Association of end-tidal and venous carbon dioxide in intubated and ventilated children

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Introduction
Capnometry (capnography), called the CO2 measurement of respiratory gases, is widely used in operating rooms and intensive care units.1 A device called a capnometer is commonly used to measure expiratory end-tidal carbon dioxide and display a capnogram waveform.2 Capnography provides a timely interpretation of expiratory CO2 changes.1

In spontaneous breathing, the respiratory center controls the rate of respiration to keep the pH and PaCO2 (pressure arterial CO2) within the normal range.3 However, in critically condition such as severe respiratory distress, patients undergoing mechanical ventilation and respiration is not positively under the control of the respiratory center.4 Therefore, the physicians and medical staff determine the amount of ventilation according to the serial ABG/VBG (arterial/venous blood gas analysis). The ABG/VBG is an invasive and painful procedure (in the absence of an arterial line) and provides only a cross-sectional view of respiratory status.5 End-tidal carbon dioxide pressure (PetCO2) measurement is a non-invasive and actual method for measuring PaCO2/PvCO2 (venous pressure of carbon dioxide) levels that do not have a delay time like ABG/VBG.6

Capnography is a convenient and valuable way to identify clinical problems quickly such as endotracheal ventilator dysfunction and other life-threatening problems, and could also be used to estimate the body’s...
metabolism and nutritional requirements of patients.7

PetCO2 monitoring has many benefits for the patients including; reducing blood sampling, reducing the number of venous catheter insertions, and as a result, the risk of infection and hospitalization, and medical costs are reduced.8

The relationship between PetCO2 and PaCO2/PvCO2 is affected by ventilation and perfusion.9 The perfect matching between ventilation and perfusion leads to a stronger relationship in the fields. So that, in critically ill patients, which have usually disturbed the ventilation-perfusion ratio the use of capnometry in ICU wards is limited.5 However, some studies have shown a good relationship between PetCO2 and PaCO2 /PvCO2 in seriously ill patients.9

Conventionally in patients, venous blood is used to measure carbon dioxide, since this is an invasive and painful method and obtaining blood from children may be difficult and potentially hazardous.10 Therefore, the current study was conducted to compare the PaCO2/ PvCO2 with PetCO2. If we do not observe any statistically significant difference between these two methods, Capnography which is a non-invasive, painless and simple method, will use for assessment the body’s dioxide status in pediatric patients undergoing mechanical ventilation.

Methods
Study design and population
The current investigation was a prospective cross-sectional study that performed on children intubated at PICU of Children hospital, Tabriz, Iran using the census method from September 2019 to September 2020. The educational and training children’s hospital is a general, governmental, and referral hospital with 150 beds and six wards in northwestern Iran.11

After obtaining the approval of the ethics committee and considering the inclusion and exclusion criteria, data including initial diagnosis, age, sex, PvCO2, and PetCO2 were provided for all patients intubated and ventilated in pediatric intensive care unit (PICU) using census method from September 2019 to September 2020.

The PvCO2 was measured after blood sampling from a vein, while the PetCO2 was calculated in the exhaled air using the capnography device. Blood sampling and capnography were performed on the first day of hospitalization in the morning shift by three observers (NM, PN, and FZ). For monitoring CO2 of the expiratory end three examiners used a capnometer device. Agreement (Cohen’s kappa) between two measurements were more than 85%.

This study was blinded so that the analyzer, supervisor, laboratory staff, and two nurses who performed the capnography did not know the results of each patient. In addition, a comparison was also performed between patients with respiratory and non-respiratory disorders.

Inclusion and exclusion criteria
Inclusion criteria for children, including (1) age less than 12 years, (2) hospitalized in PICU, (3) under tracheal intubation, and (4) under mechanical ventilation.

Exclusion criteria for children, including (1) ventilated through a tracheostomy tube, (2) with cyanotic heart, (3) age less than one month.

