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EDITORIAL COMMENTARY

Excretion of radionuclides in human breast milk after nuclear medicine examinations. Biokinetic and dosimetric data and recommendations on breastfeeding interruption

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Since the 1990s the advantages of breastfeeding have been emphasized and the number of women who nurse their infant has increased significantly. Although women in this population are generally healthy and relatively rarely need radionuclide imaging or radionuclide therapies, the issue of radiation protection of breastfed children arises because of their higher radiosensitivity [1]. Approximately 55 papers on excretion of radionuclides in human breast milk after radionuclide imaging or therapy have been published. Unfortunately, most of them are case reports or include only a small number of cases. In 1955 the first report was published about a breastfeeding woman after radioiodine treatment of thyrotoxicosis. This early study showed a higher concentration of radioiodine in breast milk than in plasma and investigated the risk to the infant, especially to the thyroid gland [2].

In this issue of the journal, Leide-Svegborn et al. [3] report data on radioactivity concentrations in breast milk from 53 breastfeeding patients. Their study included one of the largest populations of breastfeeding women studied. The milk was collected at various time-points after administration of 16 different radiopharmaceuticals. The biokinetics of the radiopharmaceuticals using the total fraction excreted in the breast milk and the effective half-life ($T½_{\,eff}$) of the radiopharmaceuticals were determined. The absorbed dose coefficients (milligrays per megabecquerel) for organs and tissues and the effective dose coefficients (millisieverts per megabecquerel) for the different radionuclide formulations were calculated using OLINDA/EXM software. Common radiopharmaceuticals were investigated including the ^{99m}Tc-labelled compounds ^{99m}Tc-DTPA, ^{99m}Tc-HMPAO-labelled leucocytes, ^{99m}Tc-MAA, ^{99m}Tc-MAG$_3$, ^{99m}Tc-MDP, ^{99m}Tc-red blood cells (^{99m}Tc-RBC) and ^{99m}Tc-tetrofosmin, and free ^{99m}Tc-pertechnetate. Other substances including ^{14}C-glycocholate (^{14}C-GCA), ^{14}C-triolein, ^{18}F-FDG, ^{51}Cr-EDTA, hippurate labelled with ^{123}I or ^{131}I, and ^{131}I-NaI were also investigated.

Because of the high sensitivity of infants to radiation exposure, administration of radionuclides to both infants and breastfeeding women should generally be avoided. In single cases of radionuclide imaging in this group of patients, a guideline on cessation or interruption of breastfeeding is essential. Rubow et al. [4] reported data on the excretion of radiopharmaceuticals in human breast milk in 60 patients. An established recommendation for cessation of breastfeeding distinguishes four categories [5]: interruption not essential, interruption for a definite period, interruption with measurement, and cessation for a longer period. Rubow et al. added a fifth category for those radiopharmaceuticals that have a sufficiently low activity concentration in milk such that no interruption of breastfeeding is required. However, with respect to the radiation exposure to the mother, close body contact between mother and child should be avoided to ensure that the dose to the infant does not exceed 1 mSv [4]. The study by Leide-Svegborn et al. [3] in this issue used only three categories as follows: no interruption, 12-hour interruption, and cessation.

Rubow et al. stated that interruption in breastfeeding is not necessary after administration of radiopharmaceuticals with fixed binding to ^{99m}Tc, such as ^{99m}Tc-DISIDA, ^{99m}Tc-sulphur

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collide, ^{99m}Tc-gluconate and ^{99m}Tc-MIBI, but close contact should be restricted after ^{99m}Tc-MIBI administration because of the higher administered activity and longer biological half-life of this agent. Leide-Svegborn et al. [3] classified the following radiopharmaceuticals in this category: ^{99m}Tc-DTPA, ^{99m}Tc-HMPAO-leucocytes, ^{99m}Tc-MAG$_3$, ^{99m}Tc-MDP, ^{99m}Tc-MIBI, ^{99m}Tc-RBC, ^{99m}Tc-tetrofosmin, ^{14}C-glycocholine acid, ^{14}C-triolein, ^{18}F-FDG and ^{52}Cr-EDTA. For the ^{99m}Tc-labelled substances, however, a 4-hour interruption (equivalent to one discarded meal) will ensure that the infant is exposed to only a low absorbed dose from free ^{99m}Tc-pertechnetate in the radiopharmaceuticals given to the mother. Fortunately, the radiostability of these ^{99m}Tc-labelled compounds is high and the radiolabelling process shows a high binding efficiency of >95 %. In contrast, Rose et al. [6] recommended an interruption of breastfeeding for 13 hours after ^{99m}Tc-RBC administration. Unfortunately, the study by Leide-Svegborn et al. [3] included only one patient who received ^{99m}Tc-RBC.

However, the issue with ^{99m}Tc-pertechnetate is more complicated. Leide-Svegborn et al. [3] reported a radioactivity concentration for ^{99m}Tc-pertechnetate of approximately 10 % of the administered activity (%ID) in contrast to a significantly lower %ID for ^{99m}Tc-compounds of approximately 0.05 % for ^{99m}Tc-MIBI to 0.11 % for ^{99m}Tc HMPAO-leucocytes. From these data a 12-hour interruption after ^{99m}Tc-pertechnetate administration is recommended. The cause of this relatively high concentration of ^{99m}Tc-pertechnetate in breast milk is the presence of a sodium iodide symporter in mammary gland cells [7], which leads to a significantly higher radioactivity concentration in breast milk than in maternal plasma. The study by Leide-Svegborn et al. [3] showed a lower excretion of radioactivity in breast milk after pretreatment with the thyroid blocking agent perchlorate: after ^{99m}Tc-pertechnetate administration without blocking a 10 %ID in breast milk was found compared with a significantly lower 0.82 %ID with blocking. These data are supported by animal data from mouse mammary gland cells which also show blocking of the sodium iodide symporter by perchlorate [7].

