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Predictive Value of Capnography for Suspected Diabetic Ketoacidosis in the Emergency Department

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**Abstract:**

**Introduction:** Metabolic acidosis confirmed by arterial blood gas (ABG) analysis is one of the diagnostic criteria for diabetic ketoacidosis (DKA). Given the direct relationship between end-tidal carbon dioxide (EtCO₂), arterial carbon dioxide (PaCO₂) and metabolic acidosis, measuring EtCO₂ may serve as a surrogate for ABG in the assessment of possible DKA. The current study focuses on the predictive value of capnography in diagnosing DKA in patients referring to the emergency department (ED) with increased blood sugar levels and probable diagnosis of DKA.

**Methods:** In a cross-sectional prospective descriptive-analytic study carried out in an ED, we studied 181 patients older than 18 years old with blood sugar levels of higher than 250 mg/dl and probable DKA. ABG and capnography were obtained from all patients. To determine predictive value, sensitivity, specificity and cut-off points, we developed receiver operating characteristic curves.

**Results:** Sixty-two of 181 patients suffered from DKA. We observed significant differences between both groups (DKA and non-DKA) regarding age, pH, blood bicarbonate, PaCO₂ and EtCO₂ values (P≤0.001). Finally, capnography values more than 24.5 mmHg could rule out the DKA diagnosis with a sensitivity and specificity of 0.90.

**Conclusion:** Capnography values greater than 24.5 mmHg accurately allow the exclusion of DKA in ED patients suspected of that diagnosis. Capnography levels lower that 24.5 mmHg were unable to differentiate between DKA and other disease entities. [West J Emerg Med. 2013;14(6):590–594.]

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Predictive Value of Capnography for Suspected Diabetic Ketoacidosis in the Emergency Department

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Introduction: Metabolic acidosis confirmed by arterial blood gas (ABG) analysis is one of the diagnostic criteria for diabetic ketoacidosis (DKA). Given the direct relationship between end-tidal carbon dioxide (ETCO₂), arterial carbon dioxide (PaCO₂), and metabolic acidosis, measuring ETCO₂ may serve as a surrogate for ABG in the assessment of possible DKA. The current study focuses on the predictive value of capnography in diagnosing DKA in patients referring to the emergency department (ED) with increased blood sugar levels and probable diagnosis of DKA.

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INTRODUCTION

Diabetes mellitus, defined by high levels of glucose and impaired carbohydrate and lipid metabolism, is the most common endocrine disorder and includes a wide group of metabolic diseases whose major characteristic is hyperglycemia caused by impaired insulin secretion and/or function.¹ Patients with diabetes mellitus are prone to important and disabling complications. One of the most important complications of the diabetes is diabetic ketoacidosis (DKA).² DKA mostly occurs in patients with type I diabetes; however, patients with type II diabetes are also prone to DKA at early ages under stress conditions including trauma, surgery, or infection.³ DKA is defined as blood sugar levels ≥250 mg/dl, ketonuria, ketonemia, and metabolic acidosis (pH<7.3 or blood bicarbonate levels <15 meq/dl).⁴ Blood sugar measurement can be quickly performed using glucometry devices widely available in emergency departments (ED). Ketones in urine could be assessed rapidly using urine...
dipsticks. However, measurement of the acid-base levels is more challenging. Commonly, arterial blood gas (ABG), pH, and bicarbonate levels are used to diagnose acidosis and evaluate its severity. Yet, obtaining ABG samples can be a painful and time-consuming procedure.5

Alternatively, capnography may be used as an alternative, non-invasive and inexpensive (in comparison with ABG) method of assessing ventilatory response to typical metabolic acidosis of DKA.5,10 In our center, the cost of capnography is 1 United States Dollar (USD) whereas each ABG costs 2.5 USD (1 USD for blood sampling and 1.5 for the analysis).

Numerous studies have evaluated the relationship between acidosis and ETCO₂, most of which are in the pediatric patients or the patients without DKA.11-15 In the current study, we aimed to evaluate the relationship between blood bicarbonate and end-tidal carbon dioxide (ETCO₂) values and the predictive value of ETCO₂ in DKA diagnosis in adult patients with increased blood sugar levels referred to the ED.

