**ORIGINAL RESEARCH**

# To assess the serum electrolyte levels, acid-base balance, and the necessity of non-invasive ventilation in patients experiencing a hypercapnic acute exacerbation of chronic obstructive pulmonary disease

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**ABSTRACT**

**Aim:** The objective of this study is to assess the serum electrolyte levels, acid-base balance, and the necessity of non-invasive ventilation in patients experiencing a hypercapnic acute exacerbation of chronic obstructive pulmonary disease.

**Material and Methods:** A prospective and observational study was conducted on a cohort of 100 patients who were admitted to the Department of Pulmonary Medicine due to exacerbation of chronic obstructive pulmonary disease (COPD). Blood investigation were performed. They include arterial blood gases (ABG) and electrolyte levels (Sodium (Na) and potassium (K).

**Results:** The mean potassium of the patients who need medical treatment only was 3.69±0.39 m E q/l and mean Sodium was 137.25±3.96 m E q/l, whereas the mean potassium for the other group was 4.29±0.55 m E q/l and mean Sodium was 135.17±4.17 m E q/l. The mean serum Bicarbonate of the group the need medical treatment only was 23.66±2.33 m Eq /l. The mean serum Bicarbonate of the other group was 29.01±2.11 m E q/l. In table 5, the Sodium and Potassium levels before treatment were 135.17±4.17 and 4.29±0.55 m E q/l, respectively, and mean Sodium and Potassium levels after treatment were 133.33±3.74 and 3.42±0.52 m E q/l, respectively.

**Conclusion:** Noninvasive positive pressure ventilation (NPPV) has the potential to facilitate the effectiveness of alternative treatments in cases of hypercapnic respiratory failure, thereby potentially circumventing the need for endotracheal intubation. While less severe instances of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) typically exhibit reversibility, the presence of more severe respiratory failure is linked to a significant mortality rate and an extended period of disability among those who survive.

**Keywords:** Serum electrolyte Acid-base balance, Non-invasive ventilation, Chronic obstructive pulmonary disease.



## Introduction

The occurrence of hypercapnia and respiratory acidosis arises from a reduction in ventilation, resulting in an inadequate removal of carbon dioxide by the respiratory system relative to its production in the tissues. Lung diseases that induce irregularities in the process of alveolar gas exchange generally do not lead to alveolar hypoventilation. Frequently, these diseases elicit an increase in ventilation and hypocapnia as a result of reflex receptors and hypoxia [1]. Hypercapnia is commonly observed in the advanced stages of pulmonary disease or when the respiratory muscles become fatigued. The topics of interest are Pediatric Respiratory Acidosis, Metabolic Acidosis, and Pediatric Metabolic Acidosis. [2]Respiratory acidosis can manifest as

either an acute or chronic condition. Acute respiratory acidosis is characterized by an elevation of PaCO2 above the upper limit of the reference range, specifically exceeding 45 mm Hg, and is accompanied by acidemia, indicated by a pH below 7.35. Chronic respiratory acidosis is characterized by an elevation of PaCO2 beyond the upper limit of the reference range. This condition is accompanied by a normal or near-normal pH due to renal compensation, as well as increased levels of serum bicarbonate (greater than 30 m E q/L). Acute respiratory acidosis is characterized by the sudden onset of ventilation failure. The lack of proper ventilation can be attributed to the suppression of the central respiratory center caused by one or more of the following factors: The etiology of respiratory depression can be attributed to either central nervous system disorders or the administration of certain drugs. The inability to achieve sufficient ventilation can arise from conditions such as neuromuscular diseases or paralysis, including myasthenia gravis, amyotrophic lateral sclerosis (ALS), Guillain-Barré syndrome, and muscular dystrophy. Additionally, airway obstruction is commonly associated with asthma or chronic obstructive pulmonary disease (COPD). [4]Chronic respiratory acidosis can arise as a result of various disorders, such as chronic obstructive pulmonary disease (COPD) [5]. Hypoventilation in chronic obstructive pulmonary disease (COPD) encompasses a range of mechanisms, which can be summarized as follows:There is a reduced level of reactivity observed in response to hypoxia and hypercapnia. The occurrence of heightened ventilation-perfusion mismatch results in an elevation in dead space ventilation. [6] The diminished functionality of the diaphragm resulting from fatigue and hyperinflation. Chronic respiratory acidosis can also arise as a result of obesity hypoventilation syndrome (OHS), commonly known as Pickwickian syndrome. It can also be associated with neuromuscular disorders like amyotrophic lateral sclerosis (ALS), as well as severe restrictive ventilatory defects seen in interstitial fibrosis and thoracic skeletal deformities. This study employed a pathophysiologic approach, guided by the principles of compensation laws, to assess acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD). In the context of acute exacerbations of chronic obstructive pulmonary disease (AECOPD), the occurrence or exacerbation of respiratory acidosis is attributed to the hypoventilation associated with hypercapnia. Given that a significant portion of these patients, particularly those who are elderly and in critical condition, are receiving multiple medications for their coexisting medical conditions, it is quite common for them to experience antibiotic (AB) and electrolyte imbalances. This prevalence of AB and electrolytic disorders can introduce a potential bias when interpreting the final values.

