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The Use of Saliva Sample Evaluating PaO2, PaCO2, pH, and HCO3 Values in Traumatic Patients under Mechanical Ventilation; as a Non-Invasive Approach Than the Arterial Blood Gas Sampling

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ABSTRACT

Background: Arterial Blood Gas (ABG) analysis is a commonly ordered test to investigate respiratory, circulatory, and metabolic status in traumatic patients with inappropriate perfusion and ventilation situations. Difficult sampling, hemorrhage risk of arterial puncture, and other vascular complications lead us to use saliva sampling as a safer non-invasive approach to evaluate PaO2, PaCO2, pH, and HCO3 values.

This study was aimed to evaluate the correlation of PaO2, PaCO2, pH, and HCO3 values between ABG and saliva gas in traumatic patients under mechanical ventilation.

Methods: This was a retrospective cross-sectional study of 18-85-year-old traumatic patients under mechanical ventilation conducted in an academic medical hospital. They were investigated based on age, sex, and ABG values as well their saliva gases values. The Paired t-test, Pearson $\chi 2$, and Pearson correlation were used to evaluate the correlation between the gases values in ABG and saliva. Data were analyzed using Mann–Whitney U test and Kolmogorov–Smirnov test.

Results: There were 120 patients including 53 men and 67 women enrolled. None of the factors of arterial and salivary gases were significantly different between men and women. And the amount of these factors is homogeneous in both groups ($P < 0.05$). The mean factors of arterial PaCO2 and HCO3 and saliva PaCO2 and HCO3 were significantly different between smokers and non-smokers.

Conclusion: The values of salivary gases correlated with these of ABG. This can expand the use of salivary gases analysis as an alternative to ABG analysis in clinical settings to reduce the logistic burden of arterial sampling as well as to better perform ventilator device settings. These results were aligned with previous studies.

Trauma is the first reason for mortality and one of the leading causes for disability and loss of life years of the active population in developing countries. A significant proportion of trauma patients require hospitalization and intensive care under mechanical ventilation [1-3]. The inappropriate situation of ventilation and perfusion subjects these patients to changes in blood gases and electrolytes [4-5]. These

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aberrant values in blood gases are important as markers to predict patient outcomes [6-7].

Arterial Blood Gas analysis is a common approach in traumatic and critically ill patients for investigating pH, partial pressures of blood gases, and electrolytes to diagnose respiratory, circulatory, and metabolic disorders [8].

Difficult sampling, hemorrhage risk of arterial puncture, bruising, and infection occur following repeated blood draws [9-10]. On the other hand, gas emission from the wall of syringes, the effects of Heparin contained in syringes on pH and PaCO2 of the blood sample, temperature effects, and also existence of air bubbles inside the syringe can influence the ABG results [11-12]. Due to these reasons, saliva sampling can be considered a noninvasive and safer alternative technique to ABG. Sampling from saliva is more convenient and accessible than other biological body fluids, since, the salivary glands are organs that secrete large amounts of fluids and electrolytes daily [13]. Saliva as a colorless liquid with a density between 18 and 35 contains maltase, serum albumin, urea, uric acid, creatinine, vitamin C, amino acids, lysozyme, lactate, and some hormones also include some gases such as CO2.O2, N2. The saliva PH is usually about 6.64 and its quantity depends on the CO2 amount in the blood [14]. There are large amounts of Potassium and Bicarbonate ions in saliva while its Sodium and Chloride ions content are several times lower than the plasma [15]. Increasing attention to non-invasive procedures has highlighted the importance of applying new techniques for saliva collection and analysis [16]. As a result, this study was performed to investigate if the values of saliva and plasma PaO2, PaCO2, pH, and HCO3 could be correlative in traumatic mechanical ventilated patients and the aim was whether Saliva analysis can be used as a non-invasive approach compared to the Arterial Blood Gas (ABG) sampling.

