Salivary Anion Gap and Na/K ratio as Predictive of Acid-Base Balance after Open Heart Surgery

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Abstract: Patients with open heart surgery need to measure arterial blood gases repeatedly to assess the acid-base status and treatment any disturbance of acid-base balance. The arterial blood gases assays are invasive and may carry infection and endocarditis. We try to use human saliva as noninvasive diagnostic fluid to access acid-base state. Our study was done in Cardiothoracic Department in Ain Shams University Hospital on 60 Patients had open heart surgery. We measured sodium, potassium, chloride, bicarbonate and pH in both saliva and blood and we calculated anion gap and sodium/potassium ratio in both. We found positive significant correlation between anion gap and Na/k ratio in saliva and blood. Moreover, in salivary anion gap, there is significant difference between acideamia and normal groups (P<0.01), and salivary anion gap cut off value ≥17.23 mmol/l (for acidosis) the sensitivity is 87.7% & specificity is 84.2%. So, measurement of salivary electrolytes and anion gap compare it with blood gases and electrolytes of the patients give an idea about the usefulness of saliva for care -monitoring strategies for patients after open heart surgery as an assessments or a replacement of arterial blood gases; as collection of saliva is a non-invasive, simple, inexpensive with minima infection and no blood loss with repeated blood sample.

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1. Introduction

Patients with prosthetic valve replacement, coronary artery bypass graft (CABG), or early post-operative after open heart surgery may be presented with low cardiac output (L.C.O), acidosis and disturbance of serum electrolyte. (1)Multiple blood samples were taken to evaluate serum electrolyte and blood gases which may be painful, carries infection and make the patients reluctant to do test. Monitoring of electrolytes in saliva has the advantages of being noninvasive; simple can be done by the patients with no need for medical personnel, inexpensive with minimal infectious risk.

The anion gap is defined as the different between measured cations and measured anions. It can be measured in plasma, serum or urine. It is calculated by the following equation:

$([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-])$.

This is a calculated measure that is representative of unmeasured ions. Under normal conditions the measurable cations are more than measurable anions, so the anion gap reference intervals are positive (3-11 mmol/l). (2)

Patient with metabolic acidosis can be classified high, normal or rarely low anion gap. High anion gap metabolic acidosis occurs in lactic acidosis, diabetic ketoacidosis, ethylene glycol, aspirin and renal failure. Normal anion gap acidosis is also called hyperchloremic acidosis as the drop in HCO_3^- is compensated by increase in Cl^-. This occurs in gastrointestinal loss of HCO_3^- in diarrhea, renal loss of HCO_3^- in renal tubular acidosis type 1 and type 2, in hyperalimentation fluids during rehydration with Na^+ containing IV solution. Low anion gap is caused by hypoalbuminemia. The anion gap is reduced by (2.5 - 3 mmol/l) for every (1 g/dl) decrease in serum albumin. (3)

Saliva is the watery substance secreted in the mouth from three pairs of major salivary gland. Human saliva composed of 98% water; the other 2% consists of electrolytes, mucus, glycoproteins, enzymes, secretory IgA and lysozyme.

2- Aim of the study:

- Use saliva as a biological fluid for monitoring acid base and electrolytes balance.
- Correlate the results with the blood gases results to confirm its reliability to replace blood gases.

2. Patients &methods:

A total of 60 patients in cardiothoracic department after open heart surgery for valve replacement using prosthetic valve (MVR, AVR or DVR) or for CABG in Ain Shams University Hospital after explaining the test for them and get their agreement with written consent.

Salivary flow was stimulated by chewing of sterile cotton swan (under tongue) for at least 2 minutes. Mixed oral saliva was collected into

17X100 mm plastic tube by hugging swab with the cover about 2 cm from the bottom of the tube and centrifugation at 500g for 15 min. at room temperature.

Arterial heparinized blood samples (Lithium heparin) are collected.

Sodium (Na^+), Potassium (K^+),, Chlorine (Cl^-), Bicarbonate (HCO_3^-), and (pH) in saliva and blood were measured on (OMNI C) blood gases and electrolytes (by ISE) analyzer. We calculated anion gap(AG) and Na/K ratio in both blood and saliva.

$$AG = ([Na^+] + [K^+]) - ([Cl^-] + [HCO_3^-]).$$

3- Result:

In the 60 patients, the mean of salivary Na^+ was 58.8 mmol/l (± 20.53), salivary K^+ 27.2 mmol/l (±17.79), salivary HCO_3^- 22.91 mmol/l (±13.844), salivary Cl^- 45.2mmol/l (±24.97), salivary AG 17.70 (±22.455) and salivary Na/K ratio 3.64 (±4,216). While the mean of plasma Na^+ was 138.8 mmol/l (±8.88), plasma K^+ 3.85 mmol/l (±.586), plasma HCO_3^- 23.89 mmol/l (±6.179), plasma Cl^- 101.5 mmol/l (±5.61), plasma AG 17.29 mmol/l (±13.363) and Na/K ratio 36.80 (±5.572)

