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Validity of pvo2 and pvco2 in measuring of desired FiO_2 and desired tidal volume on children under mechanical ventilation in PICU

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Abstract
Background: Serial arterial blood gases analysis in children with respiratory distress under mechanical ventilation is the major tool for management and treatment of these patients, which requires experienced personnel to properly arterial sampling. In pediatrics because of arterial puncture may cause complications, it is difficult to evaluate arterial blood gases repeatedly. This study was aimed to determine the validity of pvo2 and pvco2 in measuring of desired FiO2 and desired tidal volume on children under mechanical ventilation admitted to picu.
Materials and Methods*:* In this cross-sectional study, 50 patients who were admitted to the picu of Tabriz Children's Center with respiratory distress and underwent mechanical ventilation were included in the study. Arterial blood samples were taken to determine pao2 and paco2 and venous blood samples were taken simultaneously to determine pvo2 and pvco2. Pao2 and paco2 obtained from arterial blood were considered as the gold standard for measuring desired tidal volume and FiO2. All samples were assessed by a blood gas analyzer. The desired tidal volume and the desired FiO2 values were calculated using the formula.
Results: The results showed that the use of desired FiO2 by venous sampling instead of arterial sampling and use of desired tidal volume by venous sampling instead of arterial sampling have a sensitivity of 91.54% and specificity of 68.67% and a sensitivity of 90.12% and specificity of 63.89%, respectively.
Conclusion: According to the results in this study, concluded that the use of pvo2 and pvco2 in calculating desired FiO2 and desired tidal volume have acceptable validity.

Keywords: respiratory distress, Pvo2, Pvco2, Fio2, tidal volume

Introduction
Arterial blood gas (ABG) analysis is an essential part of patients' oxygenation diagnosis and management [1]. ABG analysis is also an important source for obtaining effective ventilation information in PICU patients [2]. Oxygenation and ventilation information in ABG is assessed by partial pressure of arterial oxygen (pao2) and partial pressure of arterial co2 (paco2), taking into account pao2 (75-100 mmHg) and paco2 (35-45 mmHg). ABG is routinely performed more than once in the ICU to help periodically follow a patient's treatment [3]. However, arterial blood sampling is an invasive method and has complications such as arterial injury, hemorrhage, thrombosis, distal ischemia, aneurysm and pain[2] for these reasons, many tends has been developed to perform other diagnostic methods, including venous gas analysis [4]. Venous blood gas (VBG) analysis is an alternative method for assessing pco2 and pH status in patients admitted to the ICU because the most patients have a central venous catheter [5]. Several studies have shown a good association between venous and arterial blood samples [6]. The partial pressure of venous carbon dioxide (pvco2) in VBG was (41-51 mmHg) and the partial pressure of venous oxygen (pvo2) was (35-40 mmHg) [7]. PvO_2 shows the balance between respiratory oxygen and the amount of oxygen consumed [8].

Factors that increase pvo2 were left to right shunts, high cardiac output; and factors that decrease pvo2 were low cardiac output, decreased oxygen delivery due to hypoxia, and abnormalities or deficiency of hemoglobin [9]. The need for mechanical ventilation is one of the most common causes of hospitalization in the ICU. Ventilation involves the exchange of air between the lungs and air that removes co2 from the body. Ventilation is measured as minute ventilation at the bedside, and it is calculated as the number of breaths in the tidal volume. The tidal volume is the volume of air that moves in and out of the lungs in each respiratory cycle. Oxygenation involves the supply of oxygen to the lungs, which can be gained by increasing FiO_2. FiO_2 is the percentage of oxygen in the mixed air that the patient receives [10].

A lot of ventilators have precise oxygen delivery systems, and the desired FiO_2 is used to determine the percentage of respiratory oxygen to accurately assess oxygen delivery to provide guidance for the use of supplemental oxygen in stable patients. The desired tidal volume is also used for complete evaluation of ventilation [11]. According to the literature review, since no study has been reported on the validity of pvco2 and pvo2, the aim of this study was to evaluate the Tabriz, Iran.

Materials and Methods

Study population and inclusion criteria

The study population in this study were children with respiratory distress. Inclusion criteria were age Between 1 month to 14 years, respiratory distress, under mechanical ventilated patients.

