pH and salivary sodium bicarbonate in cancer patients: Correlation with seric concentration

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Abstract

Objective: To determine the correlation between pH and bicarbonate of soda in blood and saliva in child and adolescent patients during the administration of 3g/m^2 of methotrexate. Method: A controlled clinical test was performed on 23 patients diagnosed with Acute Lymphoblastic Leukemia. Ages ranged from 4 to 18. The Spearman Correlation Coefficient was used to interpret the data. Results: No significant correlation was found between pH levels and seric and salivary sodium bicarbonate. However, there was a significant correlation between the levels of sodium bicarbonate in the body fluids evaluated (rs 0.2576, p=0.0354). Conclusions: Changes modifying the microenvironment of the oral cavity probably do not allow saliva to be used to determine blood pH and seric bicarbonate.

Key words: *Salivary pH, sodium bicarbonate, blood, saliva, methotrexate, leukemia.*

Introduction

Saliva is a secretion of the salivary glands and oral mucosa –of vital importance for maintaining oral health. For the last ten years, researchers have shown increasing interest in using saliva as a body fluid (1,2) since technological advances have provided them with useful measures for diagnosing and predicting the progression of malignant and infectious diseases, endocrine disorders, for supervising the levels of therapeutic and illicit drugs, hormonal levels and for determining antibodies that protect the body from infectious processes (3-8). It has also been reported that patients suffering from certain systemic illnesses and taking medicaments that could produce a collateral effect on the central or peripheral nervous system may present the same alterations in their saliva as those observed in their blood (7).

Easy non-invasive collection and the relationship between oral fluid concentrations and plasma confer clinical value on saliva (5,6). Whole saliva is the most frequently used for diagnosing systemic diseases, with the oral cavity receiving the seric components via the local vasculature of the salivary glands and gingival fluid (9).

A comparison of blood and saliva sampling reveals that the greatest advantage of the latter is that it can be used in clinically difficult situations, such as dealing with children, the physically impaired and anxious patients, where blood sampling would be a complex task. That is why substituting oral fluid for blood provides a clinical alternative, because it represents a diagnostic advantage (9).

In the case of pediatric cancer patients, one of the cytostatic agents contemplated in the protocols for the treatment of divers pathologies, especially of Acute Lymphoblastic Leukemia (ALL), is Methotrexate (Mtx), an acid substance which, when administered in doses over 2 g/m^2, requires the prior use of sodium bicarbonate and for 72

hours thereafter, with determination of pH being necessary for administering the optimum dose of the alkaline substance and thus obtain alkaline diuresis (10). There is evidence that the buffering action of sodium bicarbonate ($NaHCO_3$) used prior to and during the administration of high doses of Mtx probably allows the buffering capacity of saliva to be maintained at medium-high levels (11).
Clinical tests on saliva are promising. However, they may not replace blood tests on all applications, so research in this area must be continued before the clinical value of saliva as a diagnostic fluid can be determined (12). As a continuation of the study performed by Rojas de Morales T, Navas R, Viera N, Álvarez CJ, Chaparro N, Griman D (13), in which it was concluded that the dose of sodium bicarbonate considered in the administration protocol of 3 g/m^2 mtx kept pH neutral and sodium carbonate levels in saliva within normal ranges. The authors recommended that further studies should include the relationship of pH values and sodium bicarbonate in blood and saliva. The present study therefore set out to determine the correlation existing between pH and sodium bicarbonate in the blood and saliva of child and adolescent patients during the administration of 3 g/m^2 mtx.

Methods

- *Patients*

The population was made up of the children and adolescents that attended the Oncohematological Unit of the Hospital of Pediatric Specialties.
(Hep), state of Zulia, Venezuela, between April 2004 and May 2005. The sample comprised 23 patients ranging from 4 to 18 years of age. As the inclusion criterion, the patient had to present a diagnosis of acute lymphoblastic leukemia (all) in accordance with the (fab) (14) that received the total XV protocol of st jude children's research hospital, which includes the administration of 3 g/m^2 mtx and hyperhydration with sodium bicarbonate. The presence of active carious cavities was considered as the exclusion criterion. This study was approved by the HEP's Ethics Committee. Each parent or guardian signed an agreement report once the purpose of the study was explained to him or her.
To determine the relationship of pH and bicarbonate levels of the body fluids under evaluation, three samples of blood and saliva per patient were processed: a) on admission, coinciding with the preparatory phase; b) twelve hours after intravenous administration of sodium bicarbonate and c) before the administration of Mtx; the last sample was taken three hours after the application of the antineoplastic. The pH and sodium bicarbonate in saliva and blood were determined with the Chiron-Diagnostic 378.

- *Collecting the saliva sample*

The saliva sample was taken with the patient sitting upright and relaxed. Saliva production was stimulated by their chewing a paraffin capsule. 3 Cc of mixed saliva were collected, having made sure that the patient had not eaten any food during the previous two hours. To facilitate sample processing, the saliva was collected in a 15-cc syringe, extracting the air and sealing it with a rubber stopper.

- *Collecting the blood sample*

Two ccs of peripheral blood samples were extracted from the middle basilic vein, with asepsis of the area, using the Vacutainer® system, with no anticoagulant.

