Electrolyte disturbances in patients with acute exacerbation of chronic obstructive pulmonary disease

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Introduction Chronic obstructive pulmonary disease (COPD) is a cover term that includes a variety of progressively debilitating lung diseases. COPD includes both emphysema and chronic bronchitis. Although COPD is mainly a chronic disease, a substantial number of patients experience exacerbations that are related to a significantly worse survival outcome, especially with abnormal serum electrolyte level.

Aim To detect the serum electrolytes disturbances in patients with acute exacerbation of COPD.

Patients and methods A prospective study was conducted at Chest Department, El-Hussein University Hospital, Al Azhar University, on patients with acute exacerbation of COPD. The study was approved by the hospital ethics committee, and a written consent was obtained from each patient before the procedure.

Results We found a significantly low level of serum sodium (Na) (131±4.45 mEq/l), potassium (3.19±0.96 mEq/l), magnesium (1.85±0.17 mEq/l), and chloride (84.75±7.31 mEq/l) in patients with acute exacerbation of COPD than their healthy controls (Na+=138±2.28 mEq/l, potassium=4.50 ±0.02 mEq/l, magnesium=2.20±0.14 mEq/l and chloride=100.30±2.67 mEq/l) ($P<0.05$).

Conclusion In patients with acute exacerbation of COPD, there are abnormal serum electrolytes like sodium, potassium, magnesium, and chloride levels.

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by long-term breathing problems and poor airflow. The main symptoms include breathlessness and cough with sputum production [1].

COPD is the third leading cause of death worldwide. Although COPD is mainly a chronic disease, a substantial number of patients experience exacerbations. Severe exacerbations are related to a significantly worse survival outcome [2].

Following recurrent exacerbation of COPD, most patients experience decrease in the quality of life and often require re-admission, whereas others die [3].

Acute exacerbation of COPD is a sudden worsening of COPD symptoms, such as shortness of breath and quantity and color of phlegm, that typically lasts for several days. It may be triggered by an infection with bacteria or viruses or by environmental pollutants. Typically, infections cause 75% or more of the exacerbations; bacteria can roughly be found in 25% of cases, viruses in another 25%, and both viruses and bacteria in another 25%. Airway inflammation is increased during the exacerbation, resulting in increased hyperinflation, reduced expiratory airflow, and decreased gas exchange [4].

Patients with COPD present with features of acute respiratory infections, such as productive cough and dyspnea, and may be a number of metabolic changes owing to disease process or because of the treatment instituted, like hyponatremia, hypokalemia, hyperbilirubinemia, elevated transaminases, elevated blood urea, and elevated serum creatinine [3].

Aim

The main objective of this study is to determine the electrolyte disturbances in patients with acute exacerbation of COPD.

Patients and methods

A prospective study was conducted at Chest Department, El-Hussein University Hospital, Al Azhar University. The study included 80 participants, who were classified into two main groups: 60 patients and 20 healthy individuals. Blood samples were collected from the participants for the estimation of serum electrolytes using an

autoanalyzer. All participants were subjected to measurement of serum levels of potassium (K), sodium (Na), magnesium (Mg), and chloride (Cl).

Inclusion criteria

Known cases with COPD diagnosed previously with exacerbation of symptoms were included.

Exclusion criteria

Patients with COPD with other clinical conditions that may cause electrolyte disorders such as renal failure and diabetic ketoacidosis were excluded.

Statistical analysis

Data were analyzed by SPSS Microsoft Excel software (IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.). Significance of difference of average Na, K, Mg, and Cl levels in the two groups was evaluated statistically using Student's *t*-test. *P* value less than 0.05 was considered to be significant. Age was presented as mean, and other data were presented as percentage.

Results

The patient group included 60 patients with COPD exacerbation, comprising 46 males and 14 females, and the control group included 20 healthy individuals, comprising 15 males and 5 females.

Patients with COPD were in the age range of 52–77 years, with mean age at presentation being 60.22±10.45 years. In the control group, participants were in the age range of 50–70 years, with average age being 60±8.5 years. All the data are summarized in Table 1.

Average serum Na, K, Mg, and Cl levels in patients with COPD were 131±4.45, 3.19±0.96, 1.85±0.17, and 84.75±7.31 mEq/l, respectively, and the levels in the control group were 138±2.28, 4.50±0.02, 2.20±0.14, and 100.30±2.67 mEq/l, respectively. All the data are summarized in Table 2.