**Material and Methods**

A prospective and observational study was conducted on a cohort of 100 patients who were admitted to the Department of Pulmonary Medicine due to exacerbation of chronic obstructive pulmonary disease (COPD). Blood investigation were performed. They include the following:

(1) Arterial blood gases (ABG).
(2) Electrolyte levels (Sodium (Na) and potassium (K).

**Methodology**

Chest radiography has the potential to indicate the presence of chronic obstructive pulmonary disease (COPD), although it should be noted that it is not considered a definitive diagnostic tool for this condition. Radiographs were employed for the purpose of diagnosing pneumonia and ruling out alternative causes of dyspnea in patients with chronic obstructive pulmonary disease (COPD), such as the presence of ruptured emphysematous bullae. Upon admission, all patients were administered oxygen via nasal cannula or mask in order to maintain a normal arterial oxygen saturation level of at least 90%. Additionally, patients were provided with bronchodilators, corticosteroids, and antibiotics. A follow-up study was conducted on patients who underwent clinical examination and laboratory investigations. The results revealed that a portion of the patients demonstrated improvement, while others experienced a decline in their condition, leading to the administration of non-invasive ventilation (NIV). Non-invasive ventilation (NIV) was administered using an oronasal mask in conjunction with a pressure/volume ventilator. The adjustment of support pressure, Positive End Expiratory Pressure (PEEP), and triggered flows was performed in order to achieve a tidal volume within the range of 6-8 ml/kg, optimize oxygenation, and reduce respiratory rate. The adjustments to support pressure and positive end-expiratory pressure (PEEP) were made in accordance with the arterial gas measurements. The average Inspiratory Positive Assisted Pressure (IPAP) was determined to be 16 ± 4 cm H2O.

**Result**

In the table 1, the mean age of the NIV positive were 60.58±5.85 years and NIV negative were 63.15±5.98 years, who were admitted to the Department of pulmonary medicine, with hypercapnic COPD exacerbation. They were classified according to the type of management into two groups: the first group received medical treatment and the second received non- invasive positive pressure ventilation (NIPPV). The total number of patients were 100, where 80 of them were males and 20 females.

**Table 1: Distribution of sex and age**

| Gender | Need for non-invasive ventilation | | p-value |
|---|---|---|---|
| | NIV Positive (N=50) | NIV Negative (N=50) | |
| Male | 41 (82) | 39 (78) | 0.08 |
| Female | 9 (18) | 11 (22) | |
| Age | 60.58±5.85 | 63.15±5.98 | 0.33 |

**Table 2: Arterial blood gases finding of the studied group**

| **Acid–base disturbance** | **Need for non-invasive ventilation** | | **p-value** |
|---|---|---|---|
| | NIV Positive (N=50) | NIV Negative (N=50) | |
| Compensated respiratory acidosis | 14 (18) | 43 (86) | <0.0001 |
| Mixed respiratory acidosis and metabolic alkalosis | 20 (40) | 5 (10) | |
| Combined respiratory and metabolic acidosis | 16(32) | 2 (4) | |
| PO2 | 55.11±4.71 | 64.21±4.39 | <0.05 |
| PCO2 | 60.25±4.19 | 50.31±6.2 | <0.05 |

