An Pediatr (Barc). 2019;90(6):342–348

analesdepediatría

www.analesdepediatria.org

ORIGINAL ARTICLE

Level of exposure to fluorides by the consumption of different types of milk in residents from an area of Mexico with endemic hydrofluorosis☆,☆

Liliana Valdez Jiménez[a], Jaqueline Calderón Hernández[b], Rosa Isela Córdova Atilano[a], Selene Yasmín Sandoval Aguilar[c], Jorge Alejandro Alegría Torres[c], Rogelio Costilla Salazar[d], Diana Rocha Amador[c,*]

[a] *Departamento de Humanidades, Artes y Culturas Extranjeras, Centro Universitario de los Lagos, Universidad de Guadalajara, Lagos de Moreno, Mexico*
[b] *Centro de Investigación Aplicada en Ambiente y Salud, Facultad de Medicina-CIACYT, Universidad Autónoma de San Luis Potosí, San Luis Potosí, Mexico*
[c] *División de Ciencias Naturales y Exactas, Campus Guanajuato, Universidad de Guanajuato, Guanajuato, Mexico*
[d] *División de Ciencias de la Vida, Campus Irapuato, Universidad de Guanajuato, Irapuato, Mexico*

Received 10 May 2018; accepted 5 October 2018
Available online 20 May 2019

KEYWORDS
Dental fluorosis;
Breastfeeding;
Infant formula;
Raw milk

Abstract
Introduction: Several studies have shown the presence of fluorosis (DF) in primary dentition, suggesting an exposure to fluorides (F^-) in early childhood. Breast milk is recommended as an exclusive food until 6 months of age. Although it is mentioned that only a small amount of F^- can be eliminated by breast milk, studies have shown the presence of this element in milk of women living in contaminated areas, as well as in infant formulas. The objective of this project was to evaluate the exposure level to F^- through milk in children living in an area with endemic hydrofluorosis.
Methodology: The study included 110 children between 6 and 36 months of age from the municipality of Lagos de Moreno, Jalisco. Water samples were collected from the homes, as well as samples of milk (maternal, formula, whole or raw), and urine. Measurements were made with a selective ion electrode. The exposure level of F^- for milk intake was calculated using the Oracle Crystal Ball package.

☆ Please cite this article as: Valdez Jiménez L, Calderón Hernández J, Córdova Atilano RI, Sandoval Aguilar SY, Alegría Torres JA, Costilla Salazar R, et al. Dosis de exposición a fluoruros por el consumo de diferentes tipos de leche en residentes de una zona con hidrofluorosis endémica en México. An Pediatr (Brac). 2019;90:342–348.
☆ Previous presentation: This study was presented at the XV Encuentro Participación de la Mujer en la Ciencia; May 23–25, 2018; León, Guanajuato, Mexico.
* Corresponding author.
E-mail address: drochaa@ugto.mx (D. Rocha Amador).

2341-2879/© 2018 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Results: Levels greater than the reference level for DF were observed in infant formula reconstituted with public supply water, pasteurised cow's milk (whole) and untreated cow's milk treatment (raw) in the 90th, 70th, and 50th percentile, respectively, with a correlation being found between the levels of F^- in milk and F^- in urine ($r = 0.41$, $P < 0.001$).
Conclusions: The identification of sources of F^- in the early stages of child development could reduce the risk of developing DF.
© 2018 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

PALABRAS CLAVE
Fluorosis dental;
Lactancia materna;
Fórmula infantil;
Leche de vaca

Dosis de exposición a fluoruros por el consumo de diferentes tipos de leche en residentes de una zona con hidrofluorosis endémica en México

