

## Use of Medicines by Infants with Microcephaly Caused by Congenital Zika Virus Infection and Implications to Oral Health

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### Abstract

**Objective:** To analyze the use of continued-use medications by Brazilian children with microcephaly caused by Congenital Zika Virus Infection. **Material and Methods:** Cross-sectional study with 76 children of both genders. Information on age, use of continued-use medications, number and type of drugs used was collected. Data were analyzed using descriptive statistics. **Results:** Continued-use medications were used by 89.4% of the children, anticonvulsants / antiepileptics (88.1%), and those indicated for behavioral disorders (27.1%) were the most frequent. Sodium saccharin, sucrose, and sorbitol are the most common sugars in the composition of these drugs. **Conclusion:** The use of medicines is high, predominantly anticonvulsants and antiepileptics, which contain sugars in their composition. These drugs can lead to irreversible dental problems, such as tooth decay if proper oral hygiene is not present. Therefore, parents/guardians should be advised about adopting healthy oral hygiene habits after the administration of these drugs.

**Keywords:** Microcephaly; Child; Prescription Drugs; Oral Health.

## Introduction

The first description of the Zika virus was made in Uganda in 1947 in the Zika Valley. It is a mild disease with fever, erythema, and arthralgia [1]. As there is no known medical treatment for this disease, a serious attempt has been needed to eradicate the mosquito and prevent the spread of the disease to other Brazilian states and across the border [2].

According to the National Institute of Neurological Disorders and Stroke (NINDS), “microcephaly is a medical condition in which the circumference of the head is smaller than normal because the brain has not developed properly or has stopped growing” [3]. Microcephaly can be present at birth or it may develop in the first few years of life [4].

In Brazil, “thousands of cases of infants with suspected microcephaly or other developmental anomalies of the central nervous system that may be associated with ZIKV infection have been reported” [5]. Paraíba is the state with the second-highest number of suspected cases of microcephaly. Most of those were born into low-income families that reported difficulties in accessing medicine and attention from the public health system [6].

There are several studies that warn of the deleterious effects of drugs on primary teeth, due to the presence of sugars in the composition of these drugs [7-9]. This study aimed to describe the usage of continued-use drugs by children with microcephaly caused by congenital zika syndrome (CZS) and the possible implications for oral health.

## Material and Methods

### Design and Study Location

This cross-sectional study was conducted in the city of Campina Grande, State of Paraíba, northeastern Brazil. The research was developed in one rehabilitation center that offers assistance to children with congenital zika syndrome, providing physical, intellectual, auditory and visual rehabilitation treatment.

### Sampling

The sample consisted of 76 children with confirmed diagnosis of microcephaly of both sexes, attended at the Specialized Center for Rehabilitation.

### Data Collection

Through a questionnaire, information was collected by two researchers from September 2016 to April 2017 regarding the demographic situation and continued-use medicine treatments.

### Data Analysis

Data were organized and analyzed with Statistical Package for Social Sciences, Version 21.0 (IBM Corporation, Chicago, IL, USA) using descriptive statistics.

### Ethical Aspects

This study was approved by the Human Research Ethics Committee of the State University of Paraíba in compliance with Brazilian National Health Council Resolution 466/12. All parents received information

regarding the objectives of the study and provided written informed consent regarding their child's participation.

## Results

Most of the children were female (53.9%), aged between 13 and 24 months (81.6%). The average age was 21.1 months (SD  $\pm$  4.8), minimum of 8 months, and a maximum of 38 months.

Continued-use medications were confirmed in 85.9% of the children, with most using only one medication (41.0%). The average medication per child was 1.7 ( $\pm$  1.2). The most commonly used medications were Anticonvulsant/Antiepileptic (85.9%) (Table 1).