Of 60 patients with COPD, 35 (58.53%) had electrolyte disorders: hypokalemia in 20%, hyponatremia in 13.33%, hypomagnesemia in 6.66%, hypochloremia in 3.33%, and combined disturbances in 15% (Table 3).

Table 1 Age and sex distribution of patients and control groups

Groups	Age (mean±SD)	Male	Female	Total
COPD	60.22±10.45	46	14	60
Control	60.55±8.5	15	5	20

COPD, chronic obstructive pulmonary disease.

Table 2 Serum electrolytes in both study and control groups

Groups	Sodium (mEq/l)	Potassium (mEq/l)	Magnesium (mEq/l)	Chloride (mEq/l)
COPD	131±4.45*	3.19±0.96*	1.85±0.17*	84.75 ±7.31*
Control	138±2.28	4.50±0.02	2.20±0.14	100.30 ±2.67

COPD, chronic obstructive pulmonary disease. *$P<0.05$, significantly different from the control group.

Table 3 Distribution of electrolyte disorders among patients with chronic obstructive pulmonary disease

Type of electrolyte disorders	60 (100) [*n* (%)]
Hyponatremia	8 (13.33)
Hypokalemia	12 (20)
Hypomagnesemia	4 (6.66)
Hypochloremia	2 (3.33)
Combined electrolyte disturbance	9 (15)
Total	35 (58.53)

Discussion

COPD is a leading cause of morbidity and mortality worldwide. With increasing industrialization and smoking, the prevalence of COPD is increasing. Exacerbations are the most common cause of hospitalization among patients with COPD. During COPD exacerbation, the lungs experience tightening of airway passages, increase of production of mucus, and triggering of inflammation by activation of body's immune defense system. The study of risk factors associated with exacerbation is very important because the economic and social burden incurred by acute execrations of COPD is extremely high, and it has poor outcome [5].

The study of electrolyte disturbance is very important, as patients with COPD per se are predisposed to it. In turn, electrolyte imbalance can cause respiratory muscle weakness, cardiac arrhythmia, and low cardiac output. Thus, the presence of electrolyte imbalance leads to significantly poor outcome among patients with COPD. This study aimed at evaluating serum electrolyte levels in patients with acute exacerbation of COPD [6].

In this study, we measured serum electrolytes (Na, K, Mg, and Cl) in patients with COPD exacerbation. We found significantly lower levels of Na, K, Mg, and Cl in patients with COPD (131±4.45, 3.19±0.96, 1.85±0.17, and 84.75±7.31 mEq/l, respectively) than in healthy controls (138±2.28, 4.50±0.02, 2.20±0.14, and 100.30 ±2.67 mEq/l, respectively) ($P<0.05$).

The distribution of electrolyte disturbances in COPD group (total 58.53%) was found as follows: hypokalemia in 20%, hyponatremia in 13.33%, hypomagnesemia in 6.66%, hypochloremia in 3.33%, and combined disturbances in 15%.

Imbalance in serum electrolytes has been proved in patients with COPD, in both acute exacerbation and during stable disease [7].

Hyponatremia in patients with COPD developed secondary to many reasons, such as development or worsening of hypoxia, hypercapnia, and respiratory acidosis, and right-side heart failure with development of lower limb edema, renal insufficiency, use of diuretics, Syndrome of Inappropriate Antidiuretic Hormone Synthesis, malnutrition, and poor intake during acute exacerbations are common contributing factors in such patients. Activation of the renin-angiotensin-aldosterone system and inappropriately elevated plasma arginine vasopressin in COPD may aggravate the electrolyte imbalance during acute exacerbation of COPD [8].

Hyponatremia is a common electrolyte disorder that develops frequently in 15–40% of hospitalized patients, although actual incidence data are not known. Additionally, age is an independent risk factor for hyponatremia. There is a clear association between chronic pulmonary pathologies, such as chronic obstructive pulmonary disease (COPD) and Syndrome of Inappropriate Antidiuretic Hormone Synthesis, frequently concomitant with infective processes. The mechanisms involved, although not entirely clarified, suggest an effect on baroreceptors or higher release of ADH secondary to hypercapnia [9]

Hyponatremia is important, for it worsens the clinical course and is a predictor of poor prognosis in COPD, in both stable phase and exacerbation. Patients with COPD often have associated comorbidities, especially cardiovascular diseases, and hyponatremia has been associated with a higher morbidity and mortality rate in patients admitted for COPD. However, whether mortality is owing to hyponatremia or to the underlying disease remains unclear [9].