Exclusion criteria

Exclusion criteria were parents' dissatisfaction to participate in the study, patients with cyanotic heart disease associated right to left shunts and patients with hemoglobinopathies.

Study design and duration

This is a cross-sectional study that was done in Tabriz Children Hospital's PICU ward. In this study, according to previous similar studies and a pilot study conducted by our research team and using Power and Sample Size sampling software, by considering the alpha error value of 5% and power=81%, a total of 45 samples were obtained, and because of the probable rate of 10% in sample loss during the study; a final sample size of 50 patients were considered and studied.

According to the study criteria, 50 children who were admitted to the PICU of Tabriz Children's Center with a diagnosis of respiratory distress and underwent mechanical ventilation were included in the study. Demographic data such as age and gender were recorded in a data collection form designed by the researcher.

Arterial blood samples were taken to determine the amount of pao2 and paco2 and venous blood samples were taken simultaneously to determine the amount of pvo2 and pvco2. Arterial and venous samples were taken in same time by experienced nurse. Pao2 and paco2 obtained from arterial blood were considered as the gold standard for measuring desired tidal volume and FiO_2. All samples were assessed by same blood gas analyzer (IL-GEM-Premier 3000; India).

Then, using the formula, the desired tidal volume and the desired FiO_2 values were calculated. To determine the validity of pvo2 and pvco2, diagnostic analysis methods including sensitivity and specificity, positive and negative predictive value were used. The following formulas were used to calculate the desired tidal volume and the desired FiO_2 with pao2, paco2, pvo2 and pvco2:[12]

* ABG

Desired tidal volume = actual paco2 × actual tidal volume ÷ desired paco2

Desired FiO_2 = actual FiO_2 × desired pao2 ÷ actual pao2

* VBG

Desired tidal volume = actual pvco2 × actual tidal volume ÷ desired pvco2

Desired FiO_2 = actual FiO_2 × desired pvo2 ÷ actual pvo2

Statistical analysis

All obtained data were analyzed by SPSS statistical analysis software version 21 and the p-value value is considered less than 0.05 to determine the significant relationship. Demographic findings were presented in the form of tables and graphs by frequency (%) and Mean ± Standard Deviation (SD). For comparing non-parametric quantitative data, Mann-Whitney U test was used; and in the parametric ones, student's t test was used.

Results

Demographic and clinical data

In the present study, 50 children who were admitted to picu with respiratory distress and intubated and subjected to mechanical ventilation were included in the study. In part of gender distribution of patients, 29 cases (58%) were boys, and 21 cases (42%) were girls. The mean age of patients was 6.12±4.35 years with a median of 4 years (1 month to 13 years). Mean of patients' blood test values including arterial and venous blood gases is shown in Table 1.

Table 1: Test values of patients including ABG and VBG (n=50)

Variable	Mean ± SD (range)
ABG	
pH	7.35±0.14 (7-7.96)
Paco2 (mmHg)	43.12±18.21 (11.21-97.31)
Pao2 (mmHg)	88.12±29.76 (33-162)
HCO_3^- (mEq/L)	20.42±9.35 (3.6-42.7)
Desired tidal volume (cc)	146.5±33.8 (25-255)
Desired FiO_2 (%)	64.6±18.8 (40-100)
VBG	
pH	7.31±0.12 (7.03-7.69)
Pvco2 (mmHg)	46.67±20.42 (13.3-106.54)
Pvo2(mmHg)	53.42±21.65 (20-121)
HCO_3^- (mEq/L)	25.04±5.78 (4.3-38.22)
Desired tidal volume (cc)	131.7±33.5 (20-319)
Desired FiO_2 (%)	51.3±20.25 (23-100)
Ventilator	
Actual tidal volume (cc)	105.9±46.5 (26-255)
Actual FiO_2 (%)	58.5±18.12 (30-100)

ABG; Arterial blood gas, VBG; Venous blood gas, PH; Power of hydrogen, Paco2; Partial pressure of arterial carbon dioxide, Pao2; Partial pressure of arterial oxygen, Pvco2; Partial pressure of venous carbon dioxide, Pvo2; Partial pressure of venous oxygen, HCO3; Bicarbonate, Fio2; Fraction of inspired oxygen.

