Original Research Article

Serum electrolytes, Acid–base balance and need for non-invasive ventilation in patients with hypercapnic acute exacerbation of chronic obstructive pulmonary disease

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Abstract

Background: Non-invasive ventilation (NIV) is used to treat acute hypercapnic respiratory failure (AHRF) in patients with chronic obstructive pulmonary disease (COPD). In these patient acid–base and electrolyte balance are closely related. Aim of the present study was to evaluate acid–base and electrolyte alterations in these subjects and the effect of non-invasive ventilation. **Material and Method:**We analyzed 74 patients admitted to the Department of Pulmonary Medicine, Govt. Medical Collegeand Hospital, Nizamabadfor hypercapnic AECOPD. On admission, all patients underwent history taking, full examination, and arterial blood gas analysis and received oxygen with nasal cannulae or a venturi mask to preserve normal oxygen saturation, as well as received pharmacological treatment. NIV was started when patients had severe dyspnea, increased work of breathing, and respiratory acidosis despite optimum management. **Results:**Based on arterial blood gas finding, we categorized our patients into three main groups: the first group comprised 44 (59.4%) patients who had compensated respiratory acidosis, and the majority of them (35 patients) received medical treatment only. The second group comprised 17 (22.97%) patients, who had mixed respiratory acidosis and metabolic alkalosis. Overall, 13 patients needed non-invasive mechanical ventilation with the medical treatment. The third group comprised 13 (17.5%) who had combined respiratory and metabolic acidosis. Of them, 11 patients needed non-invasive mechanical ventilation with the medical treatment. **Conclusion:** Our study shows that in hypercapnic respiratory acidosis due to AECOPD, differently from previous studies, the metabolic alkalosis is not a negative prognostic factor neither determines greater NIV support need, whereas the metabolic acidosis in addition to respiratory acidosis is an unfavourable element, since it determines an increased need of NIV and invasive mechanical ventilation support.

Keywords: Acid–base balance, Hypercapnia, NIV, COPD.

Introduction

Hypercapnia and respiratory acidosis ensue when impairment in ventilation occurs and the removal of carbon dioxide by the respiratory system is less than the production of carbon dioxide in the tissues. Lung diseases that cause abnormalities in alveolar gas exchange do not typically result in alveolar hypoventilation. [1]Often these diseases stimulate ventilation and hypocapnia due to reflex receptors and hypoxia. Hypercapnia typically occurs late in the disease process with severe pulmonary disease or when respiratory muscles fatigue. (Pediatric Respiratory Acidosis, Metabolic Acidosis, and Pediatric Metabolic Acidosis). [2]Respiratory acidosis can be acute or chronic. In acute respiratory acidosis, the PaCO2 is elevated above the upper limit of the reference range (ie, >45 mm Hg) with an accompanying acidemia (ie, pH < 7.35). [3] In chronic respiratory acidosis, the $PaCO_2$ is elevated above the upper limit of the reference range, with a normal or near-normal pH secondary to renal compensation and an elevated serum bicarbonate levels (ie, >30 mEq/L) [4]Acute respiratory acidosis is present when an abrupt failure of ventilation occurs. This failure in ventilation may result from depression of the central respiratory center by one or another of the following: Central nervous system disease or drug-induced respiratory depression. [5]Inability to ventilate adequately, due to a neuromuscular disease or paralysis(eg,myasthenia gravis, amyo-trophic lateral sclerosis[ALS],Guillain-Barré syndrome, muscular dystrophy). Airway obstruction, usually related to asthma or chronic obstructive pulmonary disease (COPD).[6]chronic respiratory acidosis may be secondary to many disorders, including COPD.

