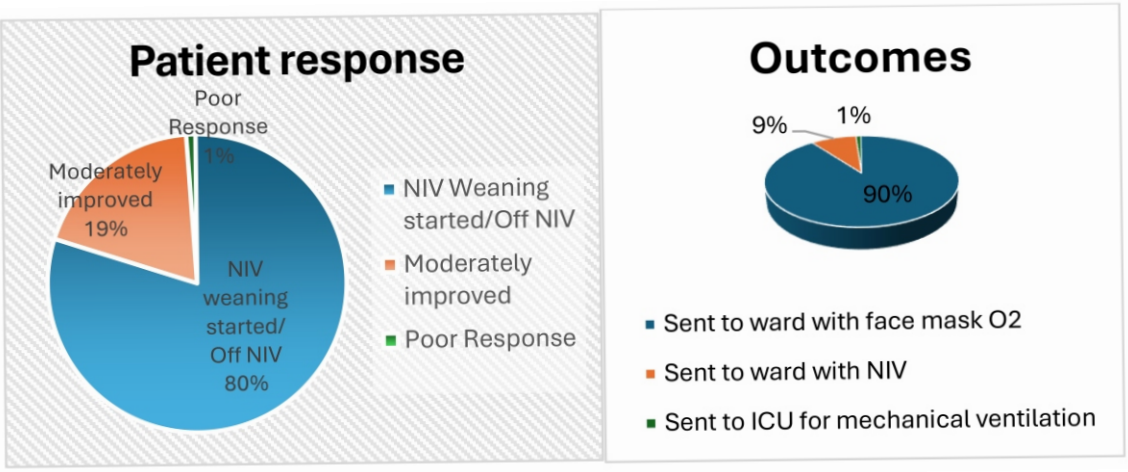

Figure 2: Response and outcomes of non-invasive ventilation (NIV)

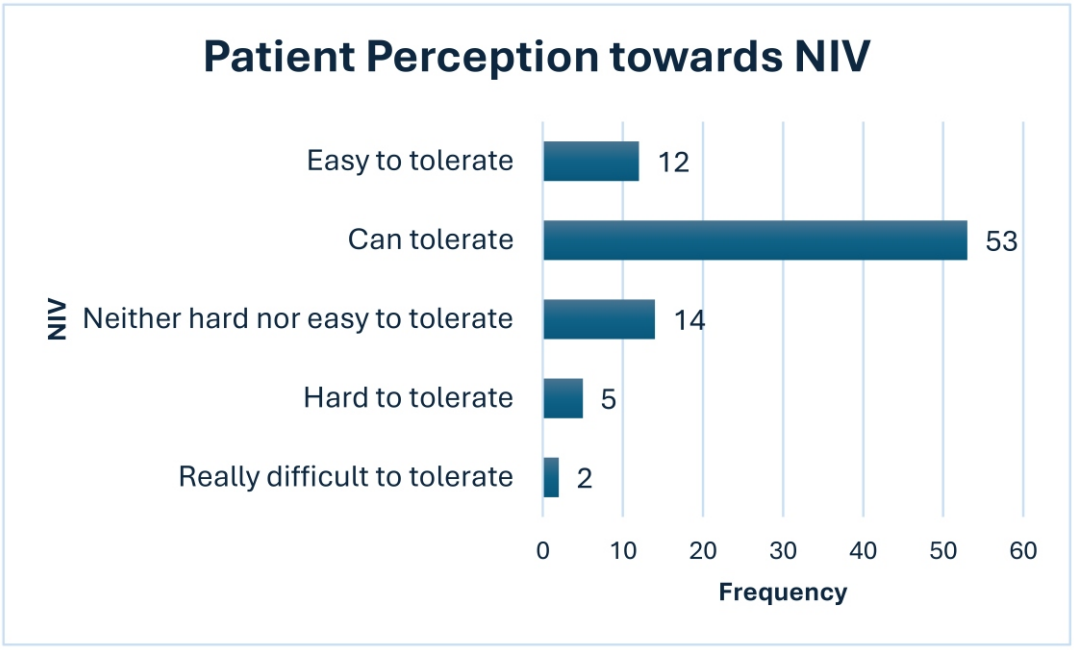

Figure 3: Patients' perception on non-invasive ventilation (NIV)

Out of 87 patients, 69 (80.2%) responded well and improved with noninvasive ventilation, while one patient (CPAP-1.2%) had a poor response and were sent to ICU for mechanical ventilation. Regarding the outcome, 78 (90.7%) patients were sent to ward with face mask O_2 and 4 (4.7%) with NIV. Two patients (2.3%) indicated that that it is difficult tolerance and 12 (14.0%) easy tolerance and 53 (61.6%) stated NIV is tolerable.

