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ORIGINAL ARTICLE

Role of Acetazolamide for the Correction of Metabolic Alkalosis in Post-NIV COPD Patients

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Abstract:

Background: *COPD is a leading cause of morbidity and mortality. Acute hypercapnic respiratory failure in acute exacerbation of COPD (AECOPD) patients can be effectively treated by non invasive ventilation (NIV). But NIV may be less successful if it induce metabolic alkalosis (MA).*

Objective: *This study aims to assess the role of acetazolamide (ACET) for the correction of metabolic alkalosis (MA) in post-NIV COPD patients.*

Methods: *This quasi experimental study was conducted in Respiratory Medicine department of National Institute of the Diseases of The Chest & Hospital (NIDCH), Mohakhali, Dhaka from april, 2017 to march, 2019 in fifty two AECOPD patients with hypercapnic respiratory failure who developed MA following NIV. Twenty six patients were treated with acetazolamide 500mg orally daily for two consecutive days (Day 0 and 1) and compared with twenty six patients without acetazolamide. Both groups were non invasively ventilated in a bilevel positive airway pressure (BiPAP). The following parameters were measured: arterial pH, PO2, PCO2, HCO3-, serum electrolytes (Na+, K+, Cl-) and urinary pH. Results were expressed as mean ± SD. A value of $p < 0.05$ was considered statistically significant for all tests.*

Results: *In this study, maximum patients were male and within age group of 60 - 69 years. Analysis within acetazolamide group showed significant reduction of arterial pH (7.41 ± 0.03 vs. 7.49 ± 0.02, p value < .001), PCO2 (55.95 ± 3.12 vs. 61.93 ± 4.87, p value < 0.001), HCO3- (35.76 ± 2.90 vs. 46.79 ± 3.48 , p value < 0.001). Moreover, acetazolamide group showed significant increase of PO2 (62.83 ± 7.64 vs. 54.19 ± 5.71, p value < 0.001) and urine pH (6.64 ± 0.33 vs. 5.87 ± 0.38, p value <0.001). Analysis between groups showed significant difference between change of arterial pH, PCO2, HCO3-, PO2 and urine pH. No adverse events were observed in both acetazolamide group and without acetazolamide group.*

Conclusions: *Acetazolamide has a role for the correction of metabolic alkalosis in post-NIV COPD patients.*

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Introduction:

Acute exacerbations of chronic obstructive pulmonary disease are critical events in the natural history of the disease and are associated with accelerated loss of lung function and poor quality of life[1].

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Non-invasive ventilation (NIV) has been shown to be an effective treatment for acute hypercapnic respiratory failure (AHRF) during COPD hospitalization. The addition of NIV to standard medical treatment for AHRF decreases the need for endotracheal intubation, reduces rate of complications, mortality and the duration of hospitalization[2,3,4].

If a chronically elevated PCO2 is rapidly lowered in patients undergoing mechanical ventilation, the plasma bicarbonate concentration may remain elevated for a period of time. Reduction of the PCO2 with a persistently elevated bicarbonate concentration results in a form of metabolic alkalosis that is called "posthypercapnic" metabolic alkalosis[5]. Metabolic alkalosis causes hypoventilation and reduce improvement of respiratory failure[6].

Acetazolamide (ACET) is a carbonic anhydrase inhibitor has been used to increase renal bicarbonate loss in metabolic alkalosis after proper fluid loading and potassium supplementation[7,8]. Correction of metabolic alkalosis also causes improvement of ventilation and helps in reduction of PaCO2[8].

Methods:

This was a quasi experimental study. Patients with AECOPD who develop metabolic alkalosis after getting NIV (BiPAP) treatment in the inpatient department of Respiratory Medicine of National Institute of diseases of the Chest and Hospital (NIDCH) during the study period from April 2017 to March 2019, were the study population and those fulfilling the inclusion and exclusion criteria were enrolled as study sample by non random purposive sampling. All patients of AECOPD with hypercapnic respiratory failure (PaCO2 e" 45 mmHg, PaO2 <60 mmHg) who develop metabolic alkalosis (pH e"7.45 and $HCO3^-$ e"30 mmol/L) following NIV treatment were included whereas patints having concomitant respiratory and neuromuscular diseases, renal failure, serum potassium levels <3.0 mEq/L, known hypersensitivity to acetazolamide or recent administration of bicarbonates were excluded.

Study Procedure:

Acute exacerbation of COPD (AECOPD) with acute hypercapnic respiratory failure patients were treated in ICU or RCU with NIV (BiPAP). Among them who developed metabolic alkalosis (pH > 7.45) as diagnosed by arterial blood gas analysis (ABG), were enrolled. Enrolled subjects were properly explained the study and written informed consent was obtained from all participants. All included subjects were concomitantly treated following international guidelines for COPD exacerbation, with systemic corticosteroids and empirical antibiotic therapy and for related comorbidities. After enrollment, 26 patients were treated with acetazolamide and 26 patients were not treated with acetazolamide. At the day of enrollment (day 0), acetazolamide 500 mg was given orally once a day at morning and continue for two consecutive days. The following laboratory parameters were measured at enrollment (day 0) and after 24 (day 1) and 48 hours (day 2): Arterial pH, partial pressure of O2 (PaO2), partial pressure of CO2 (PaCO2), Urine pH, Serum potassium, chloride, sodium and bicarbonates ($HCO3^-$). Enrolled 26 patients with acetazolamide were compared with 26 patients control group (without acetazolamide) on the basis of laboratory parameters.