In table: 2, according to ABG finding, patients were classified into three groups: the first group comprised 57(57%) patients who had compensated respiratory acidosis, and the majority of them (43 Patients) received medical treatment only. The second group comprised 25(25%) patients, who had mixed respiratory acidosis and metabolic alkalosis. Overall, 20 patients needed non-invasive mechanical ventilation with the medical treatment. The third group comprised 18 (18%) who had combined respiratory and metabolic acidosis. Of them, 16 patients needed non-invasive mechanical ventilation with the medical treatment and mean PO2 was 55.11±4.71 mmHg whereas mean PCO2 was 60.25±4.19 mmHg.

**Table 3: Electrolytes finding of the studied group**

| **Electrolytes** | **Need for non-invasive ventilation (Mean±SD)** | | **p-value** |
|---|---|---|---|
| | NIV Positive | NIV Negative | |
| Sodium (mEq/l) | 135.17±4.17 | 137.25±3.96 | 0.36 |
| Potassium (mEq/l) | 4.29±0.55 | 3.69±0.39 | <0.05 |
| Bicarbonate (mEq/l) | 29.01±2.11 | 23.66±2.33 | <0.05 |

In table 3, the mean potassium of the patients who need medical treatment only was 3.69±0.39 m E q/l and mean Sodium was 137.25±3.96 m E q/l, whereas the mean potassium for the other group was 4.29±0.55 m E q/l and mean Sodium was 135.17±4.17 m E q/l. The mean serum Bicarbonate of the group the need medical treatment only was 23.66±2.33 m E q/l. The mean serum Bicarbonate of the other group was 29.01±2.11 m E q/l..

**Table 4: Outcome and characteristic of the group that needed NIPPV from the start**

| Acid–base disturbance | Studies groups non-invasive ventilation (N=50) | | p-value |
|---|---|---|---|
| | Improved (N=47) | Failed (N=3) | |
| Compensated respiratory acidosis | 14 (29.79) | 0 (0) | <0.0001 |
| Mixed respiratory acidosis and metabolic alkalosis | 19(40.43) | 1(33.33) | |
| Combined respiratory and metabolic acidosis | 14 (29.79) | 2 (66.67) | |
| PO2 | 55.01±3.66 | 42.15±4.85 | <0.0001 |
| PCO2 | 60.05±3.63 | 57.13±3.17 | 0.21 |

**Table 5: Effect of COPD treatment on the patient electrolytes**

| | Before treatment | After treatment | P |
|---|---|---|---|
| Sodium (mEq/l) | 135.17±4.17 | 133.33±3.74 | >0.05 |
| Potassium (mEq/l) | 4.29±0.55 | 3.42±0.52 | <0.05 |

In table: 5, the Sodium and Potassium levels before treatment were 135.17±4.17 and 4.29±0.55 m Eq/l, respectively, and mean Sodium and Potassium levels after treatment were 133.33±3.74 and 3.42±0.52 m Eq/l, respectively.