Limitations

Arterial blood gas sampling was not always done, and venous gas sampling was used instead in a few instances. Therefore PaO_2/ FiO_2 calculated values included values taken from venous sampling which is not ideal. To circumvent the aforementioned issue SPO_2/ FiO_2 values were used as a surrogate marker. The study sample was collected from 2 institutions, NHSL and Base Hospital Panadura.

Therefore, may not be exactly comparable. The study had to discontinue abruptly due to the Covid pandemic, and hence unequal numbers in BiPAP and CPAP groups.

Discussion

Acute pulmonary oedema is a life-threatening condition and even though majority of the patients improve with pharmacological management, some of patients require non-invasive ventilation such as continuous positive airway pressure (CPAP) ventilation and bi-level positive airway pressure (BiPAP) ventilation to manage severe respiratory distress (16-25). CPAP therapy will improve inspiratory and expiratory flow rates as well as enhance alveolar ventilation, hence preventing micro atelectasis. This will enhance hemodynamics and diminish left ventricular afterload, thus, improving pulmonary oedema (3, 4, 17). BiPAP conveys two different pressures, thereby increasing tidal volume and diminishing respiratory workload and resolving hypercapnia and pulmonary oedema (5, 7).

Our study was designed to assess the improvement of vital parameters and blood gases following CPAP and BiPAP administration according to its duration of treatment (after standard medical therapy). Results found that SPO_2 /FiO_2 ratio after 2 hours of duration with BiPAP was increased from 84 ± 6.162 to 300 ± 70.371 mmHg and from 85 ± 7.41 to 275 ± 78.635 mmHg in CPAP therapy. SPO_2/ FiO_2 ratio was used instead PaO_2/ FiO_2 ratio as a surrogate marker to detect improvement of gas exchange (26) as venous blood gases are used in some instances. Results showed that the BiPAP may be more advantageous in diminishing the $PaCO_2$ level of patients with significant hypercapnia. Similarly, Liesching T, *et al.,* and Nouira S, *et al.,* observed that BiPAP improves the hypercapnia rapidly by diminishing breathing workload and thereby improving/ increasing cardiac output, hence more effective and reducing dyspnea scores in acute pulmonary oedema (18). Following 2 hours of treatment, both BiPAP and CPAP exhibited reducing lactate levels and improving bicarbonate levels, hence improving acidosis. Moreover, in both BiPAP and CPAP hemodynamics such as heart rate, respiratory rate, blood pressure levels were stabilized within normal parameters, even though the heart rate remains slightly elevated in the patients who were treated with BiPAP. Similar results were demonstrated in a study conducted by Summers *et al*, that hemodynamic stability showed that BiPAP was capable of improving hemodynamics such as heart rate, systemic blood pressure, ejection fraction and diastolic pressure in patients with type 2 respiratory failure and acute pulmonary oedema (27). Prior studies found that, CPAP will increase intrathoracic pressure, hence ventricular preload and afterload will be diminished. Whereas BiPAP will engage in enhancing pulmonary circulation (30). The most common co-morbidity amongst patients with ACPO was hypertension (66.3%) followed by IHD of 50%, Diabetes Mellitus 47.7% and congestive heart failure among 38.4% of the study population. Therefore, these co-morbidities may have played a pivotal role in development acute pulmonary oedema. Furthermore, regarding the precipitating factors, acute onset of myocardial ischaemia was identified as the most prevalent factor presented among 45 (53.57%) patients. Moreover, infection and poor drug compliance were evident in 14 (16.66%) patients.

