Prediction of Arterial Blood pH and Partial Pressure of Carbon dioxide from Venous Blood Samples in Patients Receiving Mechanical Ventilation

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Submission: 07-12-2012 Accepted: 28-04-2013

ABSTRACT
Substitution of arterial with venous blood samples to estimate blood gas status is highly preferable due to practical and safety concerns. Numerous studies support the substitution of arterial by venous blood samples, reporting strong correlations between arterial and venous values. This study further investigated the predictive ability of venous blood samples for arterial Acid-Base Balance (pH) and pressure of carbon dioxide (pCO₂). Participants were 51 post-brain surgery patients receiving mechanical ventilation, who had blood samples taken simultaneously from radial artery of the wrist and elbow vein. Results showed significant associations between arterial and venous blood pH and pCO₂. However, the variation of regression residuals was not homogenous, and the regression line did not fit properly to the data, indicating that simple linear regression is sub-optimal for prediction of arterial pH and pCO₂ by venous blood sample. Although highly significant correlations were found between arterial and venous blood pH and pCO₂, the results did not support the reliability of prediction of arterial blood pH and pCO₂ by venous blood samples across a range of concentrations.

Key words: Acid-base balance, blood gas analysis, carbon dioxide, respiratory insufficiency, veins

INTRODUCTION
Arterial blood gas (ABG) analysis is regarded as gold standard for assessing patient’s oxidation, ventilation, and acid-base balance status.[1-3] However, compared to venous blood sampling, arterial blood sampling needs specially trained personnel and comes with a higher risk of complications, e.g., pain, trauma, bleeding, hematoma, thrombosis with distal ischemia, aneurism formation, hemorrhage, and infection.[1,4] Reporting strong associations between venous and arterial blood gases, several studies have suggested taking venous instead of arterial blood samples to measure patient’s blood gases and acid-base balance.[2,5-8] However, other works suggest different conclusions due to no or weak associations.[2,9,10]

The aim of this study was an in-depth analysis and evaluation of associations between venous and arterial blood pH and partial pressure of carbon dioxide (pCO₂) in post-brain surgery patients receiving mechanical ventilation.

MATERIALS AND METHODS
In total, 60 adult patients completed the study. The participants were selected within two months with the inclusion criteria as follow: All patients were admitted to Shariati educational hospital, were over 18 and selected while they were on mechanical ventilation at intensive care unit (ICU) following a brain surgery. Patients were excluded if any of the following conditions existed: A positive Allen test, hypothermia (temperature <36°C), hyperthermia (temperature >38.5°C), hypotension (systolic blood pressure <90 mm Hg), hypertension (systolic blood pressure >140 mm Hg, or diastolic blood pressure >90 mm Hg, or treated), anemia (Hb < 10 mg/dl), or uncontrolled metabolic disease. Of 60 patients, 9 were excluded (4 due to hypothermia, 2 due to anemia, 1 due to hypotension, 1 due to hypertension, and 1 due to acute tubular necrosis). The data was stored and analyzed by SPSS package version 16. The study was approved by the Najafabad Medical School Research Committee. Both AVG and venous blood tests were ordered for the patients by

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Arterial and venous blood samples were taken simultaneously with heparinized syringes from radial artery of the wrist and elbow vein. After informed consent was obtained and Allen test was conducted with negative result, 0.5-1.0 cc of the blood samples were taken to measure ABG and VBG levels. Samples were analyzed in a blood gas electrolyte analyzer (AVL compact 2).

As suggested by Bland and Atman[11] and generally accepted by other researchers, the agreement between arterial and venous values was measured using plots of mean of paired arterial and venous values against their differences. Pearson’s correlation coefficient ($r$) was also used to measure the strength of association between arterial and venous pH and pCO₂. Linear regression was used to predict the arterial values from venous measures. These methods are generally accepted for evaluating the agreement of two methods of clinical measurements irrespective of the distribution of variables and residuals. [3,5,10,12-18] In the present study, the goodness of fit of the models and the distribution of residuals was graphically evaluated by checking the distribution of regression residuals against arterial values. Based on central limit theorem, normality was assumed fulfilled when regression equations and Pearson correlation coefficients were calculated.[19]

**RESULTS**

In total, 51 patients with simultaneous arterial and venous blood samples participated in this study. Mean patient age was 59.2 years (SD = 15.1, range = 38-91). Fifty-nine per cent of patients were male. Mean values for pulse rate and respiratory rate were 83 BPM (SD = 23) and 17 breaths per minute (SD = 8), respectively. Venous and arterial pCO₂ and pH statistics are presented in Table 1. As can be seen in table 1, a wide range and non-zero (biased) average of differences between venous and arterial values for the above indices are observed (mean of differences are 7.21 mm Hg, \(p < 0.001\) and -0.03 mm Hg for pCO₂ and pH, respectively, \(p < 0.001\)).