Methods

Design and eligibility

This retrospective cross-sectional study was conducted in 2019-2020 at the academic medical center, Alzahra Hospital, Isfahan, Iran. As well this is an example of non-randomized trials. The study was approved by the Ethics Committee of medical science University (cod: IR.MUI.MED.REC1399.459). Written informed consent was obtained from all participants' (legal guardians) relatives after the study was thoroughly explained.

Traumatic patients with 18 to 85 years old, under mechanical ventilation that were ordered to have ABG analysis and had a suitable artery for taking sampling according to the trained nurse, were included into the study. Pregnancy, diabetes, and any type of oral disease were non-inclusion criteria. Patients' were excluded if they had hyperglycemia during the study, also if it took more than 15 minutes for samples transferring to the laboratory, existence of any bubbles of air or blood clots in syringes, and improper saliva sampling due to dry mouth.

Procedures and assessments

Traumatic patients under mechanical ventilation admitted to the intensive care units of AL Zahra hospital were screened based on inclusion and exclusion criteria. Demographic information, smoking history, comorbidities, and vital signs, were extracted from the patient's medical records and registered in the data collection form. The patient's radial or femoral artery was investigated for ABG sampling and the Allen-test (if the sample was taken from the radial artery) was performed by the trained study nurse. The Allen test is a method to assess the arterial blood supply of the hand. A detailed description of the method has been published elsewhere [17]. Then ABG sample was taken in a heparinized syringe or special kit. (Pro-Vent, Smiths Medical SD, Keene, USA) in a standard way. It's noted that any error in sampling led us to repeat the process for outmost accuracy for up to three times. Immediately after that, saliva sampling was done; at first, the mouth was rinsed with normal saline, 15 minutes later 0.5CC of saliva was sampled in a special package. Labeled samples were sent to the laboratory within 15 minutes under standard conditions (placing on ice). ABG samples were analyzed by Blood Gas AVL441 machine and saliva samples by Blood Gas System model GASTAT-602i. The obtained result from evaluating PH, PO2, PCO2, and bicarbonate ion values were recorded in the profile of each patient.

Statistical analyses

The association between ABG and Saliva values in PH, PaO2, PaCO2, and HCO3 was evaluated by paired t-test, Pearson $\chi 2$, and Pearson correlation coefficient. Means with standard deviation (SD) for Continuous variable with normal distribution and Mann–Whitney U-test and Kolmogorov–Smirnov V-test for non-normally distribution was used and the results were presented by tables and figures. Linear regression accounting was used for Correlations and comparison analyzing too.

P-value less than 0.05 were considered significant. Statistical analysis was performed by using SPSS version 24.

Results

Of 53 men and 67women screened based on inclusion criteria with an average age of 41.33 ± 14.72 years, 32 patients were smokers. All 120 patients underwent ABG analysis and analysis of saliva gases. Information on arterial and salivary gases analysis is summarized in Table 1. The result of the Kolmogorov-Smirnov test showed that the hypothesis of normality is not established for any of the consequences. Therefore, we used non-parametric tests to test the hypotheses (Table 1).

Table 1- Summary of arterial blood and saliva gas values (n = 120)

Parameter	ABG (Mean ± SD)	AS (Mean ± SD)	ABG P value*	SG P value*
pH	7.36±0.12	7.36±0.11	< 0.001	< 0.001
$PaCO_2$ (mm Hg)	41.14±15.26	41.98±15.93	< 0.001	< 0.001
PaO_2 (mm Hg)	73.32±45.62	59.48±38.80	< 0.001	< 0.001
HCO_3^- (mEq/L)	20.69±5.58	20.82±5.73	0.032	0.004
			P value**	< 0.001
Kolmogorov-	Smirnov test	*intra Group **inter Group		

ABG, arterial blood gas; SG, saliva gas; A-S, arterial minus saliva difference; SD, standard deviation

The result of the Mann-Whitney test showed that none of the factors of arterial and salivary gases were significantly different between men and women. And the amount of these factors is homogeneous in both groups (Table 2).