Studies have been conducted to detect the superiority of BiPAP over CPAP alone. A study conducted by Meheta S, *et al.,* showed that substantial depletion in $PaCO_2$, blood pressure components including, systolic and mean arterial pressure, and hypercapnia in the BiPAP group than in the CPAP group (13). But the major limitation of this study was that approximately 71% of the BiPAP group had a high myocardial infarction rate while the rate of CPAP group was around 31% (13). In contrast to these results, Park, *et al.*, (12) and Bellone, *et al.,* (14) demonstrated that BiPAP was as effective as CPAP and both methods improved ventilation and vital signs in patients with ACPO, without any remarkable differences in hospital mortality and acute myocardial infarction rates in comparison with CPAP alone (14). The comparison data from 183 patients between CPAP and BiPAP in CPO, showed that BiPAP increases intubation rates.

A meta-analysis done with seven studies including 290 patients showed that there was fine comprehensive cohesion in most of the results

and hospital mortality and the possibility for the need of invasive ventilation were not significantly different between patients treated with CPAP and those treated with BiPAP (14, 17, 27-30). Distinguishing studies into use of BiPAP at vacillating or fixed levels of airway pressure did not have any influence towards the results. The studies appraising the higher span pressures in CPAP and BiPAP demonstrated that the time needed to resolve ACPO with NIV, the relative risk ratios for hospital mortality and requiring invasive ventilation were at a fixed level (14, 17, 27-29). Sensitivity analysis including studies that involved patients with significant hypercapnia had not change the results (21).

A randomized comparison done in the UK emergency department setting showed that efficacy of CPAP is superior to the efficacy with bilevel ventilation or with conventional oxygen therapy in patients presenting with ACPO and acidosis. However, there were no significant differences in hospital survival rate and early physiological changes (31).

A prospective multicentre randomized study done in France showed clinical improvement in respiratory distress and blood gas exchange after 1 hour of ventilation in both Boussignac CPAP and BiPAP methods in hypercapnic patients, but the patient outcome did not show any difference between CPAP and BiPAP methods (18).

Considering the outcome, this study showed that 80.2% patients responded well and improved with NIV, while only one patient required ICU support with mechanical ventilation who later passed away. In contrast, Nava, *et al.,* has shown that although NIV reduces the heart rate, improves dyspnea and enhances alveolar gaseous exchange, it does not had an impact on overall clinical outcome, such as rate of intubation, hospital mortality, and duration of hospital stay (29). However, a systematic review done by Pang D, *et al.,* concluded that CPAP is effective in stabilizing vital parameters and diminishes the intubation rate, but not had any effect on mortality rate (17). In respect of the tolerability in our study, few patients around 5 (5.8%) stated that NIV is quite difficult to tolerate. But more than 60% patients agreed that NIV was given less discomfort to them. This indicates that both BiPAP and CPA methods ameliorate acute pulmonary oedema with a higher patient satisfaction.

Conclusion and Recommendations

The results of our study found that hypertension is the most common co-morbidity and acute onset of myocardial ischemia is the most common precipitating factor associated with pulmonary oedema. Both CPAP and BiPAP are capable of improving vital parameters, gas exchange and ameliorating respiratory distress, hence effective in managing acute pulmonary oedema. Furthermore, the BiPAP group demonstrated a higher heart rate at the end of treatment than the CPAP group. Although the study does not demonstrate a significant clinical benefit of BiPAP over CPAP, it found that the BiPAP may be more advantageous in diminishing the $PaCO_2$ level of patients with significant hypercapnia. This study demonstrated that both BiPAP and CPAP methods ameliorate acute pulmonary oedema with a higher patient's perception. However, more studies in the future are essential to clarify the efficacy of CPAP vs BiPAP in the management of acute cardiopulmonary oedema.

