Short Communication
Infection Control

Zika virus infection spread through saliva – a truth or myth?

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Abstract: In this Point-of-view article we highlighted some features related to saliva and virus infection, in special for zika virus. In addition, we pointed out the potential oral problems caused by a microcephaly originated by a zika virus infection. In the end the, we demonstrated the importance of a more comprehensive exploration of saliva and their components as a fluid for diagnostic and therapeutic approaches on oral and systemic diseases.

Keyword: Saliva; Zika Virus; Microcephaly; Pediatric Dentistry; Infection; Pediatrics.

Introduction

Recent finds shown the presence of zika virus (ZIKV) in blood, semen, urine and saliva, suggesting that the transmission could be also by these corporal fluids.[1,2] However, until now, there is no any scientific evidence to support that the infection of ZIKV could be through human saliva. Besides the detection of ZIKV in saliva was reported for a neonate and his/her mother, respectively, on days 3 and 2 post partum.[3] A recent report case evidenced the ZIKV presence in a fetus with microcephaly. The authors reported the ZIKV isolation by reverse transcription polymerase chain reaction assay from the fetal brain tissue. According to the Brazilian Ministry of Health in 2015 more than 1,2 million cases of dengue and 9,000 cases of Zika were officially reported in Brazil. In addition, the total numbers of Zika cases related to microcephaly in newborn are almost 3,000 with an estimation of 200 new cases reported every month.[3] We can speculate that in the near future, the increasing number of microcephaly associated with ZIKV will significantly affect not only the general health status of their patients, but also the dental care cost in those countries affected by these conditions. Our hypothesis is based on several clinical features associated with microcephaly, such as late closure of the fontanel, characteristic facial appearance with down-slanting palpebral fissures, midfacial hypoplasia, short nose, small mouth and, in some of the children, joint anomalies (congenital hip dislocation, joint laxity and pes planus), muscle hypotonia, down-slanting palpebral fissures and mental retardation[4] could be present in these children. This is a considerable problem for public health in countries with the ZIKV epidemic and Brazil is one of these countries. The need for a multidisciplinary team to treat these patients has a direct

impact on the high cost of treatment. It should also be considered the social impact on families of these patients, as they need to be monitored all day.

In relation to saliva and virus presence, there are some viral infectious diseases that can be transmitted by saliva, such as cytomegalovirus and hepatitis (hepatitis B). However many viral infections (*e.g.* dengue) are present in saliva, but not transmitted by saliva. For example, despite the presence of HIV in saliva,[5] there have never been any reports of HIV transmission via this route. In this regard, HIV infection can be detected by saliva using a fast, and simple point-of-care detection test called OraQuick®. This "in-home test" is FDA-approved and presented a sensitivity and specificity higher than 98%,[6] which is statistically similar to the classical ELISA test carried out in laboratory to detect HIV infection. Saliva has important properties enabling its use as a diagnostic tool for viral diseases.[7] Besides the virus presence in saliva, some viruses (*e.g.* HCV), exhibit a direct correlation between viral load in and the presence of virus in saliva.[6,8] Despite the virus presence in saliva, many viruses cannot infect the host (*e.g.* HIV), highlighting the possible saliva role in modulating viral infection.[9,10] For HIV, the saliva contains many components that decrease the virus infectivity. There is evidence from studies with HIV virus, showing that saliva proteins can act at different stages of the infection cycle, since the complexes formation between macromolecules, viruses and antiviral proteins to the direct antiviral capacity or inhibiting virus invasion to susceptible cells.[11] The antiviral activity can be attributed to both the parotid saliva as the submandibular/sublingual saliva.[11,12] MUC5B and proteins related to scavenger receptors have activity against several viruses, such as HIV and influenza viruses. Other proteins do not have a well-established viral activity. Lactoferrin and histatins showed antiviral activity to HIV but not to and influenza viruses. The MUC5B can exert antiviral activity by virus aggregation and entrapment. The MUC5B function has been assigned to multivalent negative charge presence of the sialic acid or sulphated residues.[11,12] Nevertheless, the neuraminidase enzyme might play cleavage of sialic acid and gradually inactivate this protein for influenza viruses.[12]

In our point-of-view, the presence of ZIKV in saliva highlights the relevance of the use of saliva as a diagnostic tool. In this manner, in the recent years, saliva is becoming more recognized as a diagnostic fluid not only because of its multiple contributors such as serum and oral cell debris, but also because sampling is noninvasive, easy to obtain, painless and low cost.[13] Moreover, due to the fast emerging high-sensitive biotechnologies such as ELISA multiplex and mass spectrometry technology more prominent studies are underway using saliva for the identification of biomarkers for various diseases such as breast, ovarian, hepatocellular and oral cancers as well as leukoplakia and Sjogren's syndrome.[14] For example, we have recently shown correlation between end-stage renal disease and salivary nitrite and uric acid concentrations by using a colorimetric test strips.[15]

The proof-of-principle has been extended and we have also shown a strong correlation between 10 cytokines present in saliva and pulmonary disease, such as asthma, using a microsphere-based antibody array.[16] Therefore, we postulate that these new high-sensitive technologies able to measure multiples salivary biomarkers simultaneously, could become clinical tools for early detection and monitoring of prognosis and treatment for other diseases, including dengue and Zika infections.[17] Now that researchers around the world are committed to seek ways to eradicate ZIKV, all efforts in this direction should be considered. Early diagnosis using safe and non-invasive methods for ZIKV allow therapeutic measures are taken faster with less discomfort for the patient is part of this task force against this disease.

Therefore, search for a diagnostic test for ZIKA virus, as well as other viral infections as dengue and chikungunya virus in saliva is a route that should be considered.

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