Can venous blood gas analysis replace arterial blood gas analysis in patients with diabetic ketoacidosis?

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ABSTRACT
BACKGROUND: Diabetic ketoacidosis (DKA) is a life-threatening endocrine emergency, traditionally requiring arterial blood gas (ABG) analysis for diagnosis and monitoring. The aim of our study was to assess the comparability of arterial and venous blood samples for pH and bicarbonate measurements in patients with DKA.

MATERIALS AND METHODS: Prospective, observational study of patients with suspected DKA coming to ED (Emergency department) was carried out. Inclusion criteria were capillary blood glucose equal to or greater than 250 mg/dL, ketonuria, and clinical signs and symptoms of DKA. Patients with coexisting respiratory or renal diseases and hemodynamic instability were excluded from the study. ABG and VBG (Venous blood gas) samples were taken simultaneously (within 2 minutes) before treatment. Pearson’s correlation coefficient and Bland-Altman bias plot were used to compare pH and bicarbonate values of arterial and venous blood samples.

RESULTS: Data from 50 episodes of diabetic ketoacidosis in 50 patients were analyzed. Laboratory findings of those patients with diabetic ketoacidosis were as follows (mean±SD): arterial pH, 7.131±0.139; venous pH, 7.108±0.147; serum glucose, 442±113 mg/dL; arterial HCO₃⁻, 6.104±3.133 mmol/L and venous HCO₃⁻, 6.234±3.358 mmol/L. The mean difference between arterial and venous pH values was 0.022 (range 0.0 to 0.054). Arterial and venous pH results (r=0.9959) and arterial and venous HCO₃⁻ results (r=0.9025) were highly correlated and showed a high degree of agreement.

CONCLUSION: A venous blood sample is sufficiently reliable to assess pH and bicarbonate in patients with DKA suggesting that venous sampling alone is appropriate in the management of DKA.

Keywords: Arterial, Blood gas, Diabetic Ketoacidosis (DKA), Venous

INTRODUCTION
Diabetic ketoacidosis (DKA) is a life-threatening endocrine emergency characterized by hyperglycaemia, ketonaemia and metabolic acidosis. Traditionally, arterial blood gas (ABG) sampling for measurement of pH and bicarbonate has been considered an essential part of initial evaluation and monitoring of disease diagnosis and progress3,4. Arterial sampling is, however, painful for patients and carries a risk of complications such as vascular injury, vascular occlusion and infection5. There is now a growing evidence suggesting that arterial and venous pH agree within clinically acceptable limits and a small number of studies suggest that venous and arterial bicarbonate correlate closely. If this is accepted, venous blood gas (VBG) analysis can be accepted as investigation of choice rather than ABG in DKA. The aim of this study was to examine any possible correlation and agreement between venous and arterial blood gas values of pH and bicarbonate in patients with DKA.

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MATERIALS AND METHODS
We performed a single-center, prospective study to assess the agreement between ABG and VBG measurements. This study was conducted in the Emergency Department (ED) of a tertiary care center, Ahmedabad during March 2013 to December 2013. Hospital ethics committee approval was taken prior to initiation of study. A total of 50 patients who were admitted to the ED and had been suspected to have DKA (based on capillary random blood glucose more than 250 and presence of ketones in urine) were enrolled in the study. Patients with coexisting respiratory or renal diseases and hemodynamic instability were excluded from the study. A written and informed consent was taken from the patient and/or relative/legal guardian. A single sample of arterial blood was obtained from each patient by one of the investigators. A single sample of peripheral venous blood was obtained at the time of intravenous line placement or peripheral venipuncture for laboratory testing and was used for the venous blood gas analysis. Samples (arterial and venous) were obtained within 2 minutes of difference so as to avoid changes in blood gases because of time factor. All of the samples were analyzed using the same blood gas analyzer [Combiline Eschweiler blood gas analyzer (GmbH & Co. KG)] as quickly as possible. A single paired...
ABG-VBG samples were obtained per patient to prevent a single patient from dominating the data set. A total of 50 patients were included in the study. The data was entered in Microsoft excel worksheet. The values are expressed as mean ± SD. The Bland-Altman method and Pearson correlation coefficient (r) was used to assess agreement between arterial and venous measurements of pH and bicarbonate.

RESULTS
A total of 50 patients were included in our study of which 42% were men. The mean age for study population was 29.24 ± 16.93 (SD) years (range from 13 to 85 years). The main results are summarized in table-1.

Table 1: Descriptive statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pH</td>
<td>7.131</td>
<td>0.139</td>
<td>6.75–7.30</td>
</tr>
<tr>
<td>Venous pH</td>
<td>7.108</td>
<td>0.147</td>
<td>6.70–7.29</td>
</tr>
<tr>
<td>Arterial HCO3 (mmol/L)</td>
<td>6.104</td>
<td>3.133</td>
<td>2.4–15</td>
</tr>
<tr>
<td>Venous HCO3 (mmol/L)</td>
<td>6.234</td>
<td>3.358</td>
<td>2–17</td>
</tr>
<tr>
<td>Arterial-Venous pH difference</td>
<td>0.022</td>
<td>0.014</td>
<td>0–0.054</td>
</tr>
<tr>
<td>Arterial – Venous HCO3 difference (mmol/L)</td>
<td>-0.13</td>
<td>1.449</td>
<td>-2.8-3</td>
</tr>
</tbody>
</table>

Pearson correlation (r) determines the extent to which values of two variables are proportional to each other. An r closer to -1 represents a strong negative association while an r closer to +1 shows a strong positive correlation. The degree of agreement between the arterial and venous pH measurements and arterial and venous HCO3− values was evaluated by plotting the difference between the paired determinations against the mean of any two determinations, as described by Bland and Altman. This plot is bounded by limits of agreement, defined as the mean of the arterialvenous differences ±2 SD. Arterial and venous pH results (r=0.9959, Figure 1), and arterial and venous HCO3− results (r= 0.9025, Figure 2) demonstrate strong correlations. Graphic depictions of the scatter of data for arterial and venous pH measurements, and arterial and venous HCO3− values are shown in Figures 3 and 4 respectively. In our study, 95% of arterial and venous pH estimations lay within 0.054 of each other and 95% of bicarbonate estimations lay within 5.68 mmol / l of each other showing good agreement.