Resumen
Introducción: Diversos estudios han demostrado la presencia de fluorosis (FD) en la dentición primaria, lo que puede indicar una exposición a los fluoruros (F^-) en la primera infancia. La leche materna se recomienda como alimento exclusivo hasta los 6 meses de edad. Aunque se menciona que solo una pequeña cantidad de F^- puede eliminarse por leche materna, estudios han demostrado la presencia de este elemento en leche de mujeres residentes de zonas contaminadas, así como en leche de fórmulas comerciales. El objetivo del proyecto fue evaluar la dosis de exposición a F^- a través de leche en niños residentes de una zona con hidrofluorosis endémica.
Metodología: Un total de 110 niños de entre 6 y 36 meses de edad del municipio de Lagos de Moreno, Jalisco, México, participaron en el estudio. Se colectaron muestras de agua de los hogares, leche y orina. Las muestras se cuantificaron con el electrodo de ion selectivo. Se calculó la dosis de exposición a F^- a través del programa Oracle Crystal Ball.
Resultados: Se observaron dosis superiores a la dosis de referencia para FD en la leche de fórmula reconstituida con agua de abastecimiento público, de vaca pasteurizada (entera) y de vaca sin tratamiento sanitario (cruda) en el percentil 90, 70 y 50, respectivamente, así como una correlación entre los niveles de F^- en leche y F^- en orina ($r = 0,41$; $p < 0,001$).
Conclusiones: La identificación de fuentes de F^- en etapas tempranas del desarrollo infantil podría reducir el riesgo de presentar FD.
© 2018 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Fluoride (F^-) is one of the most ubiquitous natural inorganic pollutants in the drinking water supply worldwide.[1] This ion is frequently found in geological structures where subterranean water flows.[2] As a result, aquifers in many regions worldwide are naturally enriched with F^- leading to drinking water supplies with concentrations that exceed the limit of 1.5 mg/L[3] established by the World Health Organisation.[3]

Several epidemiologic studies conducted in populations residing in areas with endemic fluorosis due to fluoride-rich water have found a negative impact of F^- exposure on teeth.[4–7] The paediatric population is most vulnerable to the effects of F^- because tooth development starts during the foetal period.[8] Recent studies have demonstrated that dental fluorosis (DF) can be found in the primary dentition,[9–11] which may be indicative of prenatal and postnatal fluoride exposure.

In the first years of life, exclusive breastfeeding is recommended as the best form of nutrition for infants through age 6 months. Although there is evidence that only trace amounts of F^- are eliminated in the breast milk,[12] some studies have found this ion in the milk of women residing in areas with F^- concentrations in water exceeding the limit recommended by the WHO.[13] In some families, other types of milk are used in nutrition through age 2 years. Studies on infant and toddler formulas have shown that these can contribute to the intake of F^- at early ages.[14] This suggests that exposure to fluoride in early childhood could occur through milk, so the aim of our study was to assess exposure to F^- through milk in children residing in a geographical area of Mexico with endemic fluorosis due to high water fluoride concentrations.

Materials and methods

Study setting and sample selection

We selected the town of Lagos de Moreno in Jalisco, Mexico, due to the history of high fluoride levels in water in the area (mean, 3.2 mg/L; standard deviation [SD], 1.4).[15] We obtained the necessary approval from the Department of Public Health (Secretaría de Salud, SSA). We gave talks in 4 clinics of the SSA system in Lagos de Moreno to introduce the project to mothers and explain the objectives, risks and benefits of the study. We included children aged 6 to 36 months whose mothers signed the informed consent form. The final sample included 110 children.

Sample collection

To assess environmental and biological exposure to fluorides, we collected: (1) samples of tap water and bottled water in each household; (2) sample of whichever type of milk the child consumed, and (3) samples of the first morning urine in polypropylene bags or cups depending on the bladder control of the child. Samples were kept at 4 °C until they were transported and analysed in the laboratory.

When it came to bottled water, households acquired water from 2 types of companies: (1) companies with a registered trademark and (2) companies without a registered trademark, corresponding to small businesses dedicated to water purification without the rigorous quality control involved in the production of bottled water for registered trademarks. As for the milk samples, the mothers reported feeding their children breast milk, commercial formula reconstituted with tap water or bottled water, pasteurised cow's milk (whole) or unpasteurised (raw) cow's milk.

Analysis of specimens

To measure the concentration of fluoride in samples of water, milk and urine, we took 10 mL of each sample and added a 1:1 volume of total ionic strength adjustment buffer (TISAB). Milk and urine specimens had been previously treated with addition of 0.1 g of EDTA per 100 mL. The fluoride concentration was determined using the ion selective electrode method following protocol 8308 of the Instituto Nacional de Seguridad y Salud Ocupacional (National Institute of Occupational Safety and Health, NIOSH).[16] In the analysis of urine samples, we used the IRIS Tech ClinCheck® Urine control lyophilised for trace elements for quality control[17] and found a relative accuracy of 95% ± 2%.