Table 2- Summary of arterial blood and saliva gas values based on gender

Parameter	ABG women (Mean ± SD)	ABG men (Mean ± SD)	SG women (Mean ± SD)	SG men (Mean ± SD)	ABG P value*	SG P value*
pH	7.34±0.15	7.38±0.09	7.36±0.11	7.36±0.12	0.373	0.756
$PaCO_2$ (mm Hg)	42.39±15.76	39.31±14.49	43.68±17.33	39.16±13.05	0.359	0.233
PaO_2 (mm Hg)	77.87±53.73	67.21±31.34	58.33±35.32	61.03±43.38	0.810	0.940
HCO_3^- (mEq/L)	20.24±06.05	21.34±4.83	20.16±06.27	21.88±04.64	0.334	0.456
					P value**	0.532
Kolmogorov-	Smirnov test	*intra Group **inter Group				

ABG, arterial blood gas; SG, saliva gas; SD, standard deviation

The results of the Mann-Whitney test showed that the mean factors of arterial PaCO2 and HCO3 and salivary PaCO2 and HCO3 were significantly different between smokers and non-smokers. But the mean of other factors did not differ between the two groups (Table 3).

Table 3- Summary of arterial blood and saliva gas values based on smoking status

Parameter	ABG smoker (Mean ± SD)	ABG non-smoker (Mean ± SD)	SG smoker (Mean ± SD)	SG non-smoker (Mean ± SD)	ABG P value*	SG P value*
pH	7.33±0.14	7.37±0.12	7.38±0.07	7.35±0.13	0.144	0.601
$PaCO_2$ (mm Hg)	57.38±14.88	33.39±07.27	56.04±18.31	39.16±13.05	0.144	< 0.001
PaO_2 (mm Hg)	82.41±52.06	69.96±42.96	61.82±34.90	58.57±40.40	0.257	0.368
HCO_3^- (mEq/L)	23.77±04.89	19.22±05.32	23.00±05.43	19.91.±05.64	< 0.001	0.017
					P value**	0.192
Kolmogorov-	Smirnov test	*intra Group **inter Group				

ABG, arterial blood gas; SG, saliva gas; SD, standard deviation

The result of the Mann-Whitney test showed that the mean of arterial PaCO2 and pH and salivary PaCO2 and pH factors were significantly different in the two age groups (≥ 50 and <50) but the mean of other factors was not different between the two groups (Table 4).

Table 4- Summary of arterial blood and saliva gas values based on age range

Parameter	ABG age< 50 (Mean ± SD)	ABG age≥ 50 (Mean ± SD)	SG age< 50 (Mean ± SD)	SG age≥ 50 (Mean ± SD)	ABG P value*	SG P value*
pH	7.33±0.14	7.39±0.07	7.37±0.12	7.34±0.09	0.604	0.018
$PaCO_2$ (mm Hg)	40.91±15.55	41.65±14.54	42.04±16.64	41.87±14.74	0.898	0.875
PaO_2 (mm Hg)	74.51±45.33	41.65±14.84	64.96±42.08	48.23±28.33	0.743	0.036
HCO_3^- (mEq/L)	20.34±06.22	21.47±03.80	20.57±06.70	21.32.±02.99	0.420	0.017
					P value**	0.451
Kolmogorov-	Smirnov test	*intra Group **inter Group				