In the present study, the values of pao2 and paco2 obtained from arterial blood as the gold standard for measuring desired tidal volume and Fio2. The results showed that the use of desired fraction of inspired oxygen (FiO_2) by venous sampling instead of desired fraction of oxygen (FiO_2) by arterial sampling has a sensitivity of 91.54% (95% CI: 72.55-98.75) and specificity of 68.67% (95% CI: 52.31-81.15). The positive diagnostic value of the FiO_2 by venous sampling was 53.31% (95% CI: 43.15-64.87) and the negative diagnostic value was 93.46% (95% CI: 84.21-98.64).

Also, results showed that the use of desired tidal volume (Vt) by venous sampling instead of desired tidal volume (Vt) by arterial sampling has a sensitivity of 90.12% (95% CI: 71.3-97.46) and specificity of 63.89% (95% CI: 54.51-82.66). The positive diagnostic value of the Vt by venous sampling was 56.12% (95% CI: 41.87-67.48) and the negative diagnostic value was 94.19% (95% CI: 85.62-97.92).

Validity of pvo2 and pvco2 values in desired FiO_2 calculation

The results of evaluating the validity of pvo2 and pvco2 values in the calculation of desired FiO_2 in patients were as follow. The ROC Curve diagram (Figure. 1) shows the results for the validity of pvo2 and pvco2 in the desired FiO_2 calculation.

a. ***Pvo2:*** In pvo2 validation, the AUC value was 0.925 (95%

CI: 0.879-0.986; $p<0.001$). pvo2 sensitivity and specificity were 88.4% and 82.8%; respectively. The cutoff value of obtained pvo2 was 78.6 mmHg.

b. ***Pvco2*:** In pvco2 validation, the AUC value was 0.893 (95% CI: 0.783-0.925; $p<0.001$). The sensitivity and specificity of pvco2 was 73.2% and 75.6%; respectively. The cutoff value of obtained pvco2 was 48.5 mmHg.

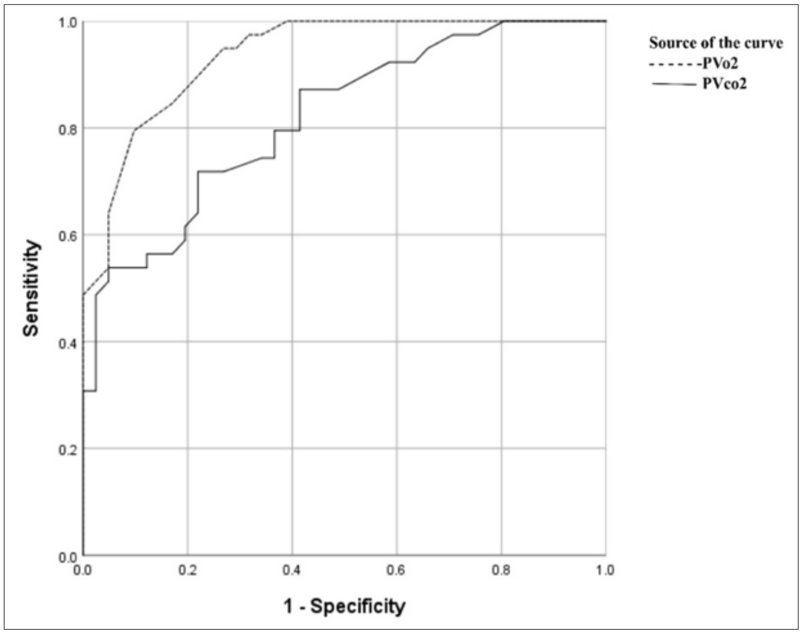

Fig 1: ROC Curve for analysis the validity of pvo2 and pvco2 values in FiO_2 calculation

Validity of pvo2 and pvco2 values in desired tidal Volume calculation

The results of evaluating the validity of pvo2 and pvco2vvalues in the calculation of desired tidal volume in patients were as follow. The ROC Curve diagram (Figure. 2) shows the results for the validity of pvo2 and pvco2bin the desired tidal volume calculation.

a. ***PvO_2*:** In pvo2 validation, the AUC value was 0.912 (95% CI: 0.866-0.991; $p<0.001$). pvo2 sensitivity and specificity were 79.8% and 75.5%; respectively. The cutoff value of obtained pvo2 was 69.8 mmHg.

b. ***$PvCO_2$*:** In pvco2 validation, the AUC value was 0.831 (95% CI: 0.723-0.911; $p<0.001$). The sensitivity and specificity of pvco2 was 69.8% and 69.6%; respectively. The cutoff value of obtained pvco2 was 44.7 mmHg.