Additional data

We administered questionnaires to the mothers to obtain additional information, such as the age of the child, the daily intake of milk, the type of milk consumed, the brand of bottled water consumed in the household and whether the brand was or not a registered trademark. We also measured the weight and height of the children at the clinics.

Calculation of fluoride intake through milk consumption

To calculate the dose of exposure, we used the measured F^- levels in milk (breast milk, formula, whole pasteurised or raw cow's milk), the body weight (BW) and daily intake (DI) by age group (6–12 months, 13–24 months, 25–36 months). We used a Monte Carlo simulation model developed with the software Oracle Crystal Ball version 11.1[18] and using the following equation:

$$\text{Dose (mg/kg/day)} = \frac{[F^-] \times DI \times AF}{BW}$$

where $[F^-]$ is the concentration of F^- in milk in mg/L, BW for body weight in kg, DI for daily intake in L/day, and AF for absorption factor, which in this case we established at 0.9 based on the findings of animal model studies.[19]

Statistical analysis

We conducted a descriptive and inferential analysis of the variables under study. We transformed the values of the F^- concentration in water, milk and urine to a logarithmic scale. We classified children into 3 age categories (6–12 months, 13–24 months and 25–36 months). We compared the detected concentrations of F^- in the drinking water supply to the threshold of 1.5 mg/L established in regulation NOM-127-SSA1-1994 for water for human use and consumption. When it came to bottled water, we compared the obtained values to the threshold established in regulation NOM-201-SSA1-2002. This regulation allows levels of up to 0.7 mg/L, the concentration currently recommended by organisations such as the American Dental Association (ADA) to prevent DF.[20] We found no threshold or recommendations for the concentration of F^- in milk, but since this is a fluid for human consumption, we applied the same threshold values of 0.7 mg/L and 1.5 mg/L. We performed bivariate analyses calculating the Pearson correlation coefficient. We defined statistical significance as a p-value of less than 0.05 (two-tailed tests). We performed all the statistical analyses with the software SPSS version 20 (SPSS Inc., Chicago, IL, United States).

Results

We analysed 110 samples of milk consumed by children aged 6 to 34 months residents in the area with high water fluoride concentrations. Table 1 presents the general characteristics of the children as well as the types of milk consumed and the proportions of children that consumed them. The body weights of participants ranged from 4.5 and 15.5 kg, and the height between 55 and 100 cm. The mean daily water intake in the sample was 0.46 L (0.1–1.5 L). Of all children, 17% consumed breast milk, 42.7% artificial formula, 24.5% pasteurised whole cow's milk and 15.5% raw cow's milk.

Table 2 presents the mean concentrations of F^- in water, milk and urine. We found that 86.4% of the tap water specimens exceeded the regulation threshold of 1.5 mg/L. When it came to the bottled water samples, we found that 16.9% and 5.6% of the samples from registered trademark companies exceeded the 0.7 and 1.5 mg/L thresholds, respectively, while 45.7% and 14.3% of the samples from bottlers without a registered trademark exceeded the same thresholds.

As for the F^- concentration in milk, we found that breast milk had the lowest levels with a mean of 0.4 mg/L (SD, 0.4) compared to formula (mean, 0.9 mg/L; SD, 0.8), whole cow's milk (mean, 0.9 mg/L; SD, 0.5) and raw cow's milk (mean, 1.6 mg/L; SD, 1.7). The proportion of samples that exceeded

Table 1 General characteristics of the children, type of milk and proportion of children consuming it.

