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Cariogenic and erosive potential of the medication used by HIV-infected children: pH and sugar concentration

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Objective The aim of this work was to analyze pH and sugar concentration in seven antiretroviral and three antibacterial medications frequently prescribed to HIV infected paediatric patients. ***Method*** Sugars (sucrose, glucose, lactose and fructose) and pH were measured from every one of ten medications with different serial numbers in two samples. The pH was determined by a previously calibrated digital pHmeter (Beckman™). Analysis of free sugars was performed using thin-layer chromatography (TLC). The pH results and the amount of sugar originated from the two samples in each lot were added. The arithmetic mean of these results were computed. ***Results*** Two antiretrovirals (Zidovudin and Abacavir Sulphate) had pH below critical level (3.55 and 3.93, respectively). All three antibacterials analyzed had pH above 5.5, and one of them (Azithromycin) had the highest pH level of the ten medications examined (9.28). Sugar was present in seven out of 10 of the medications analyzed. The antibacterials contained the highest concentration of sucrose, ranging from 40% to 54%. Glucose was found in one of the ten, sucrose was present in seven of them and none showed lactose. Fructose was not observed with the technique used. ***Conclusions*** A number of medications frequently used by HIV-infected children may cause a significant risk of both caries and dental erosion.

Key words: Child, HIV, medicines, oral health, sugars.

Introduction

There are currently more than 40.3 million HIV infected people all over the world, of which 2.3 million are children below 15 years old. Approximately two-thirds of all HIV people (25.8 million) lives in Sub-Saharan Africa (UNAIDS and WHO, 2005). After the antiretroviral therapy advent, the mortality and morbidity indexes have drastically decreased, contributing to their quality of life improvement. However, the high prevalence of dental caries in HIV infected paediatric patients makes it resemble the most important oral disease (Madigan *et al*., 1996).

There are several possible reasons to explain why an increased dental caries prevalence is observed in HIV-infected children. A hyper caloric diet (Howell and Houpt, 1991), salivary alterations, immunodeficiency as a result of HIV infection (Madigan *et al*., 1996), reduction of salivary lgA in AIDS patients (Castro *et al*., 2004) and chronic use of sucrose containing medication (Maguire *et al*., 1996) are some of them.

Sucrose is widely used in the pharmaceutical industry due to its properties as preservative, antioxidant, solvent and thickening agent. It is also a low-cost, easily processed substance, as well as a clinician's helper in paediatric therapeutics, given that its pleasantly sweetish taste encourages medicine acceptance (Nik-Hussein *et al*., 1988). However, sugars added to medicines can be fermented by oral bacteria leading to caries development. In addition, when these medicines' pH is below 5.5, they may activate dental erosion (Meurman and ten Cate, 1996).

With the objective of evaluating the children medications cariogenic and erosive potential, research was conducted to determine both pH and sucrose content. However, on antiretroviral medication, up to now modest information on these parameters is available. The aim of the present study was to analyze both pH and sugar concentration in antiretrovirals and in other medications frequently prescribed to HIV-infected paediatric patients.

Method

Ten drugs prescribed during treatment of HIV-infected paediatric patients were selected (Table 1). Seven antiretroviral products used to control HIV infection by viral load reduction and three antibacterial products used to prevent opportunistic infection. Two samples of each drug (1 pair), taken from different serial numbers lots (n=20), were analyzed.

The pH of each medicament was determined by a previously calibrated digital pHmeter (Beckman™).

Thin-layer chromatography (TLC) is a chromatographic technique useful for separating organic compounds. Because of the simplicity and speed of TLC, it is often

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used to monitor the organic reactions progress and to check products purity. This explains why the four sugars analysis was performed using thin-layer chromatography (TLC) on silica-coated plates, with the following solvent mixture: butanol/ethanol/H_2O (2:1:1, v/ v/ v). Two gms of each medication were diluted in 100mL of distilled water in a volumetric flask. Afterwards, one aliquot (500µl) of each solution was centrifuged and 2µl of supernatant were analyzed. Then, the samples were deposited as a spot on the stationary phase. The constituents of a sample can be identified by simultaneously running standards with the unknown substance. Standards of glucose, sucrose, lactose and fructose (Merck™) were used at 1 mg/mL. The plates were dried at 100º C. Spots were visualised with Orcinol – H_2SO_4 reagent (Soares *et al*., 2000).

The results were obtained by spot densitometry analysis with the Scion Image program. Data were presented as medians of the mean values of free sugar concentration (g/100mL-%).

The pH results from each matched lot were added, and the arithmetic mean of each medication was computed. The same procedure was followed for the sugar amounts.

Results

Table 1 shows the pH results of the medications. Zidovudin had the lowest pH, followed by Abacavir Sulphate, both with pH values below the critical level. For the remaining medications, the pH was above 5.5.

Thin-layer chromatography analysis proved that the majority included sugar. The presence of glucose was detected in one of the medications, sucrose was found in seven, and none contains lactose. Fructose was not observed with the technique used.

The medications that presented no sugar were Didanosine, Abacavir Sulphate and Nevirapine. The antibacterials were the medicaments that showed the highest amounts of sucrose. Zidovudin was the antiretroviral with the highest sucrose concentration which also had 13% glucose in its formula (Table 2).