Data analyses
The data were analyzed by descriptive statistical methods for means (standard deviations), and median and (interquartile ranges) in normally and non-normally distributed quantitative variables, respectively. Frequency, and percentage were used for qualitative variables. In all quantitative variables, the Kolmogorov-Smirnov test was used for checking the normality of variables when the P value > 0.05, the variables were considered to have a normal distribution. The Pearson correlation coefficient was used for the evaluation of the associations between variables. The Linear Regression test was also used for assessing the predictive values of PvCO2 for PetCO2. The confounding factors were not assessed due to low-prevalence children intubated in PICU and low diversity of causative diseases. It should be noted the children intubated due to trauma are not admitted to this center. A P value < 0.05 was considered as a significance level.

Results
Participants
In this prospective cross-sectional study, at first, 64 eligible patients were included in the study, of which 3 patients due to reasons (failure to perform 2 types of sampling at the same time, sampling error, arrest of the patient after performing one type of sampling) excluded from the study. Finally, out of 61 samples, 42 (68.9%) patients were males and 19 (31.1%) patients were females. The characteristics of patients are shown in Table 1.

The results of the Pearson correlation model showed that the correlation of PetCO2 and PvCO2 was significant (P value = 0.003, r = 0.379) as a weak positive correlation. This correlation was observed in group 1 (P value = 0.009, r = 0.374). The Correlation of PetCO2 with other variables (age and sex) was not significant (Table 2)

Table 3 presents the predictive values of PvCO2 for PetCO2. According to the Linear Regression Test results, there was a relationship between PetCO2 and PvCO2 (P value = 0.005). As for one unit increase in the PvCO2 variable, PetCO2 could increase 0.372 units (Table 3 and Figure 1).

Discussion
In this study, the correlation of PetCO2-PvCO2 was statistically significant as a positive, direct correlation but it is not very strong. This correlation also was observed between PetCO2 and PvCO2 in group 1. Furthermore, the PvCO2 variable was able to express PetCO2 changes
As for one unit increase in the PvCO2 variable, PetCO2 could increase by 0.372 units.

Advances in CO2 measurement technology have associated with increased use and importance in patients’ clinics. The importance of measuring expiratory CO2 is more important than blood samples. The CO2 measurement is a proven mechanism to confirm tracheal intubation, diagnosis of accidental esophageal intubation, diagnosis of airway outflow, displacement, and obstruction, monitoring of respiratory distress during anesthesia and after surgery. 12

Another vital importance of capnography is the evaluation the effectiveness of cardiopulmonary resuscitation (CPR) and the condition of ventilation and pulmonary perfusion. It is also used to estimate the metabolism and nutritional needs of critically patients. 13 The importance of expiratory CO2 monitoring has led to the development of recommendations for various guidelines, including the American Society of Anesthesiology (ASA), the American Heart Association (AHA), the American Respiratory Care Association, and the Medicare and Medicaid service centers. However, the examination of CO2 exhalation is often neglected. 14

In a study conducted by McDonald et al on 129 children intubated in PICU, a significant correlation was observed between PaCO2 and PetCO2. Nevertheless, only lung damage had a negative effect on PetCO2-PaCO2. The results strongly supported the use of end-tidal CO2 monitoring to assess non-invasive ventilation in critical patients except in cases with severe lung injury. 5

In a study on 38 shocked patients, a relationship was examined between PetCO2 and cardiac output. The results of this study showed that the evaluation of PetCO2 changes could be used for cardiac output monitoring and the influence of fluid injection in patients. 15

In study of Phishbin et al, on patients with metabolic acid-base disorders observed relationship between end-tidal carbon dioxide and arterial blood gas items and therefore, end-tidal carbon dioxide could be a suitable parameters for estimating blood carbon dioxide in emergency cases. 10

In a pilot study conducted by Baudin et al from 2013 to 2014 on 65 children under mechanical ventilation in the PICU, the mean gradient between Paco2 and PetCO2 was 3.35 mm Hg, and PaCO2 was measured using PetCO2 with an accuracy of ± 5 mm Hg in 95% of cases. Therefore, using non-invasive methods including the measurement of PCO2 is performed via exhalation could determinate the PaCO2 levels. It should be noted, due to the small number of studies in this field, further studies have been recommended. 16

In another study conducted in 2014 on 66 infants and 60 children under mechanical ventilation, a positive correlation was reported between PetCO2 and paco2 with r = 0.836 in infants and r = 0.914 in children.