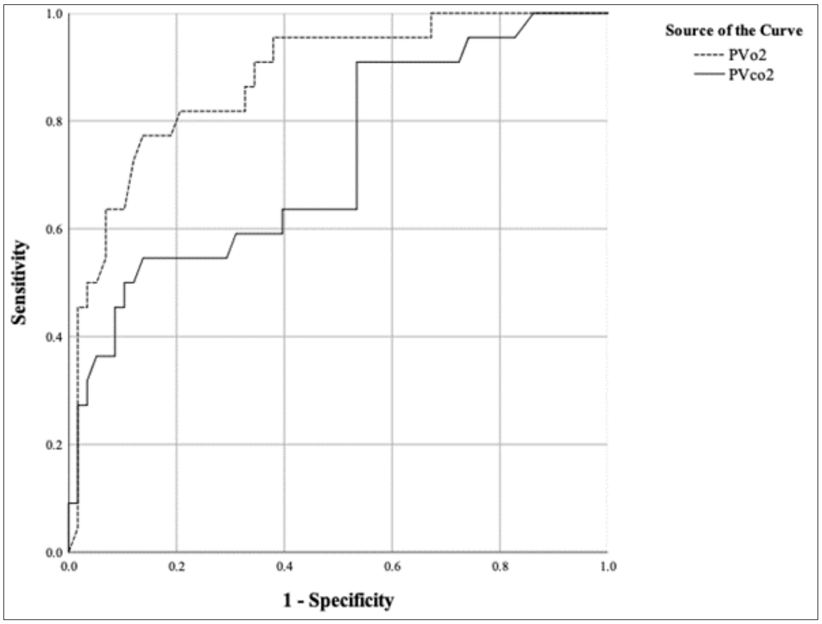

Fig 2: ROC Curve for analysis the validity of PvO_2 and $PvCO_2$ values in tidal volume calculation

Discussion

Adequate oxygen supply to body tissues is necessary for their normal functioning. Oxygen concentrations can be effective in maintaining cardiopulmonary health, proper blood flow, and the health of other tissues related to blood flow. Numerous techniques have been developed to assess oxygen supply, most of which have not been universally accepted. Arterial blood gas analysis plays an important role in assessing the condition of patients with respiratory problems. On the other hand, this experiment is a time consuming, painful and invasive process. Studies have shown that venous blood gas analysis has values related to arterial blood, but the difference between arterial and venous blood gases is sometimes high and unpredictable; So that it does not allow complete replacement [13].

Acid-base analysis is one of the most significant methods used in picu to determine the status of patients with respiratory distress [14]. Non-invasive methods such as pulse oximetry, cutaneous oxygen monitoring, and expiratory carbon dioxide are performance-proven, [15]. but these variables do not provide information on pH, bicarbonate, or pao2. For this reason, the PICU section uses ABG analysis. However, this method is invasive and has problems such as the effect of homeostasis on arterial blood sampling. This process itself is a difficult and painful technique in children. In patients admitted to the PICU, the arteries are generally accessible, but when these arteries are not accessible, clinicians use peripheral and central veins to assess the status of blood gases. Venous blood samples are taken from almost all hospitalized patients to assess the status of paraclinical tests. If the condition of patients' blood gases can be assessed by venous blood, the sample can be easily prepared and analyzed. Clinicians have been looking for alternative methods for ABG in children and adults for many years, and various studies have been performed to evaluate the relationship between venous and capillary blood gas status values [16].

Studies comparing ABG with VBG in patients with diabetic ketoacidosis and admitted to PICU have shown good results in correlation between ABG and VBG samples .[17] However, fewer studies have been conducted to randomly examine large sample sizes of stable and unstable patients admitted to the PICU. In the present study, 50 patients admitted to PICU with age over 1 month and identical and healthy cardiovascular status with respiratory distress regarding pH, po2, pco2 and HCO_3^- values along with evaluation of desired fraction of inspired oxygen (FiO_2) and the desired tidal volume have been evaluated and compared by ABG and VBG.

