The correlation between end-tidal carbon dioxide and arterial blood gas parameters in patients evaluated for metabolic acid-base disorders

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Abstract

Background: The analysis of arterial blood gas (ABG) is an invasive procedure that is used frequently in the emergency department (ED) to evaluate the acid-base status of critically-ill patients. However, capnometry is an alternative procedure that has been used in recent years to determine the metabolic status of patients' blood. Considering the correlation between end-tidal carbon dioxide ($ETCO_2$) and arterial partial pressure of carbon dioxide ($PaCO_2$) identified in the previous studies and the strong correlation between $PaCO_2$ and bicarbonate (HCO_3^-), we assumed that $ETCO_2$ might be a useful parameter in predicting the presence of metabolic acidosis. The aim of this study was to determine the correlation between $ETCO_2$ and the parameters of ABG in adult patients who were likely present metabolic acid-base disturbances in the Emergency Department of Imam Reza Hospital, the largest academic hospital in Mashhad in northeast Iran.
Methods: This was a cross-sectional study conducted during six months on 62 adult patients who presented with suspected metabolic acid-base disorders to the ED. The exclusion criteria were patients with chronic obstructive pulmonary diseases, loss of consciousness, intubated patients, and those who were unable to tolerate capnography. The patients' demographic information and vital signs were recorded. Also, ABG and $ETCO_2$ results were recorded. The Pearson product moment correlation analysis and linear regression were used to determine the correlation between $ETCO_2$ and ABG parameters.
Results: Sixty-four patients were enrolled, consisting of 37 men and 27 women with a mean age of 55.4 ± 22.7 years. The most common complaints presented were nausea and vomiting (n = 24). The average value for $ETCO_2$ was 26.2 ± 6.1. There were significant linear correlations between $ETCO_2$ level, pH (r = 0.368), HCO_3^- (r = 0.869), $PaCO_2$ (r = 0.795), and Base Excess (B.E.) (r = 0.346). HCO_3 and $PaCO_2$ were the significant predictor values for $ETCO_2$ (linear regression analysis).
Conclusion: $ETCO_2$ can be an appropriate indicator to estimate HCO_3^- and $PaCO_2$ in critical emergency situations, but it cannot be used as an indicator to estimate all ABG variables.
Keywords: capnography; blood gas analysis; acidosis

1. Introduction

The analysis of arterial blood gas (ABG) is a very common test in emergency departments (EDs) for diagnosing, planning treatment, and disposition of patients with hypoxemia, acidosis, hypercapnia, and electrolyte abnormalities (1). Since ABG analyzers are not available in all emergency departments, sometimes it may take up to an hour before ABG results are available. Sampling arterial blood is time-consuming in some patients, and the patient must tolerate the pain associated with the use of the needle several times (1). In addition, it is considered to be an invasive

measure that can lead to complications, such as hematoma, ischemia, arteriovenous fistula, and, occasionally, life-threatening infections (2-4).

ABG sampling is not always simple, and the procedure has some major limitations, including previous surgery such as cut-down and inadequate circulation in the extremities (5). One of the alternative methods for determining the metabolic status of the blood is capnometry. This method is non-invasive for measuring end-tidal CO_2 ($ETCO_2$) pressure, and, recently, it has been used as a tool for monitoring the quality of cardiopulmonary resuscitation (CPR) and determining the cause of bronchospasms (6). It has been demonstrated conclusively that, in proper ventilation/circulation cycles of the pulmonary blood, $ETCO_2$ changes can indicate blood circulation and metabolic status. Several studies have shown that $ETCO_2$ can indicate minute decreases in ventilation and increases in metabolism (7-10).

The literature review on $ETCO_2$ indicated that there were some studies that had evaluated the importance of $ETCO_2$ in diagnosing metabolic acid-base disorders in adult patients. In Barton and Wang's study, a strong correlation was observed between $ETCO_2$ and $PaCO_2$ in non-intubated patients who were referred to the ED (7). However, in studies of children with diabetic ketoacidosis (DKA), it has been reported that $PaCO_2$ can be estimated effectively by using $ETCO_2$ (8-11). Also, some studies have shown that $ETCO_2$ can indicate the status of PCO_2, especially in hemodynamically-stable patients (1, 12). Considering the correlations between $PaCO_2$, HCO_3^-, and $ETCO_2$ that have been identified in previous studies, it seems that measuring $ETCO_2$ can be useful in predicting the presence and severity of metabolic acidosis. However, the validity and usefulness of the correlations that have been identified between $ETCO_2$ and the parameters of ABG are matters of conflict in a few studies that have been conducted with adults that have metabolic disorders (1, 13, and 14). The aim of this study was to determine the correlation between $ETCO_2$ and the parameters of ABG parameters, i.e., pH, HCO_3^-, B.E., and $PaCO_2$, in adult patients in the ED of Imam Reza Hospital in Mashhad, Iran, who were likely to have metabolic acid-base disorders.