Results:

Table-I

Demographic profile of the patients in two groups (n-52)

	With Acetazolamide	Without Acetazolamide	p value
Age (years)			
50 - 59	8 (30.8)	5 (19.2)	
60 - 69	10 (38.5)	12 (46.2)	
≥70	8 (30.8)	9 (34.6)	
Mean±SD	63.34 ± 7.81	64.19 ± 7.08	0.684
Gender			
Male	25 (96.2)	25 (96.2)	1.000
Female	1 (3.8)	1 (3.8)	

Unpaired t test and Chi-Square test was done to measure the level of significance

Table-II

Smoking status of the patients in two groups (n-52)

	With Acetazolamide	Without Acetazolamide	p value
Smoker	16 (61.5)	15 (57.7)	0.958
Ex-smoker	9 (34.6)	10 (38.5)	
Biomass	1 (3.8)	1 (3.8)	

Chi-Square test was done to measure the level of significance

Table-III

Co-morbidities of the patients in two groups (n-52)

	With Acetazolamide	Without Acetazolamide	p value
Diabetes mellitus	7 (26.9)	11 (42.3)	0.382
Hypertension	12 (46.2)	15 (57.7)	0.405
IHD	10 (38.5)	12 (46.2)	0.575

Chi-Square test was done to measure the level of significance

Table-IV

Comparison of arterial pH at enrollment, after 24 hours and after 48 hours between two groups (n-52)

Arterial pH	With Acetazolamide	Without Acetazolamide	p value
At enrollment	7.49 ± 0.02	7.47 ± 0.02	0.382
After 24 hours	7.44 ± 0.03	7.49 ± 0.02	0.405
After 48 hours	7.41 ± 0.03	7.50 ± 0.03	0.575
% change after 48 hrs from enrollment	-1.10 ± 0.37	0.41 ± 0.43	<0.001
p-value (at enrollment vs after 48 hours	<0.001	<0.001	

Unpaired t test was done between groups and paired t test was done within groups (between at enrollment and after 48 hours) to measure the level of significance

Table-V

Comparison of urine pH at enrollment, after 24 hours and after 48 hours between two groups (n-52)

Urine pH	With Acetazolamide	Without Acetazolamide	p value
At enrollment	5.87 ± 0.38	5.77 ± 0.33	0.300
After 24 hours	6.35 ± 0.40	5.78 ± 0.36	<0.001
After 48 hours	6.64 ± 0.33	5.84 ± 0.33	<0.001
% change after 48 hrs from enrollment	13.66 ± 4.77	1.28 ± 3.91	<0.001
p-value (at enrollment vs after 48 hours	<0.001	0.116	

Unpaired t test was done between groups and paired t test was done within groups (between at enrollment and after 48 hours) to measure the level of significance.

Table-VI

Comparison of PO2 at enrollment, after 24 hours and after 48 hours between two groups (n-52)

PO_2	With Acetazolamide	Without Acetazolamide	p value
At enrollment	54.19 ± 5.71	54.00 ± 4.86	0.896
After 24 hours	59.31 ± 6.96	58.04 ± 5.73	0.476
After 48 hours	62.83 ± 7.64	60.08 ± 6.11	0.168
% change after 48 hrs from enrollment	16.29 ± 8.44	11.40 ± 8.03	0.043
p-value (at enrollment vs after 48 hours	<0.001	<0.001	

Unpaired t test was done between groups and paired t test was done within groups (between at enrollment and after 48 hours) to measure the level of significance

Table-VII

Comparison of PCO_2 at enrollment, after 24 hours and after 48 hours between two groups (n-52)

PCO_2	With Acetazolamide	Without Acetazolamide	p value
At enrollment	61.93 ± 4.87	60.09 ± 4.46	0.163
After 24 hours	58.57 ± 3.46	57.49 ± 3.84	0.293
After 48 hours	55.95 ± 3.12	57.58 ± 3.12	0.074
% change after 48 hrs from enrollment	-8.99 ± 6.46	-3.84 ± 6.56	0.008
p-value (at enrollment vs after 48 hours	<0.001	0.005	

Unpaired t test was done between groups and paired t test was done within groups (between at enrollment and after 48 hours) to measure the level of significance

Table-VIII

Comparison of serum electrolytes at enrollment, after 24 hours and after 48 hours between two groups (n-52)