Table 1. The characteristics of children intubated in Tabriz children’s hospital PICU

<table>
<thead>
<tr>
<th>Variables</th>
<th>Items</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (month)</td>
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<tr>
<td></td>
<td>Median</td>
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<tr>
<td></td>
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<td>96</td>
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<tr>
<td></td>
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<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Maximum</td>
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<tr>
<td>PetCO2 (mm Hg)</td>
<td>Mean</td>
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</tr>
<tr>
<td></td>
<td>Median</td>
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<td></td>
<td>Standard deviation</td>
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<td></td>
<td>Minimum</td>
<td>9</td>
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<tr>
<td></td>
<td>Maximum</td>
<td>57</td>
</tr>
</tbody>
</table>

PICU, pediatric intensive care unit.

Table 2. Correlation between PetCO2 with PvCO2, sex, and age for children intubated in Tabriz children’s hospital PICU

<table>
<thead>
<tr>
<th>Group</th>
<th>Variables</th>
<th>Pearson Correlation Test</th>
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<td>Age</td>
<td>0.4</td>
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<tr>
<td></td>
<td>Sex</td>
<td>0.3</td>
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<tr>
<td>Group 1</td>
<td>PvCO2</td>
<td>0.009</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
<td>0.6</td>
</tr>
<tr>
<td>Group 2</td>
<td>PvCO2</td>
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</tr>
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<td></td>
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<td>0.9</td>
</tr>
<tr>
<td></td>
<td>Sex</td>
<td>0.06</td>
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</table>

PICU, pediatric intensive care unit.

Group 1: Patients with pulmonary disorders, Group 2: Patients with non-pulmonary disorders.

Figure 1. The PvCO2 for predicting PetCO2 in children intubated in Tabriz children’s hospital PICU based on curve estimation.
low Pao2/Fio2 ratio (less than 200) was effective in this relationship.17

Study limitations
This study has a number of limitations. This was done on intravenous samples of children and the samples were not repeated.

Conclusion
The results showed that there is a significant correlation between PetCO2 and PvCO2 in children under mechanical ventilation when this correlation was positive, direct, but weak. Therefore, it is recommended that capnometry maybe used to monitor the adequacy of ventilation in intubated children. In addition, PetCO2 could be a predictor factor for depicting blood carbon dioxide changes and ventilation. As the correlation was weak we suggested the future studies should be performed with more with large sample size.

Strengths and weaknesses points
The low sample size of study is the weaknesses point of this study. Strength point is the comparison of venous blood CO2 (PvCO2) with expiratory air (PetCO2) because the most studies have compared arterial blood (PaCO2) with PetCO2, which is much more difficult to prepare arterial blood in children.

Acknowledgments
We would like to thank the patients for participating in this study and staffs of children hospital PICU, Tabriz, Iran because of their cooperation in the progression of this study.

Authors’ Contribution
Formal Analysis: Leila Vahedi, Amin Khameh.
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Competing Interests
The authors declare that they have no competing interests.

Ethical Approval
The present study was conducted after obtaining approval from the ethics committee of Tabriz University of Medical Sciences. All patients’ information was stored confidentially. At first, informed consent was obtained from each family patient after explaining the goals of the project and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution’s human research committee. Finally, no additional costs were received from patients for performing interventions during the study and all costs were covered by the Vice Chancellor for Research, Tabriz University of Medical Sciences (IR.TBZMED.REC.957).

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Table 3. The predictive values of PvCO2, age and sex for PetCO2 in children intubated in Tabriz Children’s Hospital PICU

<table>
<thead>
<tr>
<th>Group</th>
<th>Variables</th>
<th>Linear regression test</th>
<th>PetCO2</th>
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<tr>
<td></td>
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<td>Slope b</td>
<td>Std. Error</td>
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<tr>
<td></td>
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<tr>
<td>Total</td>
<td>Pvco2</td>
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<td>0.08</td>
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<tr>
<td></td>
<td>Age</td>
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<td>0.03</td>
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<tr>
<td></td>
<td>Sex</td>
<td>0.91</td>
<td>2.19</td>
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</table>

CI, confidence interval.
References