2. Material and Methods
2.1. Design and setting of the research
This cross-sectional study was conducted during the six-month period from September 2012 through February 2013 in the ED of Imam Reza Hospital, the largest teaching/referral hospital in Mashhad in northeast Iran. The hospital is affiliated with Mashhad University of Medical Sciences, and the ED treats approximately 150,000 patients per year.

2.2. Sample size and sampling
Considering the correlation between HCO_3^- and $ETCO_2$ as established by Fearon's study (10), the sample size was determined to be 62 patients (confidence interval = 95%, study power = 95%). A purposive sampling method was used to select the 62 patients. We used this sampling method because the selection of patients who were thought to have metabolic acid-base disorders was based on the judgment of the researcher.

2.3. Selection criteria
2.3.1. Inclusion criteria
All adult patients who presented to the ED in need of an ABG analysis due to suspected metabolic acid-base disorders were included in the study.
2.3.2. Exclusion criteria
Patients who were excluded from the study included those who had chronic obstructive pulmonary diseases, loss of consciousness, were intubated, were unable to tolerate capnography, and did not consent to participate.

2.4. Data collection
The variables of this study included demographic information (age, gender, and race), vital signs (blood pressure, pulse rate, respiration rate, body temperature, and oxygen saturation), the main presenting complaint, ABG parameters (bicarbonate (HCO_3^-)), partial pressure of carbon dioxide ($PaCO_2$), pH, base excess (B.E.), end tidal CO_2 ($ETCO_2$), and final diagnosis. The patients' demographic information and vital signs were recorded to obtain baseline information. Before ABG sampling, $ETCO_2$ was measured and recorded using sidestream nasal CO2 sampling cannula (Capnocheck® Sleep Capnograph/Oximeter, BCI^{TM} brand, provided by Smiths Medical, UK). ABG sampling was conducted for each patient, and the samples were sent to the Central Laboratory of the Hospital. The Laboratory's technician was not informed about the results of the $ETCO_2$ tests. ABG and $ETCO_2$ results were recorded.

2.5. Research ethics
The study was approved by the Ethics Committee of Mashhad University of Medical Sciences. Informed consent was obtained from all patients before their inclusion in the study. We did not perform any additional invasive procedures on the patients to acquire additional data. We collected the ABG variables from the routine laboratory records of our patients, and we used capnography, a non-invasive, bedside test that posed no harm to the patients.

2.6. Statistical analyses
SPSS version 17.0 (SPSS, Inc., Chicago, Illinois, United States of America) was used to analyze the data. All categorical variables, such as chief complaint and final diagnosis, were expressed as numbers, percentages. Continuous variables, including $ETCO_2$ and ABG variables were expressed as mean values ± the standard deviation (SD). Correlations of $ETCO_2$ with ABG variables, such as B.E., $PaCO_2$, HCO_3^-, and pH, were examined by Pearson correlation analysis. For more precise results, correlations were investigated for three subgroups of patients, i.e., those with acidemia (pH < 7.35), those with alkalemia (pH > 7.44), and those with diabetic ketoacidosis. A linear regression model was used to determine the correlations between $ETCO_2$ and ABG parameters, such as B.E., $PaCO_2$, HCO3, and pH. A p-value of more than 0.05 was required to accept the hypothesis. A multivariate linear regression analysis method was used to evaluate the influence of the other variables on $ETCO_2$.

3. Results
During the six-month study period, 67 patients who met the inclusion criteria were included in the study, and three patients were excluded from the analysis. One of these three patients had a history of chronic obstructive pulmonary diseases, and the other two required airway management and intubation before ABG sampling. Thus, the results acquired from 64 patients (37 men and 27 women) were statistically analyzed. The range of the ages of the 64 patients was 15-90, and the mean age was 55.4 ± 22.7. Nausea and vomiting (24 cases) and drowsiness (19 cases) were the most common complaints of the subjects, and the other complaints in descending order were anuria (9.3%), dyspnea (7.8%), abdominal pain (6.2%), edema (4.6%), diarrhea (3.1%), and headache (1.5%). Final diagnoses were made for the patients, and they are identified as follows: renal failure (29 cases), diabetic ketoacidosis (8 cases), sepsis (7 cases), drug toxicity (7 cases), hyperglycemia (6 cases), gastrointestinal bleeding (6 cases), and gastroenteritis (1 case).