- *Statistical analysis*

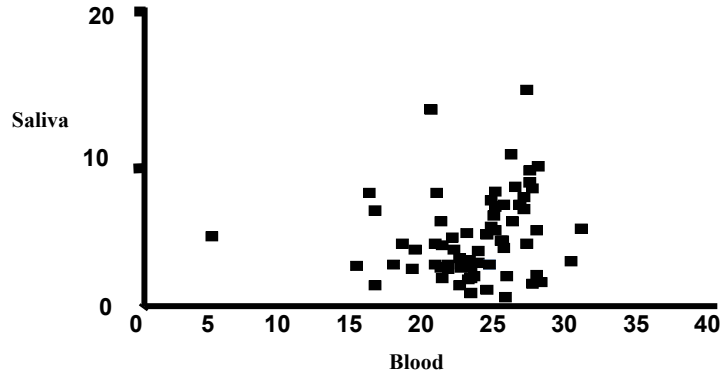
The Spearman Correlation Coefficient at 5% significance level was used to quantify the relationship between pH levels and sodium bicarbonate in blood and saliva.

Results

The blood and saliva samples of 23 patients with ages ranging between 4 and 18 years were analyzed, with the greatest frequency being observed in ages less than or equal to (≤) 5 years, followed by 5 patients of 10 to 15 years and 4 patients of 5 to 10 years and older than 15, respectively.
Relating pH values in blood and saliva produced r_s= -0.01739, considered a non-significant correlation. The result of the correlation of bicarbonate in blood and saliva was r_s= 0.2576, with a 5% significance level of $p<0.0354$ (Figure 1).
Evaluation of the correlation between the parameters under consideration in each of the body fluids produced values of pH and sodium bicarbonate in blood that were not significant (r_s = -0.04439), whereas the correlation between pH and bicarbonate of soda in saliva was r_s= 0.7371, evidencing an extremely significant statistical correlation: $p< 0.0001$ (Figure 2).

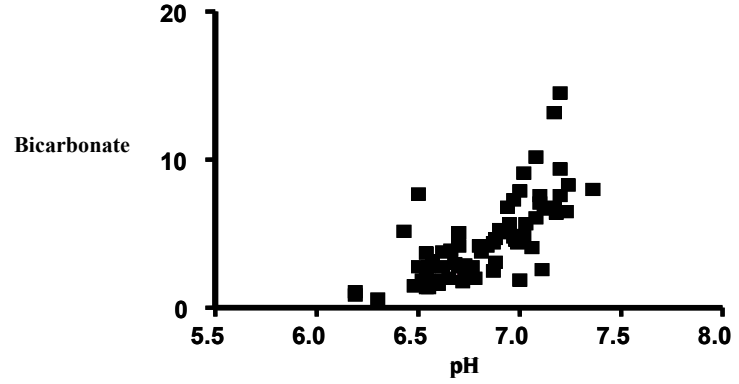
Discussion

In this study, there was no positive correlation of seric pH with salivary pH, probably because whole saliva is modified by factors such as oral hygiene, the quantity and quality of microorganisms, diet and medicaments (12). In this sense, it has been reported that consumption of milk with other sugar aggregates (15) and/or the use of syrups in long-term medication (16), tend to cause a reduction of the pH of the bacterial plaque. Moreover, the use of stimulated saliva in the experimental procedure of this study could be an intervening condition because the salivary flow produced by chewing gum (stimulated saliva) induces changes in the electrolytes and proteins secreted by the parotid and submandibular glands (17). Lynge et al. (10) evaluated a group of patients with Sjögren's Syndrome and found that the reduction of salivary flow favors aciduric oral microflora and, consequently, modifications of the pH. In the patients evaluated, the chemotherapy they receive as the basis of the antineoplastic treatment may induce changes in salivation, which produces modifications in the composition of whole saliva, as well as a reduction



Spearman Correlation r_s: 0,2576 p value: 0,0354

Fig. 1. Correlation of seric and salivary bicarbonate.



Spearman Correlation r_s: 0,7371 p<0.0001

Fig. 2. Correlation of pH and salivary sodium bicarbonate.

of the salivary flow rate (18). Under normal physiological conditions, $NaHCO_3$ concentration in saliva is similar to or below that of the plasmatic level (19). The present study evidenced a positive correlation of seric and salivary sodium bicarbonate after the administration of high doses of Mtx (an acid substance). A possible explanation may be due to the high doses of sodium bicarbonate used before and during the administration of Mtx to maintain alkaline diuresis, which coincided with sample taking. The results of this study did not show any correlation between pH and seric sodium bicarbonate, which could probably be explained because of the use of two opposing chemical substances: Mtx, an acid substance and pH, an alkaline substance, and the time at which the sample was taken. The correlation found between pH and salivary sodium bicarbonate supports the already existing theory: that sodium bicarbonate is the main buffer of salivary pH (20). It is concluded that the changes that modify the microenvironment of the oral cavity probably do not allow the use of saliva to determine blood pH. Likewise, in spite of the correlation found between seric and salivary bicarbonate, saliva is perhaps not the appropriate medium to measure seric bicarbonate. For a definitive corroboration and verification of these findings, more studies should be carried out, controlling salivary flow as the modifying variable of the event under study.

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