Variable	*n*	Mean	Standard deviation	Minimum	Maximum
Age (months)	110	16.9	7.3	6	34
Weight (kg)	110	10.6	2.4	4.5	15.5
Height (cm)	110	78	10.4	55	100
Daily milk intake (L)	110	0.46	0.29	0.1	1.5

Type of milk	*n*	Proportion (%)
Breast milk	19	17.3
Infant formula reconstituted with water out of the tap or bottled water	47	42.7
Pasteurised milk (whole)	27	24.5
Untreated cow's milk (raw)	17	15.5

Table 2 Mean fluoride concentrations in samples of water, milk and urine (mg/L).

	n	Fluoride concentration (mg/L)				% >0.7[a]	% >1.5[b]
		Mean	Standard deviation	Minimum	Maximum		
Tap water	110	3.8	2.1	0.1	11.0	90.9	86.4
Bottled water with registered trademark	71	0.4	0.4	0.4	2.0	16.9	5.6
Bottled water without registered trademark	35	0.7	0.5	0.1	2.0	45.7	14.3
Breast milk	19	0.4	0.4	0.1	0.9	21.1	0
Artificial formula reconstituted with tap or bottled water	47	0.9	0.8	0.2	3.9	55.3	10.6
Pasteurised whole milk	27	0.9	0.5	0.1	2.0	63	17.9
Untreated (raw) cow's milk	17	1.6	1.7	0.3	5.0	64.7	31.2

	n	Mean	Standard deviation	Percentile				Reference[c]	% >reference
				25	50	70	90		
Urine (mg/L)	110	1.8	1.8	0.5	1.3	2.0	4.0	1 mg/L	62

[a] NOM-041-SSA1-1993.
[b] NOM-127-SSA1-1994 and NOM-201-SSA1-2002.
[c] Singh et al., 2014.[21]

the 0.7 mg/L threshold was 21.1% for breast milk, 55.3% for artificial formula, 63% for pasteurised whole milk and 64.7% for raw cow's milk. When we applied the 1.5 mg/L threshold, none of the breast milk samples exceeded it, compared to 10.6% of formula samples, 17.9% of pasteurised whole milk samples and 31.2% of raw cow's milk samples.

The mean concentration of F^- in urine sample was 1.8 ± 1.8 mg/L; and in 62% values exceeded 1.0 mg/L, the average reported in school-aged children living in areas with endemic fluorosis due to high water F^- concentrations.[21]

Last of all, Table 3 presents the F^- intake through consumption of milk by age group. The Agency for Toxic Substances and Disease Registry (ATSDR) established a reference dose (RfD) of 0.06 mg of F^-/kg/day at which DF may develop.[7] We found doses that neared and even exceeded the RfD at the 90th percentile for formula, at the 70th percentile for pasteurised whole cow's milk and at the 50th percentile for raw cow's milk.

We found a statistically significant correlation (Pearson) between the F^- concentration in milk (logarithmic scale) and the F^- concentration in urine (logarithmic scale) ($r = 0.41$; $P < 0.001$). The correlation remained statistically significant after adjusting for age ($r = 0.39$; $P < 0.001$; Fig. 1).

Discussion

The impact on children's health of prolonged exposure to F^- depends largely on the daily intake of F^- from contaminated water or foods.

Table 3 Dose of fluoride (mg/kg/day) received through consumption of breast milk, artificial formula, pasteurised whole cow's milk and untreated (raw) cow's milk.

Type of milk	Age in months	Mean	Standard deviation		Percentile	
				50	70	90
		mg/kg/day				
Breast milk[a]	6–12	0.02	0.02	0.012	0.02	0.04
	13–24	0.02	0.03	0.015	0.03	0.05
Artificial formula reconstituted with tap or bottled water	6–12	0.04	0.06	0.03	0.05	0.09
	13–24	0.05	0.05	0.03	0.06	0.11
	25–36	0.05	0.05	0.03	0.05	0.09
Pasteurised cow's milk (whole)[a]	13–24	0.05	0.04	0.04	0.06	0.1
	25–36	0.05	0.04	0.04	0.06	0.09
Untreated cow's milk (raw)	6–12	0.08	0.09	0.05	0.08	0.17
	13–24	0.09	0.09	0.06	0.09	0.20
	25–36	0.09	0.11	0.06	0.09	0.19

Concentration of F^- in milk expressed as mean and standard deviation in mg/L (logarithmic distribution: breast milk 0.4 ± 0.4, formula 0.9 ± 0.8, pasteurised whole milk 0.9 ± 0.5, raw cow's milk 1.6 ± 1.7). Body weight expressed in kg (normal distribution: age 6–12 months 8.8 ± 1.7; 13–24 months 10.9 ± 2.0; 25–36 months 12.8 ± 1.6). Daily intake expressed as L/day (range [minimum–maximum]: age 6–12 months 0.1–1; 13–24 months 0.1–1.5; 25–36 months 0.25–1.5). Oral exposure factor (single value: 0.97). Number of simulations: 10,000.