References

1. Masip J, Páez J, Merino M, Parejo S, Vecilla F, Riera C, Ríos A, Sabater J, Ballús J, Padro J. Risk factors for intubation as a guide for noninvasive ventilation in patients with severe acute cardiogenic pulmonary oedema. *Intensive Care Medicine.* 2003; **29**:1921-1928.
2. Räsänen J, Heikkilä J, Downs J, Nikki P, Väisänen I, Viitanen A. Continuous positive airway pressure by face mask in acute cardiogenic pulmonary edema. *The American Journal of Cardiology.* 1985; **55**(4): 296-300.
3. Naughton MT, Rahman MA, Hara K, Floras JS, Bradley TD. Effect of continuous positive airway pressure on intrathoracic and left ventricular transmural pressures in patients with congestive heart failure. *Circulation.* 1995; **91**(6): 1725-1731.
4. Bendjelid K, Schütz N, Suter PM, Fournier G, Jacques D, Fareh S, Romand J-A. Does continuous positive airway pressure by face mask improve patients with acute cardiogenic pulmonary oedema due to left ventricular diastolic dysfunction? *Chest.* 2005; **127**(3): 1053-1058.

24.. Vital FM, Ladeira MT, Atallah ÁN. Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema. *Cochrane Database of Systematic Reviews.* 2013(5).

6. L'Her E, Duquesne F, Girou E, de Rosiere XD, Conte PL, Renault S, Allamy J-P, Boles J-M. Noninvasive continuous positive airway pressure in elderly cardiogenic pulmonary oedema patients. *Intensive Care Medicine.* 2004; **30**: 882-888.

7. Brochard L, Mancebo J, Elliott M. Noninvasive ventilation for acute respiratory failure. *European Respiratory Journal.* 2002; **19**(4): 712-721.

8. Lin M, Yang Y-F, Chiang H-T, Chang M-S, Chiang BN, Cheitlin MD. Reappraisal of continuous positive airway pressure therapy in acute cardiogenic pulmonary oedema: short-term results and long-term follow-up. *Chest.* 1995; **107**(5): 1379-1386.

9. Zwillich CW, Pierson DJ, Creagh CE, Sutton FD, Schatz E, Petty TL. Complications of assisted ventilation: a prospective study of 354 consecutive episodes. *The American Journal of Medicine* 1974; **57**(2): 161-170.

10. Stauffer JL, Olson DE, Petty TL. Complications and consequences of endotracheal intubation and tracheotomy: a prospective study of 150 critically ill adult patients. *The American Journal of Medicine.* 1981; **70**(1): 65-76.

11. Pingleton SK. Complications of acute respiratory failure. *Am Rev Respir Dis.* 1988; **137**(6): 1463-1493.

12. Park M, Sangean MC, Volpe MdS, Feltrim MI, Nozawa E, Leite PF, Amato MBP, Lorenzi-Filho G. Randomized, prospective trial of oxygen, continuous positive airway pressure, and bilevel positive airway pressure by face mask in acute cardiogenic pulmonary oedema. *Critical Care Medicine.* 2004; **32**(12): 2407-2415.

13. Mehta S, Jay GD, Woolard RH, Hipona RA, Connolly EM, Cimini DM, Drinkwine JH, Hill NS. Randomized, prospective trial of bilevel versus continuous positive airway pressure in acute pulmonary oedema. *Critical Care Medicine.* 1997; **25**(4): 620-628.

14. Bellone A, Monari A, Cortellaro F, Vettorello M, Arlati S, Coen D. Myocardial infarction rate in acute pulmonary oedema: noninvasive pressure support ventilation versus continuous positive airway pressure. *Critical Care Medicine.* 2004; **32**(9): 1860-1865.

15. Bersten AD, Holt AW, Vedig AE, Skowronski GA, Baggoley CJ. Treatment of severe cardiogenic pulmonary oedema with continuous positive airway pressure delivered by face mask. *New England Journal of Medicine.* 1991; **325**(26): 1825-1830.

16. Agarwal R, Aggarwal A, Gupta D, Jindal S. Non-invasive ventilation in acute cardiogenic pulmonary oedema. *Postgraduate Medical Journal* 2005; **81**(960): 637-643.

17. Pang D, Keenan SP, Cook DJ, *et al.* The effect of positive pressure airway support on mortality and the need for intubation in cardiogenic pulmonary oedema: a systematic review. *Chest*. 1998; **114**: 1185-92.