This is in agreement with the study by Das *et al.* [7], who measured the serum K+ and Na+ in 64 patients with acute exacerbation of COPD and compared the results with 20 healthy volunteers. They reported a significant decrease in serum Na+ and K+ in patients with COPD (133±6.86 and 3.39±0.96 mEq/l, respectively) than in normal controls (142±2.28 and 4.52±0.02 mEq/l, respectively).

Moreover, in the study by Teranzo *et al.* [10], 67 consecutive patients were hospitalized for hypercapnic COPD exacerbation, and hyponatremia occurred in 11 patients, hyponatremia with hypochloremia occurred in 13, hypokalemia occurred in 10 patients, and hypochloremia occurred in seven patients.

Alcindo *et al.* [11] studied the relative frequency of hypomagnesemia and other electrolyte disorders in patients with patients with chronic stable COPD taking inhaled B_2 agonists and inhaled steroids. Hypomagnesemia was reported in 27% of patients, whereas hypocalcaemia, hypokalemia, and hyponatremia reported in 52, 4.2, and 2.8% of patients, respectively.

B_2 agonists, whether inhaled like formoterol and salbutamol or oral like salbutamol or bambuterol, in addition to oral sustained-released theophylline, are the mainstay treatment in stable COPD. Unfortunately, all these treatments have been proved to cause some electrolyte disorders in patients with bronchial asthma and COPD [12].

Comparing patients with COPD with electrolyte disorders and those without any electrolyte imbalance on admission, there was a significant decrease in pH, PaO_2, and oxygen saturation in patients with electrolyte disorders, whereas there was a significant increase in $PaCO_2$. This means that patients with electrolyte disorders experience further deterioration in arterial blood gases than other group without any electrolyte disorders.

Hypoxemia that is worsening during acute exacerbation of COPD is reported to induce depletion of intracellular Mg ions. As Mg ion is involved in muscle contraction and in the maintenance of muscle tonus, a reduction in Mg ion levels in patients with chronic airflow limitation might represent one more factor that is detrimental to respiratory function or to the recovery of such function, since low levels of Mg induce muscle fatigue [3].

Moreover, respiratory acidosis with metabolic alkalosis (owing to renal compensation) in patients with COPD with chronic hypercapnia is the usual cause of hypochloremia in those patients. So, patients with severe COPD exacerbation have factors that

influence serum electrolytes levels like hypoxia, respiratory acidosis, and hypervolemia, even before starting any type of treatment that may further cause electrolyte imbalance [13].

The effect of systemic steroids, diuretics, and nebulized B_2 agonists on serum electrolytes levels has proved in many studies on both patients with COPD and those with asthma [10].

Treatment with B_2 agonists can reduce serum magnesium levels through urinary loss or intracellular shift [14].

Intravenous aminophylline therapy has been recorded to cause hypomagnesemia, hypocalcemia, and hyponatremia in susceptible individuals by increasing the urinary secretion of these electrolytes; this in turn may cause increased pulmonary irritability and consequently increased risk of exacerbation [15].

Irrespective of the underlying mechanism of development, hyponatremia itself may be a predictor of poor outcome in patients of COPD. It may lead to central nervous system dysfunction, confusion, convulsions, coma, reversible cardiac conduction defect, secondary renal insufficiency, and even death [16].

Therefore, hyponatremia should be meticulously searched for in every patient with acute exacerbation of COPD and should be actively corrected at the earliest.

Hypokalemia may be another electrolyte abnormality in the patients with COPD. It may be present independently or concomitantly with hyponatremia.

In this study, there was a significantly low level of serum potassium in patients with COPD than the healthy controls. Hypokalemia in COPD may be attributed to respiratory acidosis and metabolic alkalosis or long-standing steroid therapy [17].

Use of B_2 agonist like salbutamol may also contribute to hypokalemia in patients with COPD [12].

Moreover, acute respiratory failure associated with hypokalemia was found to have a high mortality rate among the patients with COPD [18].

This may be attributed to cardiac arrhythmias or hampered nerve-muscle conduction. So, it appears from our study that hypokalemia may be a common associated finding in the patients with COPD, which should be corrected promptly to avoid fatal outcomes.