ABG samples were drawn from the radial artery. Thirty-eight patients had acidemia (pH < 7.35) and 10 patients had alkalemia (pH > 7.44). Among the patients, 52 had hypocapnia ($PaCO_2$ < 35) and 12 had hypercapnia ($PaCO_2$ > 45). All values of the ABG parameters followed a normal distribution (Table 1). Also, the average of $ETCO_2$ was 26.2 ± 6.1, and it had a symmetric and normal distribution.

Table 1. Mean ABG variables and $ETCO_2$ with standard deviations and ranges

Variable	Mean ± SD	Range
PH	7.33 ± 0.08	7.15-7.5
HCO_3^- (mEq/L)	18.9 ± 6.2	7.10-38.8
$PaCO_2$ (mmHg)	33.1 ± 9.6	10-78.9
O_2 Saturation (%)	82.7 ± 12.8	39.8-99
Base Excess (mmol/L)	-4.4 ± 4.6	-15-15.7
$ETCO_2$	26.2 ± 6.1	11-40

There was a weak linear correlation between the level of $ETCO_2$ and pH with Pearson's correlation coefficient of 0.368 (p = 0.003). The correlation between the $ETCO_2$ level and pH in the acidemia group was (r = 0.413, p = 0.01, n = 38), and, in the alkalemia group, this correlation was (r = -0.56, p = 0.08, n = 10). The $ETCO_2$ values changed with pH in patients with diabetic ketoacidosis, and there was no significant correlation (correlation coefficient = -0.185, p = 0.66). There was a strong linear correlation (0.869, p < 0.001) between the $ETCO_2$ level and HCO_3^- with Pearson's correlation coefficient (Figure 1). The correlation between the $ETCO_2$ level and HCO_3^- in the acidemia group was (r = 0.882, p < 0.001), and it was (r = 0.933, p = 0.06) in the alkalemia group. The $ETCO_2$ changes with HCO_3^- in patients with diabetic ketoacidosis had a significant correlation (correlation coefficient = 0.942, p < 0.001). A strong linear correlation was observed between $ETCO_2$ level and $PaCO_2$ with Pearson's correlation coefficient of 0.795 (p < 0.001) (Figure 2).

The correlation between $ETCO_2$ level and $PaCO_2$ in the acidemia group was (r = 0.875, p < 0.001), and it was (r = 0.915, p = 0.08) in the alkalemia group. $ETCO_2$ changes with $PaCO_2$ in patients with diabetic ketoacidosis had a

significant correlation (correlation coefficient = 0.950, p < 0.001). There was a weak, linear correlation between $ETCO_2$ level and B.E with Pearson's correlation coefficient of 0.346 (p = 0.006). The correlation between $ETCO_2$ level and B.E. in the acidemia group was (r = 0.196, p = 0.25, n = 38), and it was (r = 0.733, p = 0.22, n = 10) in the alkalemia group. The changes in $ETCO_2$ with B.E. in patients with diabetic ketoacidosis had a significant correlation (correlation coefficient = 0.726, p = 0.041).
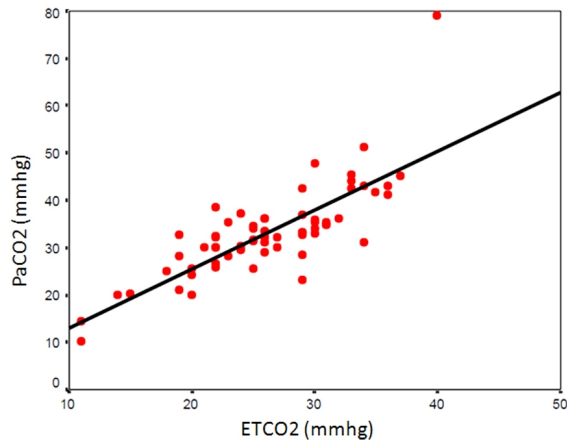