The associations of venous and arterial pH and pCO₂ values are shown graphically and mathematically in Figures 1 and 2. The figures show lines of unity (intercept = 0, slope = 1; dotted lines), regression line (solid line), and their regression equations. Figures 3 and 4 represent the distribution of the residuals. Precision and accuracy of venous values representing arterial pH and pCO₂ levels are illustrated by Bland-Altman plots [Figures 5 and 6]. The dotted lines show theoretically unbiased predictions, and the solid lines are regression lines fitted to the average and difference of arterial and venous measures to check whether differences between two measures are constant as the average of venous and arterial values increases. A horizontal regression line represents homogeneity of the differences between arterial and venous values throughout predictor variation. Figure 1 shows a strong correlation between arterial and venous pH (\(R^2 = 0.64, p < 0.001\)). However, the distribution of the residuals for the regression

<table>
<thead>
<tr>
<th>Blood gas variable</th>
<th>Venous (mm Hg)</th>
<th>Arterial (mm Hg)</th>
<th>Difference, venous-arterial (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.39 ± 0.05</td>
<td>7.42 ± 0.06</td>
<td>-0.03 ± 0.04</td>
</tr>
<tr>
<td>pCO₂</td>
<td>45.9 ± 9.8</td>
<td>38.7 ± 3.7</td>
<td>7.2 ± 8.3</td>
</tr>
</tbody>
</table>

*P value for one sample t test

![Figure 1: Correlation between arterial and venous blood gas values for pH.](image1)

![Figure 2: Correlation between arterial and venous blood pCO₂.](image2)
equation seems to be heterogeneous, as the correlation becomes weaker as the arterial values (dependent variable) increase [Figure 2]. Moreover, the significant association between residuals and arterial values ($P < 0.001$) suggests that a linear regression model is sub-optimal for prediction of arterial pH across the observed range of measurements. Differences between arterial and venous values against their averages suggest that venous values are predominantly less than arterial levels and the differences get closer to null as the average values increase [Figure 3].

Although, compared to pH, the correlation coefficient for the venous versus arterial blood pCO$_2$ values is smaller, it is also highly significant ($R^2 = 0.31$, $P < 0.001$) [Figure 4].

As shown in Figure 5, the distribution of the residuals of the regression model for venous and arterial pCO$_2$ is heterogeneous. The significant association between residuals and arterial values ($P < 0.001$) suggests that a linear regression model is sub-optimal for prediction of arterial pCO$_2$ across the observed range of measurements. The difference between venous and arterial pCO$_2$ values is predominantly positive, and increases as average arterial and venous values increase [Figure 6].

**DISCUSSION**

Arterial blood gas and acid base analysis are essential parts of medical care in ICU.[20] However, arterial blood
sampling is invasive and technically complicated, whereas venous blood sampling is easier and safer to obtain.\textsuperscript{[3,5,13]} Strong associations of arterial and venous blood gases and acid-base balance have been reported previously; all assumed sufficiency of a linear model.\textsuperscript{[1,5,9,10,17,21-23]} This study further evaluated the ability of linear models in predicting venous pH and pCO\textsubscript{2} from arterial pH and pCO\textsubscript{2}.

Consistent with other researchers,\textsuperscript{[3,10,22]} we found a significant correlation coefficient between arterial and venous blood pH ($r^2 = 0.64, P < 0.001$). However, the precision of prediction is not consistent and deteriorates as arterial blood pH increases. The distribution of residuals also indicates a significant variation in the prediction of arterial pH values from venous blood samples. The findings suggest that simple linear models may not represent the association between arterial and venous pH and pCO\textsubscript{2} values appropriately. Accordingly, using the generally accepted methods, venous blood pH value may not be a reliable proxy for arterial pH.\textsuperscript{[2]}

With respect to pCO\textsubscript{2}, a weaker but still highly significant correlation between venous and arterial measurements was observed ($r^2 = 0.31, P < 0.001$). Compared to acid-base values, the correlation between venous and arterial pCO\textsubscript{2} values is more consistent across the range of measurements. However, the distribution of residuals indicates considerable variation in the precision of predicted arterial pCO\textsubscript{2} from venous blood samples. While several studies have suggested that the substitution of arterial with venous blood pCO\textsubscript{2} values is of clinically utility,\textsuperscript{[3,5,13,24]} our findings as some others suggested otherwise.\textsuperscript{[3,10,21]}

Debate over feasibility of substitution of arterial pH and pCO\textsubscript{2} with their equivalent venous measurements is ongoing. The difference between studies in methods, analyzer machines, and types of patients may explain the contradictions in the studies’ results. Although the results of this study on the significant correlation between venous and arterial pCO\textsubscript{2} and pH are compatible with existing literature, our findings questioned the suitability of a simple linear regression and the precision and accuracy of arterial values estimated by venous values across all ranges of measurements. Multivariate or non-linear regression models could be considered as alternative methods in similar situations.

Limitations

Our conclusion is to be considered preliminary due to limited generalisability of the study results.

ACKNOWLEDGMENTS

Many thanks to Dr. Ian brown for advising on the manuscript. We also are grateful for the financial support from Azad University (Najafabad branch).

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How to cite this article: Tavakol K, Ghahramanpoori B, Fararouei M. Prediction of arterial blood pH and Partial pressure of carbon dioxide from venous blood samples in patients receiving mechanical ventilation. J Med Sign Sens 2012;3:180-4

Source of Support: This study was financially supported by Azad University of Medical Sciences, Najafabad Branch, Conflict of Interest: None declared

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