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Could Local Anesthesia While Breast-Feeding Be Harmful to Infants?

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ABSTRACT

Background: Few studies have been carried out on the levels and possible toxicity of local anesthetics in breast milk after parenteral administration. The purpose of this study is to determine the amount of lidocaine and its metabolite monoethylglycinexylidide (MEGX) in breast milk after local anesthesia during dental procedures.

Methods: The study population consisted of seven nursing mothers (age, 23–39 years) who received 3.6 to 7.2 mL 2% lidocaine without adrenaline. Blood and milk concentrations of lidocaine and its metabolite MEGX were assayed using high-performance liquid chromatography. The milk-to-plasma ratio and the possible daily doses in infants for both lidocaine and MEGX were calculated.

Results: The lidocaine concentration in maternal plasma 2 hours after injection was 347.6 ± 221.8 μg/L, the lidocaine concentration in maternal milk ranged from 120.5 ± 54.1 μg/L (3 hours after injection) to 58.3 ± 22.8 μg/L (6 hours after injection), the MEGX concentration in maternal plasma 2 hours after injection was 58.9 ± 30.3 μg/L, and the MEGX concentration in maternal milk ranged from 97.5 ± 39.6 μg/L (3 hours after injection) to 52.7 ± 23.8 μg/L (6 hours after injection). According to these data and considering an intake of 90 mL breast milk every 3 hours, the daily infant dosages of lidocaine and MEGX were 73.41± 38.94 μg/L/day and 66.1 ± 28.5 μg/L/day respectively.

Conclusions: This study suggests that even if a nursing mother undergoes dental treatment with local anesthesia using lidocaine without adrenaline, she can safely continue breast-feeding. ***JPGN 32:142–144, 2001.*** **Key Words:** Lidocaine—Monoethylglycinexylidide—Breast-feeding—Local anesthesia. © 2001 Lippincott Williams & Wilkins, Inc.

In recent years, many investigators have been interested in the risk–benefit ratios for administrating drugs during puerperium (1–4). Breast-feeding is strongly recommended by pediatricians, and the age for weaning usually varies from 4 to 8 months but may be 18 to 24 months or even more in less developed countries. Even though several studies have shown that many antibiotic and analgesic drugs are not contraindicated for women who are breast-feeding, the literature provides little information on the levels of local anesthetics in breast milk after parenteral administration (5–10). Local anesthetics used in dentistry have not been studied sufficiently regarding either their concentration in breast milk or their possible toxicity for the newborn (11). The aim of this study was to determine the amount of lidocaine and its metabolite monoethylglycinexylidide (MEGX) in breast milk after dental anesthesia.

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MATERIALS AND METHODS

Patients

The study population consisted of seven healthy, nursing mothers (age range, 23–39 years) who needed local anesthetic for dental treatment. Written informed consent was obtained from each woman before she underwent the procedure. Six women received 3.6 mL of an injection of 2% lidocaine without adrenaline, and one woman received 4.5 mL 2% lidocaine without adrenaline on the first occasion and, 3 months later, 7.2 mL 2% lidocaine without adrenaline. The patients were advised to discard their milk for 36 hours after the injection of lidocaine to allow complete elimination of the drug in the maternal system.

Assay Procedures

Two-milliliter blood samples were drawn into heparinized syringes from a maternal vein 2 hours after the injection of lidocaine, and two milk samples were collected 3 and 6 hours after the injection. The concentrations of lidocaine and its primary metabolite MEGX were assayed using high-performance liquid chromatography (12–15).

The high-performance liquid chromatographic system consisted of a Cromath 3 CDM (Biorad, Segrate, Milan, Italy) and a column (300 × 4-mm internal diameter; μ-Bondapak Phenyl, Waters Associates, Australia). Lidocaine and MEGX were supplied by Astra Pharmaceuticals (Rydalmere B.C., Sodertalje, Sweden). Stock drug standards were dissolved in absolute ethanol to give concentrations of MEGX at 2 g/L and of lidocaine at 5g/L. A working solution was prepared by diluting these standards as follows: MEGX, 0.250 mL, and lidocaine, 0.250 mL to 100 mL, with distilled water. The internal standard was a 1:200 solution of mexiletine (Mexitil; Boeringher, Milan, Italy) in distilled water. The extracting solvent was hexane:ethylacetate:methanol (60:40:0.4) (11).

Standard calibration samples were prepared by adding 10 μL lidocaine working solution and 20 μL MEGX working solution to 1.0 mL blank plasma or milk. To 1.0 mL plasma or milk were added 1) 20 μL mexiletine (1:200) internal standard, 2) 100 μL 1 mol NaOH, and 3) 10.0 mL extracting solvent. The mixture was shaken vigorously for 5 minutes and then centrifuged at 1,300 *g* for 10 minutes. A 9.0-mL aliquot of the organic phase was transferred to a second glass tube, reextracted into 0.2 mL 0.1 mol HCl by gentle shaking, and then centrifuged. The organic phase was aspirated, and the acid extract was placed in a water bath at 50°C for 5 minutes to remove the last traces of solvent. Aliquots were then injected onto the high-performance lipid chromatographic column.