[a] Children with reported consumption of breastmilk were in the 6–12 months and 13–24 months age groups, and children with reported consumption of pasteurised milk were in the 13–24 months and 25–36 months age groups.

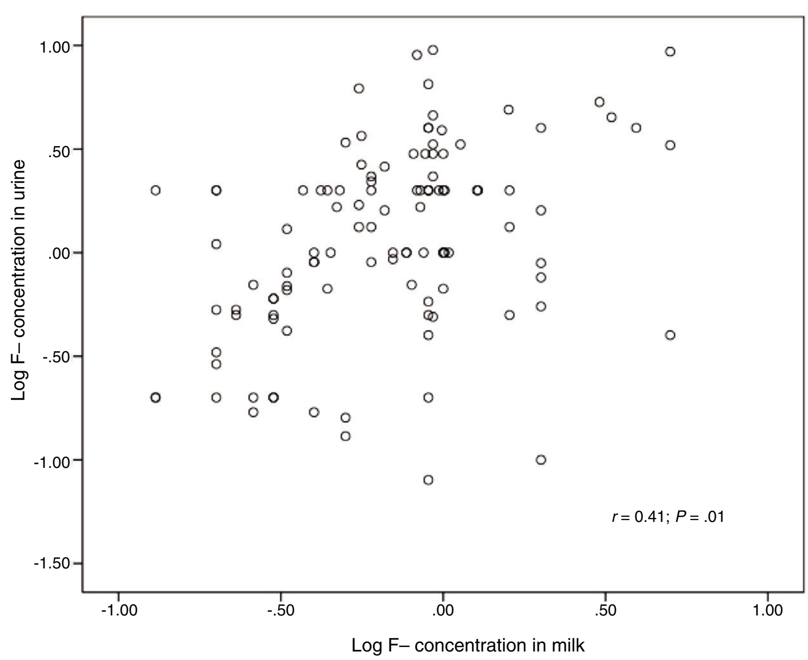

Figure 1 Pearson correlation for the concentration of fluoride in milk and in urine (logarithmic scale).

We found that 86.4% of the samples of water in the households included in the study exceeded the 1.5 mg/L limit established in regulation NOM-127-SSA1-1994. These results were consistent with the findings of Hurtado-Jiménez and Gardea-Torresdey in Lagos de Moreno in 2005 (3.2 ± 1.4 mg/L compared to 3.8 ± 2.1 mg/L in our study).[15] Some of the towns in this region have water fluoride levels that are up to 10-fold the limit established in regulation NOM-127.[22] We also analysed bottled water samples as a potential additional source of F^-, as previous studies have demonstrated that bottled water does not always meet quality standards.[23] In our study, 16.9% of bottled water samples from registered brands exceeded the NOM-201-SSA1-2002 limit of 1.5 mg/L. The proportion of samples of bottled water without a registered trademark that exceeded the NOM-201 threshold was greater (45.7%).

The type of milk that had the lowest F^- levels was breast milk, with a mean concentration of 0.4 mg/L (SD, 0.4). We found concentrations greater than 0.7 mg/L in 21.1% of breast milk samples, but none of the samples exceeded