**Table 1. Distribution of children according to continued-use medication and type of substance.**

Variables	N	%
Sex		
Male	35	46.1
Female	41	53.9
Age (in months)		
Up to 12	4	5.3
13 to 24	62	81.6
25 to 38	10	13.2
Continued-use Medications		
Yes	61	85.9
No	10	14.1
Number of Medications Utilized		
1	25	41.0
2	21	34.4
3	8	13.1
4	5	8.2
5	2	3.3
Type of Medication Utilized		
Anticonvulsant/Antiepileptic		
Yes	53	86.9
No	8	13.1
Antispastic		
Yes	16	26.2
No	45	73.8
Sedative/Anxiolytic		
Yes	6	9.8
No	55	90.2
Behavior Disorder		
Yes	16	26.2
No	45	73.8

Table 2 presents the composition and possible oral implications of the medications used. Among the sugars/sweeteners are sodium saccharin, sucrose, and sorbitol. Other substances, such as cornstarch and essences, are also present. As for the oral implications described in the leaflets are dry mouth, vomiting, dysgeusia, changes in taste, trismus and sialorrhea. Of particular note are the complications from using an anti-epileptic drug for children over 1 month of age: swelling of the lips, throat or mouth; difficulty speaking or swallowing; blisters on the mucous membranes of the lips and mouth; mouth ulcers and vomiting.

**Table 2. Distribution of the medications according to composition, class and oral implications.**

Commercial Name	Active Principle	Composition	Drug Class	Form	Manufacturer	Oral Implications	Pediatric Use
Baclon	Baclofen	Starch, Lactose Monohydrate	Antispastic	Tablet	Genomma Lab.	Myalgias, Dry Mouth, Vomiting, Dysgeusia	No
Baclofen	Baclofen	Starch, Lactose	Antispastic	Tablet	Laboratório Teuto Brasileiro S.A	-	No
Rivotril	Clonazepam	Lactose, Corn Starch	Anxiolytic	Tablet	Roche	Dysarthria	Yes
Tegretol	Carbamazepine	Caramel Flavor, Sodium Saccharin Dihydrate, Sorbitol	Antiepileptics	Tablet	Medley	Changes in Taste, Disjointed Speech	Yes
Frisium, Urbanil	Clobazam	Corn Starch, Lactose Monohydrate	Anxiolytic	Tablet	Sanofi	-	Yes, above 3 years of age
Depakene	Valproic Acid	Sacarose, Sorbitol	Anticonvulsant	Oral Solution	Abbott Laboratórios	Vomiting	Yes, preferentially above 2 years of age
Fenoarbital	Phenobarbital	Lactose Monohydrate, Amido	Anticonvulsant	Tablet	Teuto	Difficulty Speaking	No
Gardenal	Phenobarbital	Sodium Saccharin Dihydrate, Raspberry Essence	Anticonvulsant	Oral Solution (Drops)	Sanofi	Difficulty Speaking	Yes, oral pediatric use
Keppra	Levetiracetam	-	Antiepileptic	Tablet	Biopharma	Myalgias	Yes, above 6 years of age
Lamictal	Lamotrigine	Starch, Sodium Starch Glycolate	Antiepileptic	Tablet	Teuto	Vomiting	Yes, above 12 years of age
Neuleptil	Periciazine	Liquid Sucrose, Caramel, Mint Essence	Antipsychotic	Oral Solution	Sanofi	Dry Mouth, Trismus	Yes, above 3 years of age
Sabril	Vigabatrin	Sodium Starch Glycolate	Antiepileptic	Tablet	Sanofi Aventis	Vomiting	Yes
Sonebon	Nitrazepam	Lactose Monohydrate, Aluminum Red Lacquer Erythrosine 3	Sedative Hypnotic	Tablet	Ems Sigma Pharma Ltda	Dysarthria, Sialorrhea, Vomiting, Dry Mouth	No
Tegretol	Carbamazepine	Sorbitol, Sodium Saccharin, Caramel Flavor	Anticonvulsant	Oral Suspension	Novartis	Speech Disorders	Yes
Topamax	Topiramate	Lactose Monohydrate, Starch, Sodium Starch Glycolate	Anticonvulsant	Tablet	Sandoz	Increased Salivation, Speech Disorders	Yes
Trileptal	Oxcarbazepine	-	Antiepileptics	Tablet	Novartis	Swelling of the Lips, Throat or Mouth, Difficulty Speaking or Swallowing, Blisters on the Mucous Membranes of the lips and Mouth, Mouth Ulcers, Vomiting	Yes, above 1 month of age