**Figure 1:** Regression plot of arterial & venous pH measurements. (y = 1.048 x - 0.364)

**Figure 2:** Regression plot of arterial & venous HCO3− measurements (mmol/L). (y = 0.967 x + 0.330)

**Figure 3:** Differences between arterial and venous pH measurements on the vertical axis are plotted against the corresponding means on the horizontal axis.

**Figure 4:** Differences between arterial and venous bicarbonate measurements (mmol/L) on the vertical axis are plotted against the corresponding means on the horizontal axis.

DISCUSSION
Diabetic ketoacidosis is an acute, life threatening complication of diabetes which can lead to diabetic coma (brief period of unconsciousness) or even death. It is typically characterized by hyperglycemia (blood sugar levels >250 mg%), anion gap metabolic acidosis and ketonemia with ketonuria. In DKA, mortality is related to the age and state of consciousness of the patient, and the degree of acidosis, hyperglycemia, and azotemia. Determination of acid-base status, therefore, has
prognostic as well as diagnostic value. Traditionally, arterial blood gas analysis used to be an inevitable investigation to diagnose and monitor the effectiveness of treatment in case of DKA. However, arterial blood sampling has its own complications like painful prick, hematoma formation, infection and vascular occlusion leading to gangrene at times. An alternative but equivalent method to ABG analysis is desirable to avoid the complications of arterial sampling and to allow serial or frequent measurements of pH and bicarbonate. When any two methods of measurement are being compared it is important to define the clinically acceptable limits of agreement. Unfortunately there is little data regarding the same for ABG and VBG values. Rang et al in a survey of 26 clinicians, found that the clinically acceptable limits of agreement were 0.05 pH units, 3.5 mEq/L for bicarbonate and 6.6 mmHg for pCO₂. In our study, 95% of arterial and venous pH estimations lay within 0.054 of each other and 95% of bicarbonate estimations lay within 5.68 mmol/l of each other which is clinically acceptable. Brandenburg et al had studied data from 44 episodes of DKA in 38 patients and had found that the mean difference between arterial and venous pH values was 0.03 (range 0.0 to 0.11). Arterial and venous pH results (r = 0.9689) and arterial and venous HCO₃⁻ results (r = 0.9543) were highly correlated and showed a high measure of agreement in their study. Ma OJ et al studied 200 patients of DKA and found that venous pH correlated well with arterial pH (r = 0.951). Gokel Y et al studied data from 152 patients of which 21 patients had DKA. The respective mean differences between arterial and venous pH and arterial and venous bicarbonate for this group were 0.05 ± 0.01 and -1.88 ± 0.41 mmol/l. The correlation between arterial and venous pH values and bicarbonate values for DKA group was r = 0.989 and r =0.995 respectively. Hale PJ et al studied of 20 patients presenting with DKA that compared arterial blood gas results with finger capillary blood gas results. The mean arterial pH was 7.07±0.15, compared with the mean capillary pH of 7.04±0.15, with a mean difference of 0.03 (r=0.89). They found that the arterial and capillary pH and bicarbonate levels were strongly correlated (r=0.98 and 0.97, respectively). The differences in pH measurements ranged from −0.09 to +0.02. The mean pCO₂ and HCO₃⁻ values also significantly correlated between the arterial and capillary samples, although the capillary values were slightly higher than the arterial values. Our study results are in consonance with these studies. A potential disadvantage of the use of the VBG values in DKA is that it may be more difficult to determine when mixed acid-base disorders are present. Patients with DKA often have conditions such as vomiting, diarrhea, dehydration, and hyperventilation that may cause mixed acid-base disturbances. A mixed acid-base disorder is suggested when the anion gap increase does not equal the serum bicarbonate decrease. In patients who have respiratory depression, venous blood gas values may not accurately reflect the degree of respiratory acidosis or hypoxia, if present. It seems reasonable to continue to perform arterial blood gas analysis in patients with DKA in whom a mixed acid-base disorder is suspected, in those with respiratory depression, and in those in whom hypoxia is suggested by abnormally low pulse-oximetry measurements.

CONCLUSION
Although small differences were noted between pH and bicarbonate arterial blood gas and venous blood gas values, they are unlikely to be clinically significant. Venous and arterial blood gas values of pH and bicarbonate have sufficient agreement as to be clinically interchangeable in DKA patients who are haemodynamically stable without respiratory or renal failure. **Limitation:** The major limitation to this study is its small sample size and convenient number of patients leading to possibility of selection bias. We did not include patients with respiratory or renal compromise and circulatory instability in our study. So the correlation of pH and bicarbonate remains true in those patients or not is an unanswered question. We did not observe the final outcome of the patient so we can not make any conclusion as to whether use of venous instead of arterial blood gas values has any effect on clinical outcome.

REFERENCES
5. Ma OJ, Rush MD, Godfrey MM, Gaddis G. Arterial blood gas results rarely influence emergency physician management of patients with DKA.