18. Liesching T, Nelson DL, Cormier KL, Sucov A, Short K, Warburton R, Hill NS: Randomized trial of bi-level versus continuous positive airway pressure for acute pulmonary edema. *The Journal of Emergency Medicine.* 2014; **46**(1): 130-140.

19. Ferrari G, Olliveri F, De Filippi G, Milan A, Aprà F, Boccuzzi A, Converso M, Navalesi P. Noninvasive positive airway pressure and risk of myocardial infarction in acute cardiogenic pulmonary oedema: continuous positive airway pressure vs noninvasive positive pressure ventilation. *Chest.* 2007 Dec; **132**(6): 1804-9. DOI: 10.1378/chest.07-1058. Epub 2007 Oct 1.

20. Dean R Hess. Should Noninvasive Ventilation Be Used for Treatment of Acute Cardiogenic Pulmonary Edema? A Cochrane Review Summary with Commentary. *Respiratory Care.* April 2020; **65**(4): 573-574. DOI: https://doi.org/10.4187/respcare.07685

21. Fabienne Moritz, Benoit Brousse, Bruno Gellée, Abdesslam Chajara, Marie-France Hellot, Jacques Bénichou, Erwan L'Her, Continuous Positive Airway Pressure Versus Bi-level Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema: A Randomized Multicenter Trial. Airway. (Original Research) Dec 2007; **50**(6): 666-675.e1.

22. Pirracchio R, Rigon MR, Mebazaa A, Zannad F, Alla F, Chevret S. Continuous positive airway pressure (CPAP) may not reduce short-term mortality in cardiogenic pulmonary oedema: a propensity-based analysis. *Journal of Cardiac Failure*. 2013; **19**(2): 108-116.

23. Aliberti S, Rosti VD, Travierso C, Brambilla AM, Piffer F, Petrelli G, Minelli C, Camisa D, Voza A, Guiotto G. A real life evaluation of non-invasive ventilation in acute cardiogenic pulmonary edema: a multicenter, perspective, observational study for the ACPE SIMEU study group. *BMC Emergency Medicine.* 2018; **18**: 1-5.

24. Mariani J, Macchia A, Belziti C, DeAbreu M, Gagliardi J, Doval H, Tognoni G, Tajer C: Noninvasive ventilation in acute cardiogenic pulmonary edema: a meta-analysis of randomized controlled trials. *Journal of Cardiac Failure* 2011; **17**(10): 850-859.

25. Chadda K, Annane D, Hart N, Gajdos P, Raphaël JC, Lofaso F: Cardiac and respiratory effects of continuous positive airway pressure and noninvasive ventilation in acute cardiac pulmonary edema. *Critical Care Medicine.* 2002; **30**(11): 2457-2461.

26. Babu S, Abhilash KP, Kandasamy S, Gowri M. Association between SpO_2/FiO_2 ratio and PaO_2/FiO_2 ratio in different modes of oxygen supplementation. *Indian Journal of Critical Care Medicine*. Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine 2021; **25**(9): 1001.

27. Summers RL, Patch J, Kolb JC. Effect of the initiation ofnoninvasive bi-level positive air way pressure on haemodynamic stability. *Eur J Emerg Med.* 2002; **9**(1): 37-41.

28. Takeda S, Nejima J, Takano T, Nakanishi K, Takayama M, Sakamoto A, Ogawa R: Effect of nasal continuous positive airway pressure on pulmonary edema complicating acute myocardial infarction. *Japanese Circulation Journal.* 1998; **62**(8): 553-558.

29. Nava S, Carbone G, DiBattista N, Bellone A, Baiardi P, Cosentini R, Marenco M, Giostra F, Borasi G, Groff P. Noninvasive ventilation in cardiogenic pulmonary edema: a multicenter randomized trial. *American Journal of Respiratory and Critical Care Medicine.* 2003; **168**(12): 1432-1437.

30. Crane S, Elliott M, Gilligan P, Richards K, Gray A. Randomised controlled comparison of continuous positive airways pressure, bi-level non-invasive ventilation, and standard treatment in emergency department patients with acute cardiogenic pulmonary oedema. *Emergency Medicine Journal.* 2004, **21**(2): 155-161.