In the present study, the values of pao2 and paco2 obtained from arterial blood as the gold standard for measuring desired tidal volume and Fio2.The results showed that the use of FiO_2 by venous sampling instead of FiO_2 by arterial sampling in calculation of desired Fio2 has a sensitivity of 91.54% (95% CI: 72.55-98.75) and specificity of 68.67% (95% CI: 52.31-81.15). Also, the positive diagnostic value of FiO_2 by venous sampling was 53.31% (95% CI: 43.15-64.87) and the negative diagnostic value was 93.46% (95% CI: 84.21-98.64).

The results showed that the use of tidal volume by venous sampling instead of tidal volume by arterial sampling in calculation of desired tidal volume in the present study has a sensitivity of 90.12% (95% CI: 71.3-97.46) and the specificity of 63.89% (95% CI: 54.51-82.66). The positive diagnostic value of the tidal volume by venous sampling was 56.12% (95% CI: 41.87-67.48) and the negative diagnostic value was 94.19% (95% CI: 85.62-97.92).

In a study by Cole et al. [18]. a good correlation was found between pH and pco2 values compared to ABG and VBG, while this correlation was not observed in po2 study. Contrary to our study, Tin. et al, [19]. found no correlation between pH, pco2 and pco2 between ABG and VBG. The validity of pvo2 and pvco2 values in calculating desired FiO_2 and desired tidal volume in the studied patients from the AUC and Cutoff Point values obtained , showed that the use of pvo2 and pvco2 in calculating desired FiO_2 and desired tidal volume have acceptable validity.

The correlation of VBG and ABG was comparable to previous studies in neonates and pediatric patients [20, 2]. By contrast, while we observed a good correlation of pco2 between VBG and ABG, this correlation varied between studies [22]. Some studies described that correlation and agreement of PCO_2 is poor in very sick pediatric patients [23]. Bilan et al. recognized a good validity and clinical agreement based on kappa statistics for acid–base imbalance (pH, pco2, po2) for most intensive care pediatric and neonatal patients but not when there was congestive heart failure or shock [24].

As declared by McGillivray. et al, [22] there was a meaningful correlation between results of ABG and VBG analysis only in patients with perfect tissue perfusion. Adrogue. et al, [25] reported large group of children with mild to moderate disease including kidney disorders and dehydration, diabetic ketoacidosis and metabolic diseases; in such cases, obtaining ABG is not critical and VBG analysis can also be used. A study by Silverman et al [26] on 78 VBG samples taken from children admitted to the picu showed that the values obtained from the venous blood gas analysis were reliable and provided acceptable results for treatment, which not studied in our study. On the other hand, as in our study, the majority of studies have been performed on stable patients, while some studies have reported a poor correlation between arterial and venous blood gas levels under hypothermia, hypo perfusion, and shock [27] These patients require continuous and serial evaluations of pH, pco2, po2 and HCO_3^-.

Conclusion

According to the results obtained in this study, it can be concluded that the use of pvo2 and pvco2 in the calculation of desired FiO_2 and desired tidal volume of patients admitted to picu have acceptable validity. So that in evaluating the validity of pvo2 and pvco2 values in calculating desired FiO_2, the sensitivity and specificity were above 80% and 70%, respectively. In evaluating the validity of pvo2 and pvco2 values in calculating desired tidal Volume, the sensitivity and specificity were above 70% and 60%, respectively.

Conflict of interest

None.

Acknowledgements

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Ethics

In this study, a written consent form was provided to the parents, and before the study began, the parents themselves talked about the study. If they agreed, their children would enter the study. In all cases, the principle of confidentiality and trust in patients' names and personal information was observed. Also, non-inclusion in the study had no effect on the usual process of treatment of patients and patients had the option of non-cooperation at any stage of the project. Also, no additional costs were imposed on the patients and the patients were continuously supervised by pediatric pulmonology specialists and subspecialists in all stages of the research as the facilitator and collaborator of the project. It should also be noted that this plan was proposed in the ethics committee and was carried out in accordance with the laws approved by the ethics committee of Tabriz University of Medical Sciences (IR. TBZMED. REC1400. 222)

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