1 mg/L. These findings are consistent with the evidence in the literature, according to which only very small amounts of F^- are eliminated in breast milk. To demonstrate this, Sener et al. measured the levels of F^- in plasma and milk of lactating mothers, and found that the levels of F^- were lower in breast milk compared to plasma (0.006 mg/L vs 0.017 mg/L); they also found a correlation between the levels of F^- in plasma and in breast milk, which showed that while the amounts of F^- passed to the milk are small, the transfer does occur.[24] Faraji et al. found a similar correlation between the levels of F^- in the milk of lactating women and the levels of F^- in the water they consumed ($r = 0.65$; $P = 0.002$).[25] It is worth noting that the levels of F^- that the women in these studies were exposed to, ranged from 0.3 to 0.5 mg/L, so it would be fair to assume that the concentration of F^- in breast milk is higher in areas with polluted water. Poureslami et al. measured the levels of F^- in the breast milk of women with DF and found a mean concentration of 0.55 mg/L (SD, 0.25). The control group in this study consisted of women without DF, whose breast milk had lower levels of F^- (mean, 0.006 mg/L; SD, 0.003), which demonstrated that F^- concentrations may be greater in the breast milk of women exposed to this ion.[13] When it came to formula, our study found levels above 0.7 mg/L in 55.3% of the specimens and above 1.5 mg/L in 10.6% of the specimens. The formulas tested in our study were prepared as they were usually prepared in the households of each of the participants. Of all mothers, 83.7% reported preparing formula with bottled water, which could explain the high percentage of formula specimens that had F^- concentrations above 0.7 mg/L. In Mexico, there is no published evidence on the levels of F^- in artificial formula. A study conducted in Brazil reported that out of 15 commercial brands prepared with distilled water, 2 exceeded the 0.7 mg/L threshold.[14] We ought to highlight that in our study both pasteurised whole cow's milk and raw cow's milk frequently exceeded the established thresholds, with 63% and 64.7%, respectively, exceeding the 0.7 mg/L threshold and 17.9% and 31.2% the 1.5 mg/L threshold. Considering the low amounts of F^- that are eliminated in milk and that milk should not come in contact with water during the manufacturing process, this suggests the possibility that water that does not meet the quality criteria for drinking water bottled in adherence to the NOM-127 and NOM-201 regulations is being added to the milk.

When it comes to fluoride levels in urine, there is no regulation on environmental exposure in relation to this variable, but only regulations concerning occupational exposure. The American Conference of Governmental Industrial Hygienists (ACGIH) of the United States has proposed a biological exposure index (BEI) for fluoride in urine of 2 mg/L,[26] while the NOM-047-SSA1-2011 has established a BEI of 3 mg/L (both prior to shift). When it comes to the paediatric population, a study conducted in children residing in an area with water fluoride levels of less than 1 mg/L found concentrations in urine of 1 mg/L.[17] In our study, 62% had concentrations above 1 mg/L. The levels of F^- in urine increased from age 1.5 years (2.1 mg/L vs 1.6 mg/L, $P < 0.05$). In children, the risk of exposure to F^- increases with age as they stop consuming breast milk and start consuming artificial formula, cow's milk or water, in addition to foods prepared in the home. Previous data published by our working group for the town of Lagos de Moreno shows that 64.5% of households still use tap water for cooking.[22] We ought to highlight that we found a F^- concentration of 4.5 mg/L in the urine of an infant aged 6 months whose mother prepared his formula with tap water.

Knowledge of the sources and doses of exposure to F^- is of vital importance during the early stages of development, as fluoride is integrated in the teeth before they erupt,[27] increasing the risk of DF in the paediatric population. We were able to calculate a probability distribution for the dose of exposure using data obtained from our sample with the Oracle Crystal Ball software, which should approximate real values. When it came to the intake from breast milk found in our study, none of the doses calculated based on the samples exceeded the 0.06 mg/kg/day RfD established by the ATSDR. The average dose amounted to one third of the RfD. The doses obtained through consumption of artificial formula, pasteurised cow's milk and raw cow's milk exceeded the RfD from the 90th, 70th and 50th percentiles, respectively. These results suggest that the paediatric population of the region is at risk. Thus, 10% of children consuming formula reconstituted with tap water or water bottled with poor quality assurance processes, 30% of children consuming pasteurised whole cow's milk and 50% of children consuming untreated, raw cow's milk could develop DF in the primary dentition. Furthermore, we found a correlation between the concentration of F^- in milk and the concentration of F^- in urine, which supports the hypothesis that exposure to fluorides at these ages could be due to ingestion of contaminated milk ($r = 0.41$; $P < 0.001$).