**Discussion**

Numerous systematic reviews and meta-analyses have indicated a higher prevalence of chronic obstructive pulmonary disease (COPD) among individuals who smoke or have a history of smoking, male individuals, and those who are aged 40 years or older. The PLATINO study was conducted to ascertain the prevalence of post-bronchodilator airflow obstruction in several Latin American countries, namely Brazil, Uruguay, Chile, Mexico, and Venezuela. The study indicated that the highest prevalence was observed in individuals aged 60 years and older. Individuals who have pre-existing chronic obstructive pulmonary disease (COPD) and experience a worsening of their COPD symptoms, along with hypercapnic respiratory distress or respiratory failure, are the demographic that exhibits the highest probability of achieving positive outcomes through the application of noninvasive ventilation (NIV). Exacerbations in these patients lead to an elevation in the effort required for breathing, surpassing the patient's capacity to adequately ventilate. This is attributed to several mechanisms, such as heightened hyperinflation resulting in reduced diaphragmatic excursion and strength, augmented intrinsic positive end-expiratory pressure (PEEP), insufficient or ineffective generation of tidal volume, alterations in respiratory patterns, and an elevated respiratory frequency. Noninvasive ventilation has been shown to effectively relieve the respiratory muscles, resulting in an increase in tidal volume, a decrease in respiratory rate, and a reduction in the work of breathing for the diaphragm. These improvements are associated with enhanced oxygenation, reduced hypercapnia, and alleviation of dyspnea, as supported by multiple studies [7-11]. Our study included a sample of 100 patients who experienced exacerbation of chronic obstructive pulmonary disease (COPD). At the outset, a cohort of 50 patients underwent medical intervention, while an additional 50 patients required non-invasive positive pressure ventilation (NIPPV) from the onset. Based on the clinical evaluation and the patients' reaction to oxygen therapy, it was observed that only three individuals exhibited unsuccessful outcomes with non-invasive ventilation (NIV). In our study, the average age of individuals who tested positive for NIV was 60.58±5.85 years, while those who tested negative had an average age of 63.15±5.98 years. The total sample size consisted of 100 patients, with 80 being male and 20 being female. The observed disparities in sex may be attributed to various factors, including variations in airway anatomy, disparities in smoking behaviors, differences in respiratory symptoms, and variances in environmental or occupational exposures. These findings align with the outcomes reported in the investigation conducted by Struik FM et al. In the present study, the categorization of arterial blood gases was performed, resulting in the identification of three distinct groups. These groups were labeled as group A, which represented compensated respiratory acidosis, group B, which denoted mixed respiratory acidosis and metabolic alkalosis, and group C, which indicated combined respiratory and metabolic acidosis. Our findings indicate that the group characterized by respiratory acidosis and metabolic acidosis (group C) exhibited the highest level of criticality, as evidenced by the need for both non-invasive ventilation (NIV) and transfer to the intensive care unit (ICU). This finding aligns with the research conducted by Windisch W et al. [13] and Windisch W et al. [14], wherein it was posited that patients experienced a heightened severity of their condition due to muscle atrophy resulting from metabolic acidemia. Nevertheless, in certain individuals, effective medical intervention targeting the metabolic disruption, along with the rectification of hypoxia and hypercapnia through the administration of oxygen and non-invasive ventilation (NIV), may enable us to implement a secure approach that facilitates prompt recuperation. Respiratory acidosis may give rise to a mixed disorder involving metabolic alkalosis if there is an excessive elevation in bicarbonate concentration beyond the anticipated level as per the principles of renal compensation. The occurrence of metabolic alkalosis resulting in alveolar hypoventilation in our patient population can be attributed to the administration of diuretics and corticosteroids, which led to a relative reduction in circulating blood volume.As a result, the patients experienced the development of acute metabolic alkalosis, which can be linked to a significant decrease in the neural respiratory drive.[16]In addition, metabolic alkalosis has the potential to reduce cardiac output and disrupt the dissociation of oxyhemoglobin.Metabolic alkalosis has been found to be associated with an increased requirement for non-invasive positive pressure ventilation (NIPPV), as supported by the findings of a study conducted by Struik FM et al. (reference 18). However, this finding contradicts the results of a study conducted by Duiverman ML et al. (reference 19), which reported that patients in group B (respiratory acidosis + metabolic alkalosis) had a more favorable prognosis compared to those in group A (compensated respiratory acidosis), with a lower need for non-invasive ventilation (NIV). Our study revealed a statistically significant correlation ($p<0.05$) between elevated serum potassium levels and the requirement for non-invasive positive pressure ventilation (NIPPV) assistance. The increase in potassium concentration is attributed to acidosis, which prompts the translocation of potassium from intracellular fluid to extracellular fluid (plasma) in a process involving the exchange of hydrogen ions. Additionally, renal impairment is known to result in the condition of hyperkalemia. This analysis aims to elucidate the potential correlation between hyperkalemia and the necessity for non-invasive positive pressure ventilation (NIPPV). Our study found a significant correlation between acidosis and