	With Acetazolamide	Without Acetazolamide	p value
HCO_3^-			
At enrollment	46.79 ± 3.48	42.23 ± 2.79	<0.001
After 24 hours	39.85 ± 4.24	44.52 ± 2.75	<0.001
After 48 hours	35.76 ± 2.90	45.69 ± 3.86	<0.001
% change after 48 hrs from enrollment	-23.93 ± 5.08	8.34 ± 8.08	<0.001
p-value (at enrollment vs after 48 hours)	<0.001	<0.001	
K^+			
At enrollment	4.06 ± 0.38	3.90 ± 0.31	0.117
After 24 hours	3.69 ± 0.35	3.75 ± 0.30	0.530
After 48 hours	3.09 ± 1.16	3.78 ± 0.24	0.004
% change after 48 hrs from enrollment	-14.47 ± 7.21	-2.77 ± 5.93	<0.001
p-value (at enrollment vs after 48 hours)	<0.001	0.012	
Na^+			
At enrollment	138.65 ± 3.11	137.04 ± 3.12	0.067
After 24 hours	137.54 ± 2.55	136.81 ± 2.28	0.281
After 48 hours	136.78 ± 2.26	136.42 ± 1.75	0.533
% change after 48 hrs from enrollment	-1.51 ± 1.79	-0.42 ± 1.88	0.043
p-value (at enrollment vs after 48 hours)	0.001	0.232	
Cl^-			
At enrollment	96.31 ± 2.98	96.85 ± 3.09	0.525
After 24 hours	95.23 ± 2.79	96.46 ± 2.20	0.083
After 48 hours	94.86 ± 2.63	96.73 ± 1.59	0.004
% change after 48 hrs from enrollment	-1.56 ± 1.22	-0.18 ± 2.87	0.038
p-value (at enrollment vs after 48 hours)	<0.001	0.847	

Unpaired t test was done between groups and paired t test was done within groups (between at enrollment and after 48 hours) to measure the level of significance

Discussion:

In this study, maximum patients were within age group of 60 – 69 years. Mean age of the patients was 63.34 ± 7.81 years and 64.19 ± 7.08 years in acetazolamide and without acetazolamide groups respectively. In this study most of the patients were male. Out of 26 patients in each group 25 were male and 1 was female with male : female ratio of 25: 1.

More than half of the COPD patients were current smoker in both groups in this study.

Most common co-morbidity was hypertension in both groups followed by IHD and diabetes mellitus. There were no significant differences between groups in co-morbidities in this study.

Serum pH level decreased significantly in COPD patients treated with acetazolamide whereas serum pH level increased in COPD patients treated without acetazolamide. In this study serum pH significantly decreased from 7.49 ± 0.02 to 7.41 ± 0.03 (p value < .001). In the study of Fontana et al.[9] serum pH significantly decreased from 7.46 ± 0.06 to 7.41 ± 0.06 (p value = 0.004).

In this present study, urine pH level increased significantly in COPD patients treated with acetazolamide. Change of urine pH level was significantly higher in COPD patients treated with acetazolamide than that of without acetazolamide.

In this current study, urine pH increased from 5.87 ± 0.38 to 6.64 ±0.33 (p value <0.001). Fontana et al[9] found urine pH significantly increased from 5.80 ± 0.82 to 6.94 ± 0.77 (p value = 0.006).

PCO_2 level decreased significantly in both groups. But change of PCO_2 level was significantly higher in COPD patients treated with acetazolamide than that of without acetazolamide. In this study PCO2 decreased from 61.93 ± 4.87 mmHg to 55.95 ± 3.12 mmHg (p value < 0.001). Similarly in the study of Fontana et al[9] PaCO2 decreased from 63.9 ± 9.8 mmHg to 54.9 ± 8.3 mmHg (p value = 0.01).

PO_2 level increased significantly in both groups. But change of PO_2 level was significantly higher in COPD patients treated with acetazolamide than that of without acetazolamide. With acetazolamide group PO2 increased from 54.19 ± 5.71 to 62.83 ± 7.64 (p value <0.001) and without acetazolamide group PO2 increased from 54.00 ± 4.86 to 60.08 ± 6.11 (p value <0.001).

HCO_3^- level significantly decreased in COPD patients treated with acetazolamide whereas serum HCO_3^- level significantly increase in COPD patients treated without acetazolamide. Serum HCO_3^- level decreased from 46.79 ± 3.48 to 35.76 ± 2.90 (p value < 0.001). Fontana et al[9] also found serum HCO_3^- level decreased from 43.5 ± 5.9 to 36.1 ± 5.4 (p value = 0.005).

K^+, Na^+ and Cl^- level decreased significantly in COPD patients treated with acetazolamide. K^+ also significantly decreased in COPD patients treated without acetazolamide.

Conclusion:

Acetazolamide can significantly reduce arterial pH in AECOPD patients with metabolic alkalosis following NIV. It also helps to reduce PCO2 and improve PO2. So, it can be concluded that Acetazolamide has an important role for the correction of metabolic alkalosis in post-NIV COPD patients.

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