Hypoventilation in COPD involves multiple mechanisms, including the following:Decreased responsiveness to hypoxia and hypercapnia. Increased ventilation-perfusion mismatch leading to increased dead space ventilation. [7] Decreased diaphragmatic function due to fatigue and hyperinflation. Chronic respiratory acidosis also may be secondary to obesity hypoventilation syndrome (OHS—ie, Pickw-ickian syndrome), neuromuscular disorders such as ALS, and severe restrictive ventilatory defects such as are observed in interstitial fibrosis and thoracic skeletal deformities.[8]In this study, we used the pathophysiologic approach, according to the compensation laws, to evaluate the Chronic Obstructive Pulmonary Disease (COPD) acute exacerbations.In hyperacapnic AECOPD the hypoventilation produces or worsens respiratory acidosis.

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Since most of these patients, especially if elderly and critical, are multi-drugs recipients for comorbidities, the AB and electrolytic disorders are very common, producing a potential bias in the interpretation of the final values.Thus, we sought to evaluate: 1) the AB and electrolyte disorders in hypercapnic AECOPD patients; and 2) the effect of the type of treatment (pharmacological or by noninvasive ventilation [NIV]) on the AB and electrolyte disorders.

Material and Methods

This is prospective and observational study was carried out on 74 patients who were admitted with COPD exacerbation to the Department of Pulmonary Medicine, Govt. Medical College and Hospital, Nizamabad during the period of January 2020 to November 2020.

Blood investigation were performed. They include the following:

(1) Arterial blood gases (ABG).

(2) Electrolyte levels (Sodium (Na) and potassium (K).

Radiological investigations

Chest radiography can be reported as suggestive of COPD but is not diagnostic. Radiographs was used for the diagnosis of pneumonia, and exclusion of other causes of dyspnea in patients with COPD such as ruptured emphysematous bullae. On admission, all patients received oxygen through nasal cannula or mask to preserve a normal arterial oxygen saturation (≥90%) and received bronchodilators, corticosteroids, and antibiotics. Follow-up was done for patients with clinical examination and laboratory investigations, which showed that some of them improved and others deteriorated, so received NIV. NIV was performed through oronasal mask with a pressure/ volume ventilator. Support pressure, Positive End Expiratory Pressure (PEEP) and triggered flows were adjusted to obtain a tidal volume of 6– 8 ml/kg, the best possible oxygenation, and a decrease in respiratory rate. Support pressure and PEEP were modified based on the arterial gases. The mean Inspiratory Positive Assisted Pressure (IPAP) was 16 ± 4 cm H_2O.

Result

In the table 1, the mean age of the NIV positive were 59.23 years and NIV negative wre 62.32 years, who were admitted to the Department of TB and Chest, 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).

Table 1:Mean Age of the studied group

	Need for non-invasive ventilation		p-value
	NIV Positive (N=33)	NIV Negative (N=41)	
Age (Years) Mean±SD	59.23±7.2	62.32±7.3	0.236

Table 2: Distribution of sex of the studied group

Sex	Need for non-invasive ventilation		p-value
	NIV Positive (N=33)	NIV Negative (N=41)	
Male	27 (81.8)	32 (78.0)	0.074
Female	6 (18.1)	9 (21.9)	

In table 2, the total number of patients were 74, where 59 of them were males and 15 females.

Table 3: Arterial blood gases finding of the studied group

Acid–base disturbance	Need for non-invasive ventilation		p-value
	NIV Positive (N=33)	NIV Negative (N=41)	
Compensated respiratory acidosis (n=44)	9 (27.2)	35 (85.3)	<0.0001
Mixed respiratory acidosis and metabolic alkalosis(n=17)	13 (39.3)	4 (9.7)	
Combined respiratory and metabolic acidosis(n=13)	11 (33.3)	2 (4.8)	
PO2	54.32±8.7	63.32±8.9	<0.05
PCO_2	59.63±8.1	49.36±6.2	<0.05

In table 3, according to ABG finding, patients were classified into three groups: the first group comprised 44 (59.4%) patients who had compensated respiratory acidosis, and the majority of them (35 patients) received medical treatment only. The second group comprised 17 (22.97%) patients, who had mixed respiratory acidosis and metabolic alkalosis. Overall, 13 patients needed non-invasive mechanical ventilation with the medical treatment. The third group comprised 13 (17.5%) who had combined respiratory and metabolic acidosis. Of them, 11 patients needed non-invasive mechanical ventilation with the medical treatment and mean PO_2 was 54.32 mmHg whereas mean PCO_2 was 59.63 mmHg.

