

## Case Report

# Excretion of Gadopentetate Dimeglumine in Human Breast Milk

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The excretion of iodinated contrast media in human breast milk has been documented [1–6]. Magnevist (gadopentetate dimeglumine, Berlex Inc., Wayne, NJ), a relatively new paramagnetic contrast agent for MR imaging with an extracellular distribution pattern similar to that of iodinated contrast agents, has been approved for clinical use in Europe and the United States. Although studies in rats have shown evidence that gadopentetate dimeglumine is excreted in breast milk [7], excretion of gadopentetate dimeglumine in human breast milk has, to our knowledge, not been reported or quantified. With the increasing use of contrast-enhanced MR procedures, knowledge of whether gadopentetate dimeglumine is excreted in breast milk and the time course of such excretion is important for treating lactating patients. We studied a lactating patient in whom a gadopentetate dimeglumine-enhanced MR study was performed. Serial measurements of gadolinium excretion in the patient's breast milk and urine form the basis of this report.

### Subject and Methods

The patient, a 29-year-old lactating woman with a 13-year history of left ear deafness and mild left ear tinnitus, was referred for MR imaging to rule out an acoustic neuroma. After consulting with the patient and discussing the risks and options, it was decided to proceed with the contrast-enhanced MR study at the time because of personal and logistical considerations. After informed consent was obtained, Magnevist was injected IV at a dose of 0.1 mmol/kg. The total amount of administered gadopentetate dimeglumine was 5.8 mmol. Breast feeding was discontinued for 48 hr after the examination

to minimize any potential risk to the infant. Serial samples of all expressed breast milk were collected at 135 min, 290 min, 12 hr 40 min, 17 hr 30 min, 22 hr 40 min, and 32 hr 40 min after injection of Magnevist. The patient attempted to empty both breasts completely at the time of each collection. Serial urine samples were obtained at the same time as the breast milk, together with a total urine collection for the 33-hr period of observation. Five-milliliter aliquots of all samples were lyophilized and analyzed for gadolinium concentration by using inductively coupled plasma atomic emission spectrometry (ICP-AES, wavelength 342.247 nm; Schering AG, Berlin). The lowest detectable gadolinium concentration with this method is  $1 \times 10^{-7}$  mol/l. The concentrations of gadolinium in the urine and milk samples were essentially equivalent to the concentration of gadopentetate dimeglumine as there is no endogenous source of gadolinium and no significant dissociation of the chelate within the body has been reported.

### Results

A cumulative amount of gadolinium that accounted for only 0.011% of the total IV administered dose was excreted in the breast milk during the observation period of almost 33 hr. The cumulative excreted amounts of gadolinium in milk and urine vs time are shown in Figure 1. The highest concentration of gadolinium in breast milk was noted 4 hr 50 min after administration, and measured 5.1  $\mu\text{mol/l}$ . At 22 hr after gadopentetate dimeglumine administration, the concentration in breast milk measured less than 1.0  $\mu\text{mol/l}$ . The time course of gadopentetate dimeglumine concentration in excreted breast milk compared with that in urine is shown in Figure 2.

Received November 27, 1990; accepted after revision February 1, 1990

This work was supported in part by Schering AG, Berlin, W. Germany.

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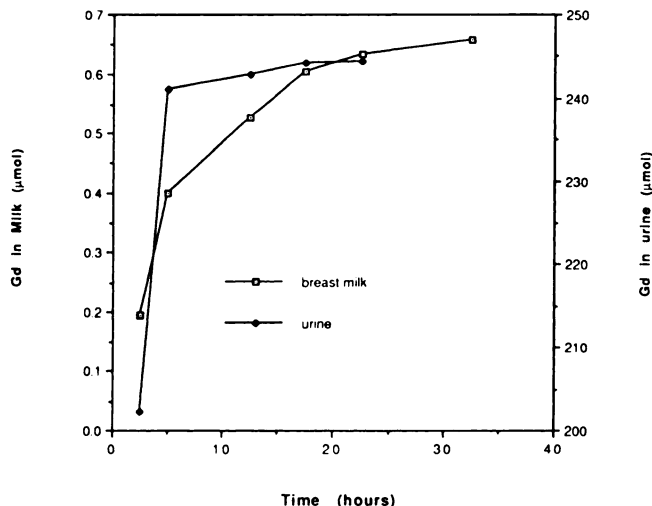


Fig. 1.—Total (cumulative) excretion of gadolinium in breast milk and urine over time after IV administration.