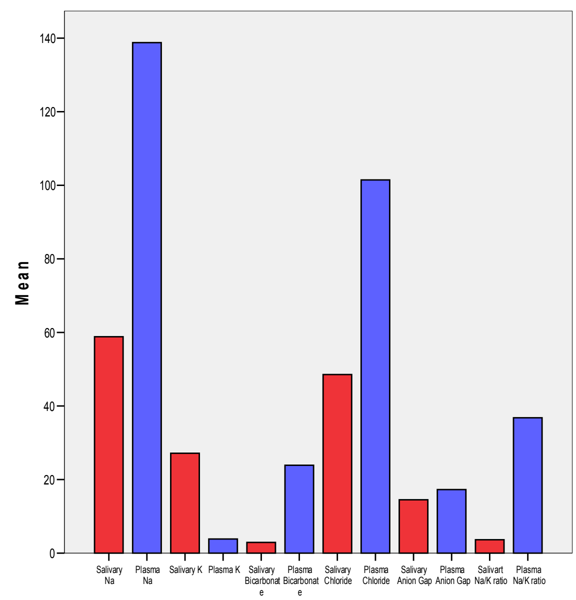

Fig (1): show comparison between results of saliva (red) and plasma (blue).

Table (1): show correlation between saliva and plasma results.

Paired Samples Correlations

		N	Correlation	Sig.
Pair 1	Salivary Na & Plasma Na	60	.227	.081
Pair 2	Salivary K & Plasma K	60	.195	.135
Pair 3	Salivary Bicarbonate & Plasma Bicarbonate	60	.155	.237
Pair 4	Salivary Chloride & Plasma Chloride	60	.128	.330
Pair 5	Salivary Anion Gap & Plasma Anion Gap	60	.444	.000
Pair 6	Salivart Na/K ratio & Plasma Na/K ratio	60	.323	.012

There is positive significant correlation between salivary anion gap and plasma anion gap (P <0.1) and between salivary Na/K ratio and plasma Na/K ratio (P <0.05), but there is no significant correlation between salivary Na, K, HCO_3^- and Cl^- and plasma ones.

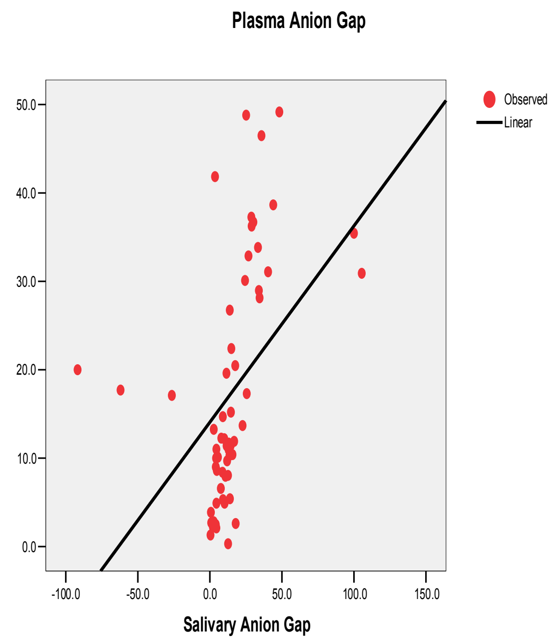

Fig (2): show positive significant correlation between salivary and plasma AG.

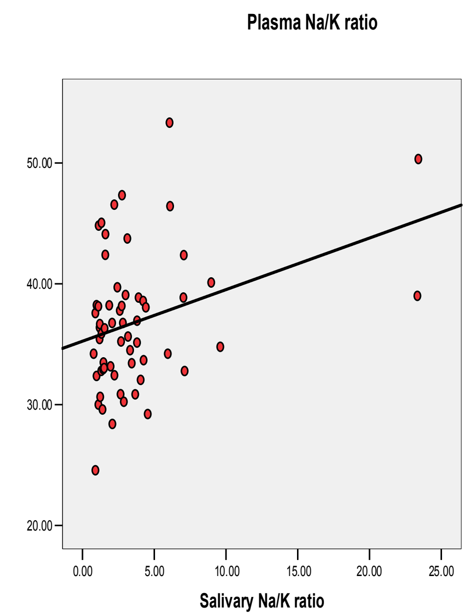

Fig (3): show positive significant correlation between salivary and plasma Na/K ratio.

Table (2) ANOVA test for salivary AG and Na/K ratio with pH groups (acideamia, normal and alkaleamia).