Table 4: Electrolytes finding of the studied group

Electrolytes	Need for non-invasive ventilation (Mean±SD)		p-value
	NIV Positive (N=33)	NIV Negative (N=41)	
Sodium (mEq/l)	134.7±3.8	136.9±4.1	0.293
Potassium (mEq/l)	4.32±0.73	3.73±0.52	<0.05
Bicarbonate (mEq/l)	28.21±5.7	22.63±4.3	<0.05

In table 4, the mean potassium of the patients who need medical treatment only was 3.73mEq/l and mean Sodium was 136.9 mEq/l, whereas the mean potassium for the other group was 4.32 mEq/l and mean Sodium was 134.7±3.8mEq/l. The mean serum Bicarbonate of the group the need medical treatment only was 22.63mEq/l. The mean serum Bicarbonate of the other group was 28.21mEq/l.

Table 5: Outcome and characteristic of the group that needed NIPPV from the start

Acid–base disturbance	Studies groups non-invasive ventilation (N=33)		p-value
	Improved (N=31)	Failed (N=2)	
Compensated respiratory acidosis	9 (29.0)	0 (0)	<0.0001
Mixed respiratory acidosis and metabolic alkalosis	15(48.3)	1(50)	
Combined respiratory and metabolic acidosis	7 (22.5)	1 (50)	
PO_2	54.3±7.3	41±6.3	<0.0001
PCO_2	59.4±6.6	57.4±7.8	>0.05

Table 6: Effect of COPD treatment on the patient electrolytes

	Pre-treatment	Follow-up	Wilcoxon signed rank test	P
Sodium (mEq/l)	136.1±6.1	134.2±6.3	1.3	>0.05
Potassium (mEq/l)	4.3±0.71	3.3±0.64	1.8	<0.05

In table 6, the Sodium and Potassium levels before treatment were 136.1±6.1 and 4.3±0.71 mEq/l, respectively, and mean Sodium and Potassium levels after treatment were 134.2±6.3 and 3.3±0.64 mEq/l, respectively.

Discussion

Patients with underlying COPD who present with an exacerbation of their COPD and hypercapnic respiratory distress or respiratory failure are the group most likely to be successfully treated with noninvasive ventilation (NIV). Exacerbations increase the work of breathing in these patients and may exceed the patient's ability to adequately ventilate through a variety of mechanisms, including increasing hyperinflation with decreased diaphragmatic excursion and strength, increasing intrinsic positive end-expiratory pressure (PEEP),ineffective or inadequate tidal volume generation, respiratory patterns,and increased respiratory frequency. Noninvasive ventilation effectively unloads the respiratory muscles, increasing tidal volume, decreasing the respiratory rate, and decreasing the diaphragmatic work of breathing, which translates to an improvement in oxygenation, a reduction in hypercapnia, and an improvement in dyspnea[9-13]. In our study was 74 patients with COPD exacerbation. Initially, 41 patients received medical treatment and 33 patients needed NIPPV from the start; according to the patients clinical assessment and response to oxygen therapy, only 2 of them failed NIV. In our study patient's age ranged from 43 to 74 years old. In the present study, COPD exacerbation was found more in males (n=59, 79.7%) than females (n=15, 20.2%). The sex differences may be a result of many factors such as sex-related differences in airway anatomy, smoking habits,respiratory manifestations,and environ-mental or occupational exposures, and this is in agreement with the result of the study conducted by Struik FM et al. [14]In our study, Arterial bloodgases were categorized into three groups, group A (compensated respiratory acidosis), group B (mixed respiratory acidosis and metabolic alkalosis), and group C (combined respiratory and metabolic acidosis). We found that the group C with respiratory acidosis +metabolic acidosis (group C) was most critical, in terms of both NIV and ICU transfer. This is in agreement with the study conducted by Windisch Wet al. [15] and Windisch W et al. [16], who stated that patients' condition was more critical owing to muscle wasting because of the metabolic acidemia. However, in some patients, good medical treatment of the metabolic disturbance, and the correction of hypoxia and hypercapnia by oxygen and NIV may permit us a safe management with rapid recovery. In respiratory acidosis, if there is an excessive increase of bicarbonate concentration(above the expected level with renal compensation laws), a mixed disorder with metabolic alkalosis should be suspected. In our patients, the use of diuretics and corticosteroids with a relative decrease in circulating blood volume was the cause of metabolic alkalosis leading to alveolar hypoventilation.[17] As a consequence, the acute metabolic alkalosis developed in these patients can be associated with a severe depression of the neural respiratory drive.[18]Moreover, metabolic alkalosis may decrease cardiac output and disturb oxyhemoglobin dissociation.[19] Metabolic alkalosis increases the need for NIPPV, and this is in agreement with the result of the study conducted by Struik FM et al. [20], but it is in contrast to the study conducted by Duiverman ML et al. [21], who reported that patient belonging to group B(respiratory acidosis+metabolic alkalosis) had a better prognosis than those of group A (compensated respiratory acidosis) with a lower need of NIV. In our study showed a highly significant relation ($p<0.05$) between increased serum potassium level and need for NIPPV support. The elevated potassium level is caused by acidosis that causes movement of potassium to extracellular fluid (plasma) in exchange for hydrogen ions.