The presence of DF in the primary dentition of children residing in areas with high fluoride concentrations in water has already been documented in the literature.[9–11] Levy et al. found an association between different periods of exposure to F^- and the prevalence of DF in the primary dentition. This association was strongest in infants aged 6–9 months ($P < 0.001$).[11] A study conducted in Mexico that investigated the presence of DF in the primary teeth of children aged 3–6 years found that its prevalence increased with increasing concentrations of fluorides in the water supply (0–1.2 mg/L, FD 66.2%; 1.3 and 3 mg/L, FD 81.3%; >3 mg/L, FD 92.3%).[28]

Dental associations in different parts of the world recommend the use of F^- for prevention and control of tooth decay in children, determining the use of F^- by balancing the risk of tooth decay and the risks associated to the toxic effects of fluorides.[29] When it comes to fluoridated water, European dental associations recommend concentrations of fluoride between 0.3 and 0.6 mg/L as optimal for prevention of both tooth decay and DF (with these levels in water, further exposure to F^- other than through tooth paste is not recommended in children aged 2–3 years).[30] In Mexico, regulation NOM-013-SSA2-1994 recommends fluoride supplementation in children that for health reasons do not consume fluoridated salt and live in areas where the concentration of F^- in drinking water is less than 0.7 mg/L.

The identification of sources of F^- in addition to drinking water during early child development may reduce the risk of DF and other unfavourable outcomes in the future.[22,30] Breast milk continues to be the optimal food for infant development in areas with high F^- levels in water, as it provides the best nutrition and reduces the risk of exposure to this pollutant. It is also important to ascertain the quality of the dairy or nutritional products in which water is used in the manufacturing process, especially those produced in geographical areas where the water is known to contain pollutants.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgments

This study was carried out during the second year of the postdoctoral fellowship of the first author (Conacyt grant no. 239404).