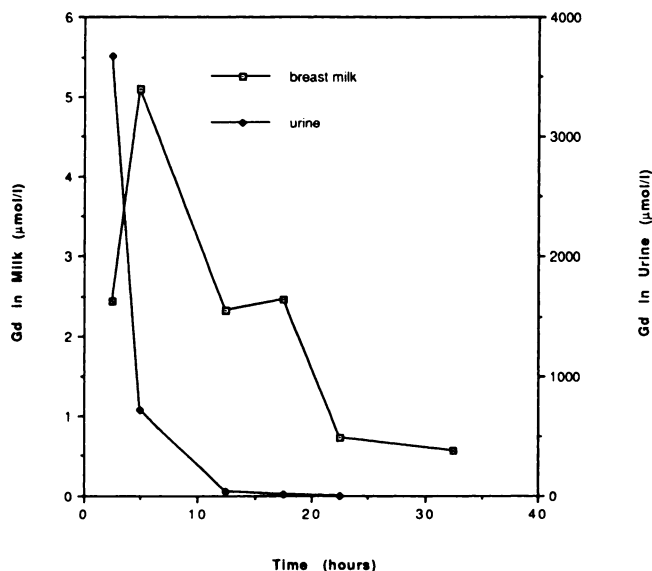


Fig. 2.—Concentration of gadolinium in breast milk and urine over time after IV administration.

## Discussion

We have found that gadopentetate dimeglumine, which is an ionic contrast medium, is transferred to the breast milk in a very limited amount. Compared with the nonionic contrast agent iohexol, which is reported to be excreted in the breast milk in amounts of 0.5% of total injected dose [5], the excretion rate of gadopentetate dimeglumine appears even lower. Compared with the reported excretion of diatrizoate (<0.05%), an ionic contrast agent, the excretion of gadopentetate dimeglumine as measured in our study seems to be on the same order of magnitude [6]. Experimental studies of gadopentetate dimeglumine in lactating rats at a dose of 0.5 mmol/kg indicated an estimated cumulative mammary excretion of 0.2% [7]. One reason for the lower measured excretion

found in our patient might be that she was weaning the infant at the time of the study, which resulted in a reduced amount of breast-milk production during this study. This effect was shown in an earlier study of iodinated contrast agents [5]. Other factors that have been shown to influence the degree of secretion of a substance from plasma to milk include: (1) the route, frequency, and dose of administered drug; (2) degree of protein binding; (3) molecular weight and degree of ionization at plasma and milk pH; (4) lipid solubility; and (5) time after parturition and frequency of breast feeding [1–3].

The extent of protein binding and blood cell partitioning of gadopentetate dimeglumine is not known [7]. Magnevist is a water-soluble gadopentetate dimeglumine salt that, upon injection, is completely dissociated, and the gadopentetate moiety is eliminated in the urine with  $91 \pm 13\%$  of the total dose excreted by 24 hr after injection [7]. The small difference in molecular weight between the anion (the gadopentetate moiety) of Magnevist (550 daltons) and diatrizoate (614 daltons) may contribute to their similar excretion in breast milk.

The peak gadolinium concentration in breast milk (5.1  $\mu\text{mol/l}$ ), measured 5 hr after administration of Magnevist, equals approximately one tenth of estimated plasma concentration at this time (G. Schuhmann-Giampieri, personal communication). Assuming a body weight of 3 kg, the amount of gadolinium transferred to a nursing infant during the first 24 hr after injection would amount to only 0.21  $\mu\text{mol/kg}$ . Theoretically, contrast media, if excreted in the breast milk, can cause either direct toxic effects on the nursing infants or allergic sensitization. Neither of these effects have been reported, to our knowledge, for gadopentetate dimeglumine or for iodinated contrast media. Although the present observation is limited because it is based on only one patient, our data indicate a low excretion rate of gadopentetate dimeglumine in the breast milk. The time course of excretion indicates that breast feeding can probably be safely resumed 24 hr after IV administration of gadopentetate dimeglumine. This conclusion is based on setting an arbitrary cutoff for gadopentetate dimeglumine concentration in breast milk at less than 1  $\mu\text{mol/l}$ . Because of the uncertainties arising from the fact that our measurements are based on a single case, an additional waiting period of 12 or 24 hr could be used as an added safety factor, and breast feeding could be suspended for a total of 36–48 hr after gadopentetate dimeglumine administration.

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