METHODS

We carried out a prospective cohort study of a convenience sample of patients in the ED of Imam Reza Medical Research and Training Hospital, Tabriz, East Azarbaijan, Iran, 110,000 admission per year, during a 4-month period (December 2011–March 2012).16 Sample size determination was based on the previous studies (11) in which capnography sensitivity in diagnosing DKA was reported to be 83%. Considering α=0.05, power of 80% and 6 units acceptable absolute difference in the reported sensitivity, we selected 176 people which was later increased to 181 people to compensate for expected dropouts or missing data. Patient collection was performed from 8AM until 4PM seven days a week, while no sample collection was performed in the evening or night shifts.

Inclusion criteria for the study: All adult patients older than 18 years old with suspected DKA by an attending emergency physician in charge of the shift and blood sugar levels of higher than 250 mg/dl referred to our ED. Patients likely to have metabolic disturbances from other causes were excluded from the study, including:

1. Gastroenteritis
2. Chronic renal failure
3. Patients unable to tolerate capnography
4. Respiratory diseases
5. Impaired consciousness

This study was approved by the Ethics Committee of “Tabriz University of Medical Sciences” and registered under the Code Number 90104.

On arrival vital signs of all patients were checked and blood sugar levels were measured by glucometer (Clever check, model TD 4209, San Chung, Taipei). Complete blood count, serum levels of sodium, potassium, urea and creatinine, urine ketone levels, and ABG were measured. Patients with blood sugar levels higher than 250 mg/dl, probable DKA diagnosis, and symptoms including nausea, vomiting, abdominal pain, and fatigue were further evaluated. ABG samples were taken for all patients by the same person, and in order to avoid human error in registering ETCO₂ values by different people, capnography values were recorded by one person simultaneously using a RESPIRONICS device (model number: 7100, RESPIRONICS California Inc, California).

Capnography was performed for 1 minute at the same time the ABG sample was taken, and the total number of the registered ETCO₂ in every breath in 1 minute was divided
by the respiratory rate per minute; the calculated mean was
considered as the ETCO2 value of each patient.

At the time of discharge, patients were divided into 2
groups, DKA and non-DKA, based on clinical consensus of
their course and other supporting data.

DKA patients were hospitalized after consultation with
the internal medicine service whereas non-DKA patients,
after calculation of their serum osmolarity, were hospitalized
in case of having hyperosmolar sera or discharged from the
ED. We analyzed the results using SPSS (model number:
17.0.1, SPSS Inc, Chicago). We used descriptive statistical
approaches (domains, frequency, percentage, mean ± SD and
variance). To compare the qualitative data, chi-square test
was used. To compare quantitative data, we used t-test and, if
required, Non-Parametric Mann-Whitney U tests.

We studied normal distribution of the data using
Kolmogorov-Smirnov test. Non-Parametric Mann Whitney U
test was used in case of non-normal distribution of the data.

To evaluate the relation between ETCO2 and ABG findings
(pH, arterial carbon dioxide [PaCO2] and HCO3) in patients
with increased levels of blood sugar, we used the Spearman
correlation coefficient and regression curves. To define ETCO2
as cut-off point in diagnosing DKA, we used receiver operating
characteristic curve analysis ROC). In all cases, we considered
p-value less than 0.05 significant. A flow diagram of our study
is presented in Figure 1.

RESULTS
In the current study, 181 patients including 107 females
were studied. The mean age was 57.9 ± 17.8 years. Sixty-
two patients had DKA (%) while 119 had other conditions
associated with metabolic acidosis. Table 1 shows a
statistically significant difference between the 2 groups (DKA
and non-DKA) regarding age, blood pH, bicarbonate, PaCO2,
blood sugar and ETCO2. Table 2 presents the difference
between groups for associated symptoms at admission.

Spearman test revealed a significant linear correlation between
pH and ETCO2, (p>0.0001, r=0.253) (Figure 2), PaCO2 and
ETCO2, (p>0.0001, r=0.572) (Figure 3) and HCO3 and ETCO2
(p>0.0001, r=0.730) (Figure 4).

To study the sensitivity and specificity of capnography in
diagnosing DKA patients with increased blood sugar levels,
we used ROC curves. The surface area under the curve is
0.037. Given the low surface area and low sensitivity and
specificity of the ETCO2 test, a determination of the cut-off
point was not possible. ROC curves were also used to evaluate
the sensitivity and specificity of capnography in ruling out
DKA in patients with increased blood sugar levels. In Figure
5, the area under the curve is 0.963. Using this curve, a cut-off
point of 24.5 with a sensitivity of 0.90 and specificity of 0.90
was achieved for ETCO2 revealing that ETCO2 >24.5 mmHg
rules out DKA with a moderate confidence (Figure 5).