## Discussion

In most cases of microcephaly, there is severe neurological damage that can result in impaired cognition and motor coordination. Therefore, episodes of epileptic seizures and mood swings are common, leading children with microcephaly, even at an early age, to use continued-use medications [10].

Children with special needs are mostly dependent on their caregivers for their daily living activities [9,11], including tooth brushing. Parents and/or caregivers of children with microcephaly have an intense routine of therapies, which often occur in different places and may compromise the persistence and routine necessary to perform oral hygiene [12]. Added to this is the low age of most of the children in this study (81.6% of them were 13 to 24 months old), which can potentiate these oral hygiene difficulties.

Children with microcephaly have delayed eruption chronology, altered tooth eruption sequence [12-14], altered muscle tone, with consequences for suction, swallowing, lip seal, and mouth breathing [9]. Literature has also mentioned a higher prevalence of enamel defects, which entails a higher risk of dental caries [13].

Analysis of the drug leaflets revealed that anticonvulsants and antiepileptics, the class of drugs most commonly administered by the children in the study, can cause vomiting. At these times, intrinsic acids in the organism, present in the gastric juice, are taken to the oral cavity through the atypical flow of content from the stomach [15], and this is responsible for making the dental surface soft and susceptible to abrasion and friction wear [16]. Because of the higher risk of dental erosion development in these cases, the constant monitoring of the children who use this type of medication by a dentist is recommended.

Special attention is advised to possible oral symptoms resulting from the use of Trileptal®, an antiepileptic medicine that, in addition to inducing vomiting, may cause swelling of the lips, throat or mouth, difficulty to speak or swallow, blistering of mucous membranes of the lips and mouth, and mouth ulcers, which can negatively affect the quality of life of these children.

More than half of the children use more than one drug, possibly due to the number of sequelae resulting from neurological damage, such as visual alterations, speech and hearing disorders, hypertonia, intracranial calcifications, choroid plexus enlargement, ventriculomegaly, and hydrocephalus [13]. Therefore, it is cautioned that undesirable oral effects may be added to children exposed to more than one drug.

Most pediatric drugs contain high levels of sucrose [7,9]. The analysis of the leaflets reveals that this substance is present in the composition of the medications administered to the children in this study. The addition of sucrose improves palatability, favoring acceptance and continuity of the children; sucrose also has preservative, antioxidant, solvent and thickening properties [17]. Children who use this substance are exposed to a cumulative harmful effect, which can manifest as carious lesions [18].

Recommendation to immediately rinse in water and delay tooth-brushing after ingestion of syrup medications could be proposed at the time of prescription. Previous authors reported that “medicine labels should also alert in relation to the possibility of causing dental caries and erosion since many products could be consumed for prolonged periods, several times a day, at bedtime, and without adequate oral hygiene, which would certainly contribute to dental caries and erosion” [19].

Microcephaly is a condition that causes numerous problems in children's health; so knowing which medications are used is extremely relevant. Therefore, dentists should be aware of sugars in child medicine and the parents should be informed of the need for proper oral hygiene after medication administration.

## Conclusion

The use of medicines that contain sugars in their composition is high, predominantly anticonvulsants and antiepileptics. These drugs can lead to irreversible dental problems, such as tooth decay if proper oral hygiene is not present. Therefore, parents/guardians should be advised about adopting healthy oral hygiene habits after the administration of these drugs.

## Authors' Contributions

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All authors declare that they contributed to critical review of intellectual content and approval of the final version to be published.

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## Conflict of Interest

The authors declare no conflicts of interest.

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