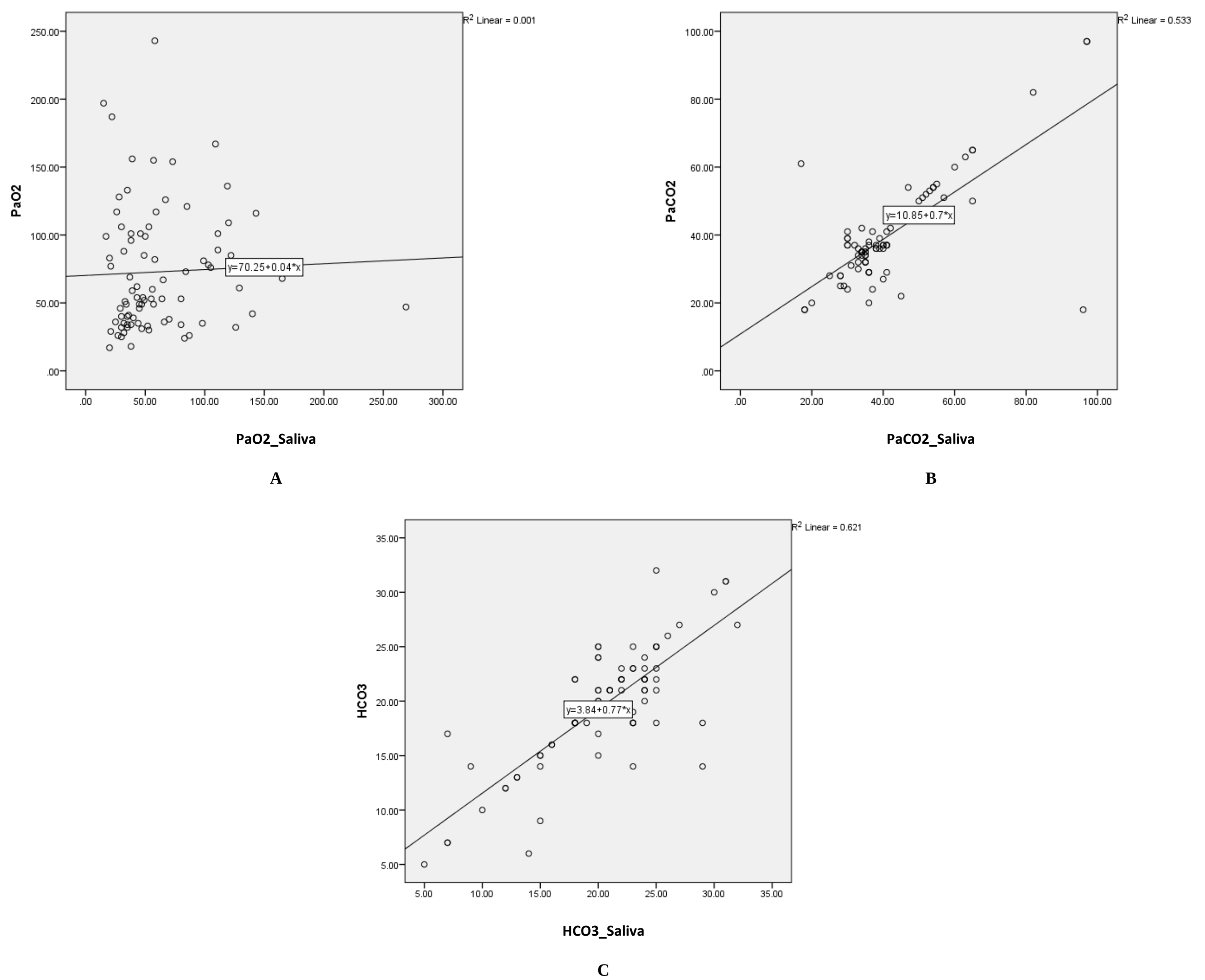
ABG, arterial blood gas; SG, saliva gas; SD, standard deviation

Pearson correlation showed that there was a significant positive correlation between arterial and salivary pH, arterial and salivary PaCo2, and arterial and salivary HCO3 (P <0.0001, r> 0) but no significant correlation between arterial and salivary PaO2 (P = 0.72) (Table 5).