Moreover, renal impairment causes hyperkalemia. This may explain the relation between hyperkalemia and need for NIPPV. In our study, there was a significant relation between acidosis and NIPPV failure; this is in agreement with the study conducted by Diaz O et al. [22] who considers severity of academia as a predictive factor for the success of NIPPV in COPD cases. Moreover, there was a significant relation between decreased PO_2 and NIV failure, and this is in agreement with the study conducted by Contreras M et al [23], who showed that failure to improve oxygenation is the main cause for NIV failure.In our study, there was no significant relation between the patient's PCO_2 and NIV failure; this is in agreement with the study conducted by Kisaka T et al. [24], who failed to find any relationship between baseline ABG tension and success of NIV, but is in contrast to the study conducted by Titlestad IL et al. [25] who showed a correlation between the failure of NIV and elevated PCO_2. The medical treatment of COPD decreases the patient's electrolytes (Na and K); this is in agreement with the study conducted by Chu CM et al. [26] The routine use of titrated oxygen treatment is recommended in hospitalized AECOPD, due to the lower riskof death and lower likelihood of respiratory acidosis or hypercapnia than in patients who received high flow oxygen.[27] Blood gases should be monitored to ensure a good level of oxygenation without carbon dioxide retentionand/or worsening acidosis; the PaO_2 should be maintained at 7.3–10 kPa (SaO_2 85–92%) to avoid the dangers of hypoxia and acidosis.[28] A recently developeddevice (Free O_2) automatically adjusts the oxygenflow rates based on patients' needs, in order to limit hyperoxia and hypoxemia in hospitalized AECOPD patients.[29] In comparison to manual oxygen titration this device improved the percentage of time within the target SaO_2 (significantly higher with Free O_2) and the time with severe desaturation and hyperoxia (reducedwith Free O_2); furthermore, the length of hospital staywas lower in patients using Free O_2. [30]Limitation of the present study is observational design and a relatively small sample size,being performed at a single center. Furthermore,data on smoking status could not be obtained.

Conclusion

AECOPD afflict millions of patients with COPD annually and account for substantial health care costs. AECOPD episodes can be triggered or complicated by other comorbidities. Oxygen, physical therapy, mucolytics, and airway clearance devices may be useful in selected patients. Pharmacologic management includes broncho-dilators, corticosteroids, and antibiotics in most patients. In hyper-capneic respiratory failure, NPPV may allow other therapies to work and thus avoid endotracheal intubation. Although mild episodes of AECOPD are generally reversible, more severe forms of respiratory failure are associated with a substantial mortality and a prolonged period of disability in survivors.

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