We studied the following parameters:

- Lidocaine concentrations in maternal plasma 2 hours after injection
- Lidocaine concentrations in maternal milk 3 hours after injection
- Lidocaine concentrations in maternal milk 6 hours after injection
- MEGX concentrations in maternal plasma 2 hours after injection
- MEGX concentrations in maternal milk 3 hours after injection
- MEGX concentrations in maternal milk 6 hours after injection
- Milk-to-plasma ratio for lidocaine and MEGX (using the milk sample taken 3 hours after injection)
- Possible daily doses of lidocaine and MEGX that an infant might assume consuming 90 mL breast milk every 3 hours

Statistical Analysis

The mean ± standard deviation and range of all parameters were measured. The Shapiro Wilk's normality test was performed to verify distributions. Nonparametric rank signed and rank tests for paired and unmatched data were performed when appropriate.

RESULTS

The lidocaine concentration in maternal plasma 2 hours after injection was 347.6 ± 221.8 μg/L (LD^P), the lidocaine concentration in maternal milk 3 hours after injection was 120.5 ± 54.1 μg/L (LD^{M1}), the lidocaine concentration in maternal milk 6 hours after injection was 58.3 ± 22.8 μg/L (LD^{M2}), the MEGX concentration in maternal plasma 2 hours after injection was 58.9 ± 30.3 μg/L ($MEGX^P$), the MEGX concentration in maternal milk 3 hours after injection was 97.5 ± 39.6 μg/L ($MEGX^{M1}$), the MEGX concentration in maternal milk 6 hours after injection was 52.7 ± 23.8 μg/L ($MEGX^{M2}$), the lidocaine milk-to-plasma ratio was 0.38 ± 0.09 μg/L, and the MEGX milk-to-plasma ratio was 1.61 ± 0.48 μg/L. All measures were calculated using plasma and milk samples taken 2 and 3 hours respectively after injection.

Assuming an infant intake of 90 mL breast milk every 3 hours, the daily infant dosages of lidocaine and MEGX were 73.41 ± 38.94 μg/L/day and 66.1 ± 28.5 μg/L/day respectively (10). The mean ± standard deviation and range of all parameters are shown in Table 1. The differences between LD^{M1} versus LD^{M2}, and $MEGX^{M1}$ versus $MEGX^{M2}$ were significant ($P = 0.008$) and not significant ($P = 0.0078$) respectively. The differences between LD^{M1} versus LD^P, and $MEGX^{M1}$ versus $MEGX^P$ were significant ($P = 0.002$ and $P = 0.046$ respectively).

DISCUSSION

As our data show, the amount of lidocaine seems to be very small, given the poor systemic bioavailability of the drug along with its short half-life, and considering that an infant can tolerate much higher doses of lidocaine (16). In addition, a clinically important aspect must be con-

TABLE 1. *Maternal and neonatal data*

	Mean ± SD	Range
Maternal Age (years)	29.6 ± 5.5	23–29
Maternal Weight (kg)	68 ± 6.7	53–92
Dose of Lidocaine (mg/kg)	1.24 ± 0.15	1.0–1.47
LD^P (μg/L)	347.6 ± 221.8	195.6–868.8
LD^{M1} (μg/L)	120.5 ± 54.1	78.2–250.1
LD^{M2} (μg/L)	58.3 ± 22.8	28.3–107.2
LD M/P ratio	0.38 ± 0.09	0.27–0.53
$MEGX^P$ (μg/L)	58.9 ± 30.3	22.2–122.5
$MEGX^{M1}$ (μg/L)	97.5 ± 39.6	33.3–143
$MEGX^{M2}$ (μg/L)	52.7 ± 23.8	23.5–96
MEGX M/P ratio	1.61 ± 0.48	1.16–2.5
LD (infant daily dose) (μg/L/day)	73.41 ± 38.94	56.3–180.1
MEGX (infant daily dose) (μg/L/day)	66.1 ± 28.5	24.0–103.0

Data are mean ± SD.

LD^P, lidocaine concentrations in maternal plasma 2 hr after injection; LD^{M1}, lidocaine concentrations in maternal milk 3 hr after injection; LD^{M2}, lidocaine concentrations in maternal milk 6 hr after injection; $MEGX^P$, MEGX concentrations in maternal plasma 2 hr after injection; $MEGX^{M1}$, MEGX concentrations in maternal milk 3 hr after injection; $MEGX^{M2}$, MEGX concentrations in maternal milk 6 hr after injection; M/P, milk/plasma ratio for lidocaine and MEGX calculated using the milk sample taken 3 hr after injection.

sidered: these anesthetic agents are used on a single-dose basis, thus preventing their accumulation in maternal milk.

The current study suggests that an infant may safely continue to breast-feed from a mother who has undergone dental treatment after local anesthesia with lidocaine without adrenaline. Because there have been reports of several idiosyncratic reactions resulting from additives (e.g., methylparaben or sulfite) often used with local anesthetics (17,18), it may be advisable to use local anesthetics without adrenaline, even if adrenaline is destroyed during its passage through the gastrointestinal tract and its appearance in breast milk is unlikely (19).

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