References

1. Ryczel ME. Flúor y agua de consumo – Su relación con la salud – Controversias sobre la necesidad de fluorar el agua de consumo. Bol ATA. 2006;20:21–6.
2. Galicia Chacón L, Molina Frenchero N, Oropeza A, Gaona E, Juárez López L. Análisis de la concentración de fluoruro en agua potable de la delegación Tláhuac, Ciudad de México. Rev Int Comun Ambient. 2011;27:283–9.
3. World Health Organization (WHO) [Internet]. Guidelines for drinking-water quality, 4th edition, incorporating the 1st addendum; 2017 [accessed 10 Sep 2018]. Available in: http://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/
4. Khan A, Moola MH, Cleaton-Jones P. Global trends in dental fluorosis from 1980 to 2000: a systematic review. SADJ. 2005;60:418–21.
5. Browne D, Whelton H, O'Mullane D. Fluoride metabolism and fluorosis. J Dent. 2005;33:177–86.
6. Newbrun E. What we know and do not know about fluoride. J Public Health Dent. 2010;3:227–33.
7. Integrated Risk Information System (IRIS) [Internet]. Fluorine (soluble fluoride). Environmental Protection Agency US; 1985 [accessed 12 Apr 2018]. Available in: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0053_summary.pdf
8. Jheon AH, Seidel K, Biehs B, Klein OD. From molecules to mastication: the development and evolution of teeth. Wiley Interdiscip Rev Dev Biol. 2013;2:165–82.
9. Warren JJ, Kanellis MJ, Levy SM. Fluorosis of the primary dentition: what does it mean for permanent teeth? J Am Dent Assoc. 1999;130:347–56.
10. Warren JJ, Levy SM, Kanellis MJ. Prevalence of dental fluorosis in the primary dentition. J Public Health Dent. 2001;61:87–91.
11. Levy SM, Broffitt B, Marshall TA, Eichenberger-Gilmore JM, Warren JJ. Associations between fluorosis of permanent incisors and fluoride intake from infant formula, other dietary sources and dentifrice during early childhood. J Am Dent Assoc. 2010;141:1190–201.
12. Ekstrand J, Boreus LO, de Chateau P. No evidence of transfer of fluoride from plasma to breast milk. Br Med J (Clin Res Ed). 1981;283:761–2.
13. Poureslami H, Khazaeli P, Mahvi AH, Poureslami K, Poureslami P, Haghani J, et al. Fluoride level in the breast milk in Koohbanan, a city with endemic dental fluorosis. Fluoride. 2016;49:485–94.
14. Nagata ME, Delbem ACB, Kondo KY, de Castro LP, Hall KB, Percinoto C, et al. Fluoride concentrations of milk, infant formulae, and soy-based products commercially available in Brazil. J Public Health Dent. 2016;76:129–35.
15. Hurtado-Jiménez R, Gardea-Torresdey J. Estimación de la exposición a fluoruros en Los Altos de Jalisco, México. Salud Públ Méx. 2005;47:58–63.
16. The National Institute for Occupational Safety and Health (NIOSH) [Internet]. Fluoride in urine; 2016 [accessed 10 Sep 2018]. Available in: https://www.cdc.gov/niosh/docs/2014-151/pdfs/methods/8308.pdf
17. RECIPE. ClinChek urine controls, lyophilised for trace elements; 2016 [accessed 10 Sep 2018]. Available in: https://www.recipe.de/en/products_qa_chek_884749.html
18. Riccio F. Simulación Monte Carlo. Oracle Crystall Ball; 2018 [accessed 12 Jun 2018]. Available in: http://www.oracle.com/technetwork/es/articles/oem/oracle-crystal-ball11-1-4434142-esa.html
19. Agency for Toxic Substances and Disease Registry (ATSDR) [Internet]. Resumen de Salud Pública: Fluoruros, fluoruro de hidrógeno y flúor (Fluorides, hydrogen fluoride and fluorine); 2003 [accessed 12 Apr 2018]. Available in: https://www.atsdr.cdc.gov/toxprofiles/tp11.pdf
20. American Dental Association (ADA) [Internet]. Fluoride clinical guidelines; 2018 [accessed 12 Apr 2018]. Available in: https://www.ada.org/en/public-programs/advocating-for-the-public/fluoride-and-fluoridation/fluoride-clinical-guidelines
21. Singh N, Gupta Verma K, Verma P, Sidhu GK, Sachdeva S. A comparative study of fluoride ingestion levels, serum thyroid hormone & TSH level derangements, dental fluorosis status among school children from endemic and non-endemic fluorosis areas. Springerplus. 2014;3:1–5.
22. Valdez Jiménez L, López Guzmán OD, Cervantes Flores M, Costilla-Salazar R, Calderón Hernández J, Alcaraz Contreras Y, et al. In utero exposure to fluoride and cognitive development delay in infants. Neurotoxicology. 2017;59:65–70.
23. Cruz Cardoso D, Castillo Chaires I, Arteaga Mejía M, Cervantes Sandoval A, Pinelo Bolaños P. Análisis de la concentración de fluoruro en aguas embotelladas de diferentes entidades federativas de la República Mexicana. Rev ADM. 2013;70:81–90.
24. Sener Y, Tosun G, Kahvecioglu F, Gökalp A, Koç H. Fluoride levels of human plasma and breast milk. Eur J Dent. 2007;1:21–4.
25. Faraji H, Mohammadi AA, Akbari-Adergani B, Vakili Saatloo N, Lashkarboloki G, Mahvi AH. Correlation between fluoride in drinking water and its levels in breast milk in Golestan Province, Northern Iran. Iran J Public Health. 2014;43:1664–8.
26. American Conference of Governmental Industrial Hygienists (ACGIH) [Internet]. Fluorides: BEI(R) 7th edition documentation; 2012 [accessed 12 Apr 2018]. Available in: https://www.acgih.org/forms/store/ProductFormPublic/fluorides-bei-r-7th-edition-documentation
27. Rivas Gutiérrez J, Huerta Vega L. Fluorosis dental: metabolismo, distribución y absorción del fluoruro. Rev ADM. 2005;62:225–9.
28. Loyola-Rodríguez JP, Pozos-Guillén A, Hernández-Guerrero JC, Hernández-Sierra JF. Fluorosis en dentición temporal en un área con hidrofluorosis endémica. Salud Públ Méx. 2000;42:194–200.
29. Documento de consenso de la European Academy of Paediatric Dentistry (EAPD) con la Sociedad Española de Odontopediatría [Internet]. Protocolo para el uso del flúor en niños; 2018 [accessed 12 Jun 2018]. Available in: https://www.odontologiapediatrica.com/protocolos/fluor/
30. Tang Q, Du J, Ma H, Jiang S, Zhou X. Fluoride and children's intelligence: a meta-analysis. Biol Trace Elem Res. 2008;126:115–20.