Discussion

It is known that the chronic use of medication in syrup form has been reported as one of the risk factors associated with dental caries. Taking this into consideration, the cariogenic potential of medicines taken by paediatric patients has been previously studied. Lima *et al*. (2000) found pH values below 5.5 in 78% of 40 paediatric medicines. At the same time Drumond *et al*. (2005) reported similar findings in 100% of the medicaments evaluated. In 2001, Silva *et al*. ascertained that the mean pH of 10 antibacterials for paediatric use was 5.46. In the present study, all three antibacterials analyzed showed pH above 5.5, and one of them (Azithromycin) presented the highest pH level of the ten medicines examined (9.28). Concerning antiretrovirals, two of the seven analyzed medications had pH values below the critical level, and Zidovudin showed the lowest value (3.55). Ingestion of medication with low pH level has also been related to severe cases of dental erosion (Moss, 1998). Since 28.5% of the antiretrovirals analyzed have pH values below the critical level, and as they are used in syrup form and with great frequency (Moss, 1998), they may be considered to have high erosive potential. Furthermore, as tooth brushing is not suggested soon after acid medication ingestion, caries risk in these cases is also high.

Table 1. Medicaments used by HIV-infected children

Acitve Substance	*Trademark*	*Action Mechanism*	*pH Values*
Zidovudin	AZT	antiretroviral	3.55
Didanosine	DDI	antiretroviral	8.22
Lamivudine	Iquego-Lamivudina	antiretroviral	5.75
Nelfinavir	Viracept	antiretroviral	7.62
Nevirapine	Viramune	antiretroviral	5.74
Abacavir Sulphate	Ziagenavir	antiretroviral	3.93
Stavudine	Svudin	antiretroviral	6.74
Amoxicillin	Amoxicillin (drug)	antibacterial	5.82
Azithromycin	Azi	antibacterial	9.28
Sulphametaxone + Bacitracin	Sulphametaxone + Bacitracin (drug)	antibacterial	2.95

Table 2. Sugar concentration in antiretroviral and antibacterial medicines.

Medicines / *Sugar(%)*	*Zidovudin*	*Didanosine*	*Lamivudine*	*Nelfinavir*	*Nevirapine*	*Abacavir Sulphate*	*Stavudine*	*Amoxicillin*	*Azithromycin*	*Sulphametaxone + Bacitracin*
Sucrose	28	0	20	14	0	0	5	50	54	40
Glucose	13	0	0	0	0	0	0	0	0	0
Lactose	0	0	0	0	0	0	0	0	0	0

In a review about sugars analysis in traditional Chinese drugs (Wang and Fang, 2004), the authors employed chromatography and electromigration methods. Paper chromatography (PC) and thin-layer chromatography (TLC) are usually applied for measurement of purity and identification of monosaccharides of oligosaccharides and polysaccharides constituents. In their conclusion, the authors considered that the PC and TLC of sugars are high-speed and require simple instrumentation, but the results are limited and can only be used as reference about constituent mono-or oligosacchides identification.

The objective of the present study was to determine the presence and concentration of sucrose, glucose, lactose and fructose in paediatric drugs used in HIV therapy. This methodology may be considered acceptable, mainly when the spot densitometry analysis with the Scion Image programme is also undertaken. This assumption corroborates another study findings that used the same methods (Khedr and Sheha, 2003).

Concerning the percentage of medicines with sucrose in their compositions, studies have shown values ranging from 0% (Drumond *et al*., 2005) to 58.30% (Lima *et al*., 2000). In the present work, of the 10 medicaments studied, seven have shown sugar. As regards the average sucrose concentration present in the drugs, Silva *et al*. (2001) have found a percentage of 29.80%. In the present study, the antibacterials displayed the highest sucrose concentration (40% to 54%). Of the four antiretrovirals with sugar in their formulas, Zidovudin was found to contain glucose as well as sucrose. This finding is particularly important in view of the fact that this is one of the most frequently prescribed drugs to HIV-infected patients. The situation is further aggravated because multiple therapy, taking two or more antiretrovirals, an antibacterial and further medication, in cases with infection, may be prescribed to these patients. Taking into consideration the importance of assessing the medications' cariogenic potential, further studies should be undertaken to test their cariogenic and erosive potential.

There are further aspects concerning patterns of medicament ingestion to be considered. The simultaneous ingestion of medicines and sweet food products in order to improve the taste of the drug and encourage its ingestion, is one of them. Furthermore, oral hygiene instruction by paediatricians after the ingestion of medicaments has been considered unsatisfactory, reaching only 40.6% (Silva Pierro *et al*., 2004). A significant relationship may be suggested between the prolonged ingestion of these medicines containing sugar and the occurrence of carious lesions. This may be particularly important considering the world population percentage of HIV-infected people, particularly in Africa, where this percentage is higher. Health policies are being evolved there to enable the infected population to have antiretroviral treatment, and these policies should show results in the next few years. Thus the African victims of the AIDS epidemic will have access to this antiretroviral therapy, already in use in other parts of the world (UNAIDS and WHO, 2005).

That is why information regarding the cariogenic and erosive potential of all medicines should be included in the directions which come with them, especially prolonged-use paediatric drugs, such as those analyzed in this study. This practice is already in place for some products, which alert diabetic patients to the presence of sugars in their formulas. The present situation could be further improved if sugar substitutes were included in these medicines. In addition the adoption of preventive measure including use of fluoride should be promoted.

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