Conclusion

In patients with acute exacerbation of COPD, there are abnormal serum electrolytes like Na, K, Mg, and Cl levels. The diagnosis of electrolyte disturbances in patients with COPD exacerbations is a challenge for the clinician because of its frequency, different etiologies, and implications for prognosis. Suspicion should be raised by directed anamnesis and complete physical examination in those patients with suggestive symptoms or at risk (alcoholics with malnutrition, patients on diuretic treatment, etc.), and then subsequently confirmed by serum electrolyte analysis.

Recommendation

Serum electrolytes levels should be monitored routinely in patients with COPD, and an attempt should be made to correct them at the earliest to avoid poor outcomes.

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Conflicts of interest

There are no conflicts of interest.

References

1 Borup H, Kirkeskov L, Hanskov DJA, Brauer C. Chronic obstructive pulmonary disease and construction workers. *Occup Med (Lond)* 2017; **67**:199–204.

2 Lozano R, Naghavi M, Foreman K. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; **380**:2095–2128.

3 Mohan A, Premanand R, Reddy LN, Rao MH, Sharma SK, Kamity R, Bollineni S. Clinical presentation and predictors of outcome in patients with severe acute exacerbation of chronic obstructive pulmonary disease requiring admission to intensive care unit. *BMC Pulm Med* 2006; **6**:27.

4 Rabe KF, Hurd S, Anzueto A. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary. *Am J Respir Crit Care Med* 2007; **176**:532–555.

5 Sapey E, Stockley RA. COPD exacerbations 2: aetiology. *Thorax* 2006; **61**:25–28.

6 Filippatos TD. Hyponatremia in the elderly: challenges and solutions. *Clin Interv Aging* 2017; **12**:1957–1965.

7 Das P, Bandyopadhyay M, Baral K, Paul R. Dyselectrolytemia in chronic obstructive pulmonary diseases with acute exacerbation. *Niger J Physiol Sci* 2010; **25**:25–27.

8 Bauer FK, Telfer N, Herbst HH. Hyponatremia and increased exchangeable sodium in chronic obstructive lung disease. *Am J Med Sci* 1965; **250**:245–253.

9 Burguera V. Epidemiología de la hyponatremia. *Nefrología* 2011; **2.6**:13–20.

10 Terzano C, Di Stefano F, Conti V, Di Nicola M, Paone G, Petroianni A, Ricci A. Mixed acid-base disorders, hydroelectrolyte imbalance and lactate production in hypercapnic respiratory failure: the role of noninvasive ventilation. *PLoS One* 2012; **7**:e35245.

11 Cerci Neto A, Ferreira Filho OF, Parreira Jde S. The relative frequency of hypomagnesemia in outpatients with chronic airflow limitation treated at a referral center in the north of the state of Paraná, *Brazil. J Bras Pneumol* 2006; **32**:294–300.

12 Yang CT, Lin HC, Lin MC, Wang CH, Lee CH, Kuo HP. Effect of beta 2-adrenoceptor agonists on plasma potassium and cardiopulmonary responses on exercise in patients with chronic obstructive pulmonary disease. *Eur J Clin Pharmacol* 1996; **49**:341–346.

13 Saini V, Saini N, Kaur J, Singh GP. Acid base status in chronic obstructive pulmonary disease patient. *Indian J Clin Biochem* 2008; **28**:36–38.

14 Rolla G, Bucca C. Hypomagnesaemia and bronchial hyperreactivity: a case report. *Allergy* 1999; **44**:519–521.

15 Knutsen R, Bohmer T, Falch J. Intravenous theophylline induced excretion of calcium, magnesium and sodium in patients with recurrent asthmatic attacks. *Scand J Clin Lab Invest* 1994; **54**:119–125.

16 Suri P, Habeeb K, Alai MS, Rather HA, Jalal S. Hyponatremia presenting as cardiac conduction defect. *J K Sci* 2009; **11**:85–86.

17 Porcel A, Díaz F, Rendón P. Dilutional hyponatremia in patients with cirrhosis and ascites. *Arch Intern Med* 2002; **162**:323–328.

18 Hussain SF, Irfan M, Naqi YS, Islam M, Akhtar W. Acute respiratory failure in Pakistani patients: risk factors associated with mortality. *J Coll Physicians Surg Pak* 2006; **16**:287–290.