A 12-hour interruption has also been recommended for ^{99m}Tc-MAA, ^{125}I-iodo-hippurate and ^{131}I-iodo-hippurate [3]. The %ID in breast milk is higher for ^{99m}Tc-MAA (3.7 %) than for other ^{99m}Tc-labelled compounds (<0.1 %). This is in accordance with the findings of other studies [8, 9] and indicates a lower radiostability of this radiopharmaceutical. Leide-Svegborn et al. [3] found a %ID between 2.0 and 2.4 for radioiodine-labelled hippurate, which led to higher expected radiation absorbed doses of 1.0 mSv$_{infant}$/MBq$_{mother}$ for ^{125}I-iodo-hippurate and 5.3 mSv$_{infant}$/MBq$_{mother}$ for ^{131}I-iodo-hippurate. These results are in line with data reported by Rose et al. [6] showing radioactivity concentrations in breast milk of 1.2 % to 4.9 % for ^{123}I, ^{125}I and ^{131}I.

The longest mandatory interruption of breastfeeding is associated with the administration of ^{131}I-NaI for which an interruption of at least 3 weeks is necessary. Although 29 studies on this radionuclide have been published, most of them are only single case reports [10]. Leide-Svegborn et al. [3] found high radioactivity concentrations of ^{131}I-NaI in three patients after diagnostic administration of 1.00 to 1.85 MBq per patient (13, 32 and 48 %ID, respectively) [3]. These levels led to effective radiation absorbed doses to the infant of 106, 70 and 29 mSv$_{infant}$/MBq$_{mother}$, respectively, although the highest dose was expected in the thyroid.

The important factor for recommendations for interruption or cessation of breastfeeding is the effective radiation absorbed dose to the infant. These both depend especially on the $T½_{eff}$ and the total fraction excreted in the breast milk. The ^{99m}Tc radiopharmaceuticals have comparable $T½_{eff}$ values in the range 3.5 hours (for ^{99m}Tc-DTPA) to 5.4 hours (for ^{99m}Tc-MIBI). Depending on the physical half-life, a range of $T½_{eff}$ values from short to long have been reported: 1.8 hours for ^{18}F-FDG, 5.0 to 6.3 hours for ^{125}I/^{131}I-labelled hippurate, 14 hours for ^{131}I-NaI, 15 hours for ^{14}C-triolein, and 143 hours for ^{14}C-CGA [3]. The long $T½_{eff}$ of ^{14}C-labelled radiopharmaceuticals is not a problem in infants because of the very low doses of radioactivity administered to the mother of 0.065 to 0.02 MBq. The highest radiation absorbed dose to infants has been observed after ^{131}I-NaI administration as a result of a high radioactivity concentration in breast milk, a longer $T½_{eff}$ and a higher biological effectiveness of the beta particles of ^{131}I. Medium radiation absorbed doses to infants are associated with radioiodine-labelled hippurate, ^{99m}Tc-MAA and ^{99m}Tc-pertechnetate because of their high excretion into breast milk. The expected radiation doses to infants corresponds well with the recommendations on interruption times for breastfeeding.

Summary

The paper by Leide-Svegborn et al. [3] reports important data on radiation exposure in infants after radionuclide imaging in breastfeeding mothers. In particular, application of the recommendations on interruption of breastfeeding for a large number of investigated radiopharmaceuticals is essential in clinical practice.

References

1. Romney B, Nickoloff EL, Esser PD. Excretion of radioiodine in breast milk. J Nucl Med. 1989;30(1):124–6.
2. Miller H, Weetch RS. The excretion of radioactive iodine in human milk. Lancet. 1955;269(6898):1013.

3. Leide-Svegborn S, Ahlgren L, Johansson L, Mattsson S. Excretion of radionuclides in human breast milk after nuclear medicine examinations. Biokinetic and dosimetric data and recommendations on breastfeeding interruption. Eur J Nucl Med Mol Imaging. 2016. doi:10.1007/s00259-015-3286-0
4. Rubow S, Klopper J, Wasserman H, Baard B, van Niekerk M. The excretion of radiopharmaceuticals in human breast milk: additional data and dosimetry. Eur J Nucl Med. 1994;21(2):144–53.
5. Mountford PJ, Coakley AJ. A review of the secretion of radioactivity in human breast milk: data, quantitative analysis and recommendations. Nucl Med Commun. 1989;10(1):15–27.
6. Rose MR, Prescott MC, Herman KJ. Excretion of iodine-123-hippuran, technetium-99m-red blood cells, and technetium-99m-macroaggregated albumin into breast milk. J Nucl Med. 1990;31(6):978–84.
7. Rillema JA, Yu TX, Jhiang SM. Effect of prolactin on sodium iodide symporter expression in mouse mammary gland explants. Am J Physiol Endocrinol Metab. 2000;279(4):E769–72.
8. Ahlgren L, Ivarsson S, Johansson L, Mattsson S, Nosslin B. Excretion of radionuclides in human breast milk after the administration of radiopharmaceuticals. J Nucl Med. 1985;26(9):1085–90.
9. Ahlgren L. Excretion of radionuclides in human breast milk after administration of radiopharmaceuticals. Error in table. J Nucl Med. 1986;27(1):151.
10. Simon SL, Luckyanov N, Bouville A, VanMiddlesworth L, Weinstock RM. Transfer of 131I into human breast milk and transfer coefficients for radiological dose assessments. Health Phys. 2002;82(6):796–806.