failure of non-invasive positive pressure ventilation (NIPPV), which aligns with the findings of Diaz O et al. [20]. Diaz O et al. also identified the severity of acidosis as a predictive factor for the success of NIPPV in patients with chronic obstructive pulmonary disease (COPD). Furthermore, a notable correlation was observed between reduced partial pressure of oxygen (PO2) and non-invasive ventilation (NIV) failure, which aligns with the findings of a previous study conducted by Contreras M et al [21]. This study demonstrated that failure to enhance oxygenation is the primary factor contributing to NIV failure.In our investigation, we observed no statistically significant association between the patient's partial pressure of carbon dioxide (PCO2) and the failure of non-invasive ventilation (NIV). This finding aligns with the research conducted by Kisaka T et al. [22], which also failed to identify any connection between baseline arterial blood gas (ABG) tension and the success of NIV. However, our results differ from the study conducted by Titlestad IL et al. [23], who demonstrated a correlation between NIV failure and elevated PCO2 levels. The medical intervention for chronic obstructive pulmonary disease (COPD) has been found to result in a reduction in the levels of electrolytes, specifically sodium (Na) and potassium (K), as reported in the research conducted by Chu CM et al. The utilization of titrated oxygen therapy is advised for patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) during hospitalization. This approach is preferred as it has been associated with reduced mortality rates and a decreased probability of developing respiratory acidosis or hypercapnia compared to patients receiving high flow oxygen therapy [24].[25] Monitoring blood gases is crucial in order to maintain optimal oxygenation levels and prevent the accumulation of carbon dioxide and the exacerbation of acidosis. It is recommended to maintain a partial pressure of oxygen (PaO2) within the range of 7.3-10 kilopascals (kPa), corresponding to a saturation of arterial oxygen (SaO2) between 85% and 92%. This range is considered essential to mitigate the risks associated with hypoxia and acidosis.[26]

## Conclusion

The pharmacological management of patients typically involves the administration of bronchodilators, corticosteroids, and antibiotics. Noninvasive positive pressure ventilation (NPPV) has the potential to facilitate the effectiveness of alternative treatments in cases of hypercapnic respiratory failure, thereby potentially circumventing the need for endotracheal intubation. While less severe instances of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) typically exhibit reversibility, the presence of more severe respiratory failure is linked to a significant mortality rate and an extended period of disability among those who survive.

## References

1. Deep A, Behera P R, Subhankar S, et al. Serum Electrolytes in Patients Presenting With Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) and Their Comparison With Stable COPD Patients. Cureus.2023;15(4): e38080. doi:10.7759/cureus.38080
2. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. Fontina WI: Global Initiative for Chronic Obstructive Lung Disease; 2019. https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf. Accessed April 19, 2019.
3. Murphy PB, Rehal S, Arbane G, et al. Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation: a randomized clinical trial. *JAMA*. 2017;317(21):2177-2186.
4. Siddharthan T, Pollard SL, Quaderi SA, Rykiel NA, Wosu AC, Alupo P, Barber JA, Cárdenas MK, Chandyo RK, Flores-Flores O, Kirenga B, Miranda JJ, Mohan S, Ricciardi F, Sharma AK, Das SK, Shrestha L, Soares MO, Checkley W, Hurst JR, GECo Study Investigators. Discriminative Accuracy of Chronic Obstructive Pulmonary Disease Screening Instruments in 3 Low- and Middle-Income Country Settings. JAMA. 2022 Jan 11:327(2):151-160.
5. Sana A, Somda SMA, Meda N, Bouland C. Chronic obstructive pulmonary disease associated with biomass fuel use in women: a systematic review and meta-analysis. BMJ open respiratory research. 2018:5(1):e000246.
6. Combes A, Tonetti T, Fanelli V, Pham T, Pesenti A, Mancebo J, Brodie D, Ranieri VM. Efficacy and safety of lower versus higher CO2 extraction devices to allow ultraprotective ventilation: secondary analysis of the SUPERNOVA study. Thorax. 2019;74(12):1179-1181.
7. Husain-Syed F, Birk HW, Wilhelm J, Ronco C, Ranieri VM, Karle B, et al Extracorporeal Carbon Dioxide Removal Using a Renal Replacement Therapy Platform to Enhance Lung- Protective Ventilation in Hypercapnic Patients With Coronavirus Disease 2019-Associated Acute Respiratory Distress Syndrome. Front Med (Lausanne). 2020;7:598379.
8. Seiler F, Trudzinski FC, Kredel M, Lotz C, Lepper PM, Muellenbach RM. Update: akutehy perkapnische respiratorische Insuffizienz [Update: acute hypercapnic respiratory failure]. Med Klin Intensivmed Notfmed. 2019;114(3):234-239
9. Kraut JA, Madias NE. Intravenous sodium bicarbonate in treating patients with severe metabolic acidemia.Am J Kidney Dis. 2019; 73: 572-575
10. Raphael KL. Metabolic acidosis in CKD: core curriculum 2019.Am J Kidney Dis. 2019; 74: 263-275.
11. Casanova C, Celli BR, Tost L, et al. Long-term controlled trial of nocturnal nasal positive pressure ventilation in patients with severe COPD. Chest 2000; 118: 1582–1590.
12. Struik FM, Lacasse Y,Goldstein RS, et al. Nocturnal noninvasive positive pressure ventilation in stable COPD: a systematic review and individual patient data meta-analysis. Respir Med 2014; 108: 329–337.