Figure 1. Linear correlation curve of baseline $ETCO_2$ and HCO_3^- for the entire group
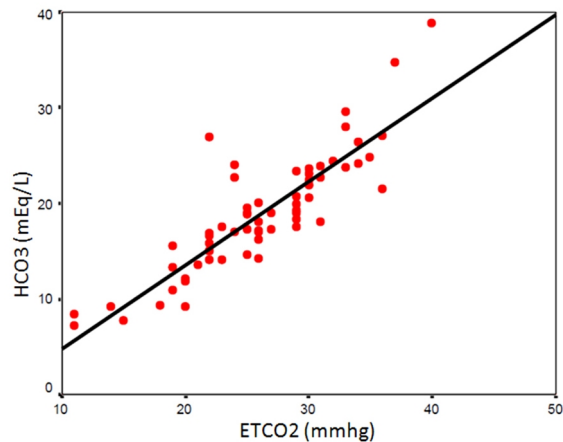

Figure 2. Linear correlation curve of baseline $ETCO_2$ and $PaCO_2$ of the entire group

Regression analysis was used to determine the correlation of $ETCO_2$ and all related ABG parameters. Demonstrating the correlation of baseline $ETCO_2$ with each of the ABG parameters as a model, we found that the correlations of $ETCO_2$ with HCO_3^- and $PaCO_2$ were significant, while no significant correlations were observed for any of the other parameters. This showed that HCO_3^- and $PaCO_2$ are the significant predictors of $ETCO_2$ among the ABG variables (Table 2).

Table 2. Results of linear regression displaying (β), p-values, and 95% confidence intervals for baseline $ETCO_2$

Variable	(β)	p-value	95% Confidence Interval
pH	0.088	0.42	(-9.0–21.1)
HCO_3^-	0.530	0.01	(0.13–0.92)
$PaCO_2$	0.353	0.04	(0.00–0.44)
O_2 Saturation	0.041	0.52	(-0.04–0.08)
Base Excess	0.093	0.89	(-0.17–0.19)

4. Discussion

This study was conducted with the assumption that there might be a significant correlation between $ETCO_2$ and ABG parameters. Determining such a correlation we allow us to use the $ETCO_2$ level instead of arterial blood sampling. The results did, in fact, show that there was a significant correlation between all ABG parameters and $ETCO_2$ in all 64 patients (including those with normal pH, acidemia, and alkalemia). Dividing patients into two groups, identified as those having acidemia and those having alkalemia, showed that the correlation was significant for all patients with acidemia, with the only exception being the correlation between $ETCO_2$ and B.E. However, for the patients with alkalemia, none of the ABG parameters had a significant correlation with the $ETCO_2$ level. Therefore, as previous studies have shown, measuring $ETCO_2$ is very useful in patients with acidemia. However, not all such studies have produced the same results (7-11).

In most studies of children, $ETCO_2$ has been reported to have a strong linear and significant correlation with PCO2, and capnometry can be used to estimate PCO_2 (8, 11). In both studies conducted on children with DKA, regarding the correlation of PCO_2 and $ETCO_2$, these two variables had a strong and significant correlation with correlation coefficients of r = 0.92 and r = 0.79 (8, 11). Thus, using $ETCO_2$ is considered useful in estimating PCO_2 in children with DKA. Also, in the current study, the changes in $ETCO_2$ had a significant correlation with $PaCO_2$ in adult patients with diabetic ketoacidosis. Thus, it seems that $ETCO_2$ might be a useful estimator in patients with diabetic ketoacidosis. However, more studies on adults with diabetic ketoacidosis are required. Studies conducted on adults have been limited mostly to patients with acute dyspnea who were referred to emergency departments, and acidosis was observed in most cases. However, various results have been reported. For example, one study reported that $ETCO_2$ cannot be used to estimate $PaCO_2$ in patients with respiratory distress (15), while another study on patients with the average age of 60.9 found a moderate correlation between $ETCO_2$ and $PaCO_2$ with r = 0.407 and p < 0.001 (16). In another study on adults who had been referred to the emergency department and diagnosed with COPD, there was a moderate correlation between PCO_2 and $ETCO_2$ (17). In our study, the correlation between $ETCO_2$ and $PaCO_2$ was linear and significant, which was in good agreement with the results of another study (1). However, more studies on the correlation of $ETCO_2$ and PCO_2 in adults with respiratory distress are necessary to assess confounding factors, such as respiratory rate and other diseases.