DISCUSSION
Numerous factors are used to diagnose DKA, including
blood sugar levels higher than 250 mg/dL, ketones in
urine and metabolic acidosis. A conventional method
determining metabolic acidosis is to use ABG, which
can be a painful, time-intensive and expensive procedure
with undesirable complications. Venous blood gases have
been shown to closely approximate arterial for DKA. An
alternative method suggested by our study is to replace ABG
with noninvasive capnography for determining ETCO2 and
severity of metabolic acidosis.

Numerous studies have been performed on the association
of metabolic acidosis and capnography; these, however, have
been of small sample sizes mostly focusing on either pediatric
patients or other metabolic acidosis disorders. Diedre et al, in
a study of 42 pediatric patients, concluded that ETCO2
t-values have a direct linear relation with blood bicarbonate

| Table 1. Demographics characteristics and laboratory findings of both groups (diabetic ketoacidosis [DKA] and non-DKA). |
|---------------------------------------------------------------|
| **** | **DKA Patients** | **Non DKA patients** | **p-value** |
| Age (years) | 51.01 ± 18.86 | 61.53 ± 16.13 | 0.001 |
| Sex | 23 male | 51 male | 0.454 |
| Blood sugar levels (mg/dL) | 458.66 ± 193.16 | 361.88 ± 92.94 | 0.001 |
| pH | 7.24 ± 0.13 | 7.36 ± 0.07 | <0.0001 |
| Bicarbonate (mEq/dL) | 12.76 ± 4.00 | 21.81 ± 3.61 | <0.0001 |
| PaCO2 | 28.99 ± 7.92 | 37.93 ± 6.74 | <0.0001 |
| ETCO2 | 17.98 ± 5.24 | 31.23 ± 5.45 | <0.0001 |

| Table 2. Comparison of the associated symptoms between two groups at admission. |
|---------------------------------------------------------------|
| **** | **All patients** | **DKA patients** | **Non-DKA patients** |
| Nausea/vomiting | 114 (63%) | 40 (64%) | 74 (62%) |
| Abdominal pain | 120 (66%) | 45 (72%) | 75 (63%) |
| Polyuria/polydipsia | 94 (52%) | 39 (63%) | 55 (46%) |
| History of diabetes mellitus | 165 (91%) | 46 (74%) | 119 (100%) |
| Fatigue | 172 (95%) | 62 (100%) | 11 (92%) |

DKA, diabetic ketoacidosis
et al. found (r=0.84 and r=0.79 respectively). Moreover, Gilhotta et al. conducted a study on 58 pediatric patients (1-18 year-olds) with type 1 diabetes. Capnography was felt to be of predictive value for DKA in combination with the clinical evaluation. ETCO₂ values more than 30 could rule out DKA diagnosis with sensitivity of 100% and specificity of 86%. The study of Garcia et al. on 126 DKA patients suggested a statistically significant and direct relation between ETCO₂ and PaCO₂ and pH.

In our study, we focused on predictive value of ETCO₂ in the diagnosis of DKA in adult patients with blood sugar levels higher than 250 mg/dl and probable diagnosis of DKA. ETCO₂ levels were significantly lower in patients with DKA compared to other patients with high blood sugar levels. The more severe the acidosis and the more reduction in the blood bicarbonate levels, the more we found reduction in ETCO₂ levels. Finally, based on our results, capnography can be used to rule out DKA in the patients with increased blood sugar levels; cut-off point of 24.5, sensitivity of 0.90 and specificity of 0.90.

We studied adults, and a larger sample of patients than previous investigators, 4 times (181 versus 42 people) and 3 times (181 versus 58 people) the studies of Dierdre and Gilhotra, respectively.

LIMITATION

Our study had some limitations as it was of a descriptive nature and lacked a control group. Patient collection was performed in specific hours of the day only (8 AM until 4 PM); we did not track nor report the number of the patients with high blood glucose levels referring to the ED. Moreover, some patients were unable to undergo capnography due to their severe nausea and were excluded.
from the study (Figure 1). Based on the study design, we included the results of the ABG and capnography only once and did not evaluate the changes in ABG and capnography values throughout the treatment course.

CONCLUSION
DKA patients do require decisive and prompt treatment. The aim of the current study was to introduce capnography as a screening tool for DKA diagnosis. Capnography is a simple, noninvasive and inexpensive method that could be performed at bedside. A linear relation could be detected between capnography and blood bicarbonate values. Capnography could be used to rule out DKA in patients with increased blood sugar levels with a cut-off point of 24.5 mmHg, with sensitivity of 0.90 and specificity of 0.90.

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