13. Windisch W, Kostic S, Dreher M, et al. Outcome of patients with stable COPD receiving controlled noninvasive positive pressure ventilation aimed at a maximal reduction of Pa(CO2). Chest 2005; 128: 657–662.
14. Windisch W, Dreher M, Storre JH, et al. Nocturnal non- invasive positive pressure ventilation: physiological effects on spontaneous breathing. Respir Physiol Neurobiol 2006; 150: 251–260.
15. Katalinić L, Blaslov K, Pasini E, Kes P, Bašić-Jukić N. [Acid- base status in patients treated with peritoneal dialysis]. Acta Med Croatica. 2014;68(2):85-90.
16. Kohnlein T, Windisch W, Kohler D, et al. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. Lancet Respir Med 2014; 2: 698–705.
17. Murphy PB, Rehal S, Arbane G, et al. Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation: a randomized clinical trial. JAMA 2017; 317: 2177–2186.
18. Struik FM, Sprooten RT, Kerstjens HA, et al. Nocturnal non- invasive ventilation in COPD patients with prolonged hypercapnia after ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group study. Thorax 2014; 69: 826–834.
19. Duiverman ML, Wempe JB, Bladder G, et al. Nocturnal non- invasive ventilation in addition to rehabilitation in hypercapnic patients with COPD. Thorax 2008; 63: 1052–1057.
20. Diaz O, Begin P, Andresen M, et al. Physiological and clinical effects of diurnal noninvasive ventilation in hypercapnic COPD. EurRespir J 2005; 26: 1016–1023.
21. Contreras M, Masterson C, Laffey JG. Permissive hypercapnia: what to remember. CurrOpinAnaesthesiol. 2015 Feb;28(1):26- 37.
22. Kisaka T, Cox TA, Dumitrescu D, Wasserman K. CO2 pulse and acid-base status during increasing work rate exercise in health and disease. Respir Physiol Neurobiol. 2015;218:46-56.
23. Titlestad IL, Lassen AT, Vestbo J. Long-term survival for COPD patients receiving noninvasive ventilation for acute respiratory failure. Int J Chron Obstruct Pulmon Dis 2013; 8: 215–219.
24. Chu CM, Chan VL, Lin AW, et al. Readmission rates and life- threatening events in COPD survivors treated with non-invasive ventilation for acute hypercapnic respiratory failure. Thorax 2004; 59: 1020–1025.
25. Niewoehner DE. The impact of severe exacerbations on quality of life and the clinical course of chronic obstructive pulmonary disease. Am J Med 2006; 119: 38–45.
26. Mc Ghan R, Radcliff T, Fish R, et al. Predictors of rehospitalization and death after a severe exacerbation of COPD. Chest. 2007; 132: 1748–1755.