Most of the studies of the correlation between $ETCO_2$ and HCO_3^- have been conducted with children. In a study by Agus et al. (11) on 42 patients suspected of having DKA, the correlation between $ETCO_2$ and venous HCO_3^- variables was reported as r = 0.84 and p < 0.001. Also, in other studies (24, 25) on children with DKA, correlation coefficients for $ETCO_2$ and venous HCO_3^- were determined to be r = 0.88 and r = 0.80. In a study by Gilhotra et al. (9) with children under 18 with DKA, a strong linear correlation was observed between $ETCO_2$ and HCO_3^- (r = 0.72). Like the correlation between $ETCO_2$ and PCO_2, the correlation between $ETCO_2$ and HCO_3^- in children with DKA has been demonstrated in almost all studies. In the current study, this correlation was significant in adults with DKA. However, no study has been conducted to assess the correlation between these two variables in adults. In a study by Mutlu et al. (18) on 240 adults who were referred to the emergency department with suspected metabolic disorders, a moderate correlation was observed between $ETCO_2$ and HCO_3^- (r = 0.50). In a study by Fearon et al. (10), a significant linear correlation was observed between $ETCO_2$ and HCO_3^- (r = 0.80, p < 0.0001), and we found the same correlation as well. Different measuring methods, various sample sizes, and concurrent diseases can describe the differences in the correlation coefficient of the current study, Fearon's study, and Multu's study. In a study by Joshua (19) on children with gastroenteritis, r = 0.80 was reported on the correlation between $ETCO_2$ and blood HCO_3^- level, and it is reported that $ETCO_2$ can be used to estimate HCO_3^- in children with diarrhea and vomiting. It seems that using $ETCO_2$ to estimate HCO_3^- has been demonstrated in most studies so it can be appropriate to use $ETCO_2$ as an indicator of HCO3 especially in emergency situations.

Only one study has been conducted to determine the correlation between $ETCO_2$ and pH, i.e., a study by Garcia et al. (8). A correlation coefficient of r = 0.88 with a significance level of p < 0.001 was reported for the correlation between $ETCO_2$ and pH. In the current study, this correlation was not strong, but it was moderate and linear in patients referred to the emergency department in general and in patients with acidemia and alkalemia. However, one cannot form a definite conclusion based on the two studies, and more research seems necessary. Although a significant correlation was observed between $ETCO_2$ and some ABG parameters in the current study as in all similar studies, there have yet to be any studies to determine the possible correlation between $ETCO_2$ and all ABG parameters as a unique model. Since ABG interpretation is based on all parameters, $ETCO_2$ can be used as a substitute for ABG when there is a significant correlation with all ABG parameters. We used regression analysis in this study in an attempt to investigate the indicator power of $ETCO_2$ regarding the change in each ABG variable as a

model. This is a major contribution of our study. The analysis showed that among ABG parameters as a model, only HCO_3^- and $PaCO_2$ have a significant correlation with $ETCO_2$. Thus, $ETCO_2$ cannot be considered as an indicator that is correlated with all ABG variables. However, it can be an appropriate indicator to estimate HCO_3^- and $PaCO_2$ in critical emergency situations. In order to use $ETCO_2$ as the gold standard in diagnosing metabolic disorders, its sensitivity and specificity must be determined, but that was not the purpose of this study.

Considering the expenses involved, our sample size had to be minimized, and we suggest larger sample sizes in future studies. Since most patients referred to the emergency department during the study were diagnosed with chronic renal disease and diabetic ketoacidosis, it was not possible to precisely estimate $ETCO_2$ function in more diseases with various acid-base disturbances. Thus, it is recommended that future studies divide patients into four groups, i.e., acidosis, alkalosis, respiratory, and metabolic, which should provide a better comparison of $ETCO_2$ application between the groups. Since there were no healthy individuals in the groups, it was not possible to estimate the correlation between $ETCO_2$ level and ABG parameters in healthy individuals and compare that with acid-base disturbances. Therefore, it is recommended that future studies include a control group of healthy individuals.

5. Conclusions
The findings of this study indicate that $ETCO_2$ may not be useful as an indicator in estimating all ABG variables; however, as a fast, inexpensive, and non-invasive test, it can be an appropriate indicator to estimate HCO_3^- and $PaCO_2$ in critical, emergency situations. Further studies are needed to determine whether capnography can be used to accelerate the recognition of metabolic disturbances in the emergency department and decrease the time required to identify the appropriate therapy in critical situations.

Conflict of Interest:
There is no conflict of interest to be declared.

Authors' contributions:
All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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