Table 5- Pearson correlation between arterial and salivary gas values

ABG/SG	r	p
pH	0.41	< 0.001
$PaCO_2$ (mm Hg)	0.72	< 0.001
PaO_2 (mm Hg)	0.03	0.72
HCO_3^- (mEq/L)	0.79	< 0.001

Figure 1- Linear regression plot of Arterial blood gas and Saliva gas (A) Po2, (B) $PaCO_2$, and (C) HCO_3^-



Discussion

Traumatic patients with mechanical ventilation are usually subject to respiratory, circulatory, and metabolic disorders due to their abnormal ventilation and perfusion situation. Abnormal blood gas and electrolyte values in these patients have been identified as predictor for morbidity and mortality [6-7, 18].

Arterial blood gas analysis is one of the necessary tests in these patients to investigate their partial pressures of gas in blood, acid-base content, and metabolic status [8]. However, difficult sampling with its belonged (associated) complications supports the use of some simple and safe replacement methods. Following the growing body of evidence that supports the use of Salivary Gases (SG) analysis instead of ABG analysis, we compared ABG indexes with indexes of saliva. This study showed a clear correlation between PH, PaCO2, and HCO3 values in Arterial blood gases with those of Salivary gases in traumatic mechanically ventilated (under mechanical ventilation) patients although the correlation of the PaO2 values were not significant. Pearson correlation showed that there was a significant positive correlation between arterial and salivary pH, arterial and salivary PaCo2, and arterial and salivary HCO3 (P <0.0001, r> 0) but no significant correlation between arterial and salivary PaO2 (P = 0.72). This correlation may be consistent with the study by Amann et al. that stated the level of pH, PaCO2, HCO3, and PaO2 in saliva could be associated with these same blood indexes in patients with mechanical ventilation [19]. Fueda et al. by examining arterial and salivary gas values in young patients concluded that PH, PaCO2, and HCO3, as well as PaO2 in saliva and blood, were closely correlated nevertheless, they mentioned smoking as one of the important factors influencing this consistency [20]. In the present study, the mean of arterial and salivary PaCO2 and HCO3 values were significantly different in the smokers and non-smokers patients as well; the arterial and salivary PaCO2 and HCO3 levels in non-smokers were lower than those of smokers.

evaluating the factors based on patients' age, showed a significant difference between the mean of salivary PaCO2 and pH values in two age groups ≥ 50 and <50. However, the mean of ABG values and other SG values didn’t (did not) have any difference between the two age groups. Examining ABG and SG values based on gender likewise, didn’t confirm any significant difference between men and women.

Some studies investigated the features of salivary gases [21-22]. However, limited studies have been conducted to investigate the relationship between ABG and SG values. Effros et al. found that exhaled gases were correlated with salivary gas [23]. Another study by Inomata et al. stated that another method could be used instead of ABG sampling to reduce recurrent blood draws and their complications in patients [24]. Ambrosino et al. acclaimed that prolonged use of mechanical ventilation could lead to general weakness of the body. They attributed this weakness to a lack of nutrients as well as frequent blood draws to adjust the mechanical ventilation system [25]. They suggested that using less invasive methods could improve patients' treatment outcomes. This study result presented that the use of salivary gas index can be replaced with arterial gas, and more studies should be performed on major populations in this area.

Limitations

Noticeable limitations

In our study were first, the rinsing of mouth before saliva sampling may be able to change the values of saliva gases. While, there was15 minutes interval between rinsing and sampling. In addition, these results were obtained from a group of traumatic ventilated patients, so future studies are required to examine if can consider an acceptable correlation between ABG and SG values in all types of patients.

Conclusion

We found a good correlation between pH, pCO2, and HCO3 values in ABG with pH, pCO2, and HCO3 values in SG. However, there was no significant correlation between arterial and salivary PaO2. Also, smoking and age range were identified as effective factors on results. These results may suggest using the SG values instead of ABG to investigate the clinical status and also to set the ventilator device in patients under mechanical ventilation. Our study was consistent with previous studies, but further studies are suggested conducting in this area as well as other influential factors.

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