Multiple Comparisons

LSD

Dependent Variable	(I) Plasma ph	(J) Plasma ph	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Salivary Anion Gap	acideamia	normal	23.3349*	5.6839	.000	11.953	34.717
		alkaleamia	30.5370*	6.2968	.000	17.928	43.146
	normal	acideamia	-23.3349*	5.6839	.000	-34.717	-11.953
		alkaleamia	7.2021	6.0591	.240	-4.931	19.335
	alkaleamia	acideamia	-30.5370*	6.2968	.000	-43.146	-17.928
		normal	-7.2021	6.0591	.240	-19.335	4.931
Salivary Na/K ratio	acideamia	normal	1.15728	1.27864	.369	-1.4032	3.7177
		alkaleamia	1.85118	1.41651	.197	-.9853	4.6877
	normal	acideamia	-1.15728	1.27864	.369	-3.7177	1.4032
		alkaleamia	.69390	1.36304	.613	-2.0355	3.4233
	alkaleamia	acideamia	-1.85118	1.41651	.197	-4.6877	.9853
		normal	-.69390	1.36304	.613	-3.4233	2.0355

*. The mean difference is significant at the .05 level.

In salivary AG, there is significant difference between acideamia and normal groups (P <0.01), but no significant difference between alkaleamia and normal groups.

While in Na/K ratio, there is no significant difference between the 3 groups.

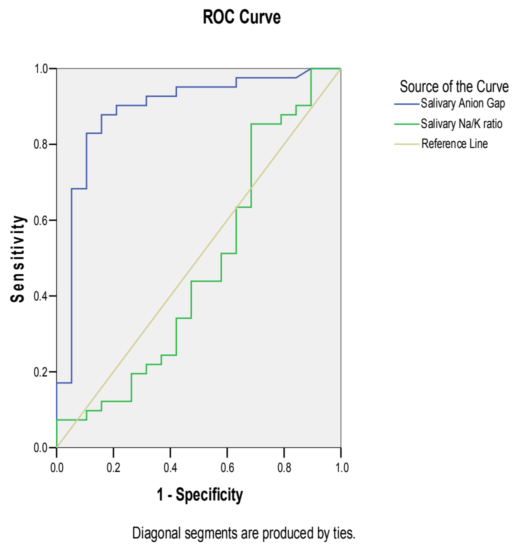

Fig (4) ROC Curve for diagnosis of acidosis (plasma pH≤7.35).

Salivary AG cut off value ≥17.23 mmol/l (for acidosis) the sensitivity is 87.7% & specificity is 84.2%.

4-Discusion:

Acid-base disorders might by described by analysis of plasma HCO_3^- (4), use of base excess (BE) (5) and AG constitutes an additional diagnostic contribution. (6) The anion gap is a sensitive indicator of metabolic derangement independent of acute respiratory changes, while the pH can be impacted by a compensatory respiratory alkalosis. (7)The combination use of AG, BE and HCO_3^- might be enough for an evaluation of acid-base balance in critically patients. (8) Acidosis is present in many patients with cardiac diseases probably because of tissue hypoxia renal dysfunction. (9). Acidosis may decrease myocardial contractility and a reduction in the threshold for cardiac dysrhythmias. (10)

Saliva is secreted from salivary glands in two stages; first, saliva is secreted as a primary secretion like extra-cellular fluid, which change as it pass in acinar duct by actively reabsorb or secrete some ions in the second stages. (11) Various components of saliva are passively diffused or actively transported from serum into the saliva through the gingiva or oral mucosa which may reflect their serum composition.(12). Salivary Na^+ and Cl^- are lower than those of serum, while salivary K^+ is higher. Salivary Na^+ and Cl^- appear to vary with changes in serum, while K^+ and HCO_3^- do not. Salivary Na/K ratio may be inversely related to the rate of aldosterone secretion. (13) Salivary Na/K ratio is also directly related to Na^+ balance, under conditions of dietary salt intake. (14)

In our study, measurement of salivary electrolytes and acid-base compare with arterial blood gases and electrolytes revealed a positive significant correlation between plasma AG and Na/K ratio and salivary ones, while there was no significant correlation between plasma Na^+, K^+, Cl^- and HCO_3^- and salivary ones. On the other hand, there is a significant difference between plasma pH and salivary AG in patients with acideamia than others and cut off value ≥17.23 mmol/l for salivary AG may differentiate those acideamic patients form others with sensitivity 87.7% & specificity 84.2%. So, measurement of salivary electrolytes and AG compare it with blood gases and electrolytes of the patients may reflect a correlation between them and may give an idea about the usefulness of saliva for care -monitoring strategies for patients after open heart surgery as an assessments or a replacement of arterial blood gases; as collection of saliva is a non-invasive, simple, inexpensive with minima infection and no blood loss with repeated blood sample.

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