EDITORIAL

Excretion of Radioiodine in Breast Milk

Over the past decade or so the advantages of breast feeding have been emphasized and the number of women who nurse their children for at least some fraction of the daily intake has increased, particularly during the first few months after birth. Although this population of women is generally healthy, it is not rare for them to have medical problems for which diagnostic radionuclide studies would ordinarily be a routine part of the work-up. An issue of radiation protection thus arises concerning the breast feeding child. With a few recent exceptions the literature on this has consisted largely of case reports in which breast milk activity was measured following diagnostic radionuclide studies, and recommendations were made regarding the safe resumption of nursing, frequently without any explicit consideration of target organ dosimetry. With this as a background, we attempted to summarize the existing literature and derive from it a more uniform and objective approach to the problem (*1*). We hoped that further work would validate our method and refine our recommendations.

We have thus read with interest and would like to comment upon the recent case report by Dydek and Blue regarding breast milk excretion of iodine-131 (^{131}I) following diagnostic and therapeutic doses at $Na^{131}I$ (*2*). In this article, Dydek and Blue recommended that ^{123}I administration should be avoided in those patients who wished to resume nursing. In our article, which discussed many different radiopharmaceuticals, we had recommended a 3-day cessation of nursing following the administration of pure ^{123}I. We would like to consider the controversy which has developed over the use of $Na^{123}I$ as an alternative for diagnostic studies in nursing women (see References *3* and *4*, and Letters to the Editor in this issue of the Journal).

The long-term data provided by Dydek and Blue clearly document that there is a second slow component to the effectively biexponential disappearance of ^{131}I from breast milk after administration of $Na^{131}I$. We anticipated this from older metabolic data which indicate that plasma iodide reaches a near constant level at about 1 wk after administration of $Na^{131}I$ to the nonlactating individual (*5*). Our analysis ignored breast milk elimination and it is not unexpected that the effective half-life in breast milk of 5.9 days found by Dydek and Blue is significantly less than the physical half-life which we assumed with our "worst case" approach. The implications of this are no different, however, since it is still necessary to withhold nursing for an impractical 40 days if the same maximum permissible dose (MPD) of 150 mrad to the child's thyroid is accepted.

In view of their apparent confirmation of our basic assumptions, we were initially surprised to note the very discrepant opinion of Dydek and Blue regarding $Na^{123}I$. This caused us to reconsider our own analysis, and we wish to modify our previous recommendation for this agent and concur with the conclusion of the above authors. Although we were aware that current preparations of $Na^{123}I$ necessarily include iodine-124 (^{124}I) as a contaminant, we did not calculate for its contribution. Our data was essentially based upon pure ^{123}I with a slight adjustment to the dose factor, D. We used the physical half-life of ^{123}I for the effective half-life in breast milk. This is invalid for ^{123}I which contains impurities of ^{124}I or ^{125}I. It fails to correct for the much longer half-life and larger target organ dose of ^{124}I which persists in breast milk well after the contribution of ^{123}I becomes relatively insignificant from a dosimetric point of view. In fact, if we properly apply our model to impure ^{123}I containing 5% ^{124}I, all we really need to consider is the ^{124}I contaminant itself.

Since the biologic half-life of ^{124}I should be no different than that of ^{131}I, we can use the value of 21.9 days calculated by Dydek and Blue together with the physical half-life of ^{124}I (4.2 days) to derive an effective half-life in breast milk of 3.5 days. In Dydek and Blue's paper two discrepant infant dose factors of 10.3 and 36 rad/μCi of ^{124}I were cited.

For this reason, we performed our own calculations for the dosimetry to the thyroid pertaining to ingestion of various iodine radioisotopes in breast milk consumed by a new born infant. We obtained values of 0.43 rad/μCi for ^{123}I, 25 rad/μCi for ^{124}I and 35 rad/μCi

for ^{125}I. The results are dependent upon the assumptions utilized in the calculations. Nevertheless, these values are in reasonable agreement with those given by Hedrick.

If we apply our formula using the lower value given by Dydek and Blue together with an effective half-life of 3.5 days, a volume of 1,500 ml breast milk/day, and an MPD to the thyroid of 150 mrad, then we derive a value of 1.9×10^{-6} μCi/ml as the breast milk concentration of activity at which nursing may safely resume. We can use Dydek and Blue's data to estimate when this concentration would be achieved after a 30 μCi dose of ^{123}I containing 5% or 1.5 μCi of ^{124}I. Over the first 3 days, breast milk excretion of ^{124}I will occur at or about the same rate as ^{131}I, since the first component of its biexponential elimination from breast milk is almost completely determined by the biologic half-life (11.8 hr, according to Dydek and Blue) which is much shorter than its physical half-life. From Table 2 in Dydek and Blue's paper, it is noted that at 3 days following the administration of 9.6 mCi of $Na^{131}I$, breast milk concentration is 1.69×10^{-1} μCi/ml or 1.76×10^{-5} of the administered dose on a μCi/ml basis. By proportionality it is to be expected that breast milk concentration will be 2.6×10^{-5} μCi/ml at three days following 1.5 μCi of $Na^{124}I$. The latter is ~14 times the previously calculated concentration at which nursing can safely resume. With an effective half-life of 3.5 days, this level would be reached in another 10-14 days. Not unexpectedly this is in agreement with Dydek and Blue since they used the same daily milk volume and MPD which we assumed, and we have accepted their biologic half-lives as reasonable estimates of reality.

We also performed a more precise calculation using the equation for the clearance of radioiodine from the mother given by Dydek and Blue and the highest dosimetry values. We based the results upon limiting the dose to the infant thyroid below 0.150 rad and used integral calculus to solve the equations for a 30 μCi administered dose of ^{123}I. For a consumption of 850 ml/day of breast milk, the data indicate that a 16-day delay for a 4.9% contamination of ^{123}I with ^{124}I and a 91-day delay for a 1.9% contamination of ^{123}I with ^{125}I would be required.

Although there may be some individual variation in biologic half-life this is unlikely to be of practical importance with respect to the conclusions under consideration here. The long physical half-life and high dose factor of ^{124}I dominate the calculations. It is also worth noting that we have considered ^{124}I contamination of ^{123}I to be 5%, which is essentially the value at the time of calibration. This is a minimum value which assumes that the dose is administered at that time. If administration is delayed, as will undoubtedly be the case for logistical reasons, the percentage of ^{124}I will increase to as high as 12.9% at the time of expiration (package insert for $Na^{123}I$, Medi-Physics, Inc., Richmond, California, 1986).

Hedrick et al. have argued that nursing may resume at 1.5 to 3 days following administration of diagnostic doses of $Na^{123}I$ but they initially ignored the contribution of ^{124}I (*3*). Subsequently they claimed to have reached the same conclusion after making allowances for this oversight (*4*). However, their only reasoning in support of this is a dosimetric analysis of ^{124}I which is only peripherally relevant. They never considered the kinetics of ^{124}I excretion in breast milk, implying that it follows a monoexponential disappearance similar to that which they erroneously postulated for ^{123}I because their data collection was too short to appreciate the second slow component. The latter cannot be ignored with ^{124}I and ^{131}I because of their long half-lives and high dose factors.

More recently, Hedrick et al. have criticized Dydek and Blue's model as greatly overestimating the activity in breast milk (see Letters to the Editor in this issue of the Journal). However, the analysis which Hedrick et al. provide in support of this uses the activity concentration obtained from daily volumes of 100 ml of breast milk. It is unknown whether these 100 ml aliquots were the full extent of this woman's daily milk supply. Since she was merely pumping her breasts and not actually nursing, it is unlikely that she was producing anything close to 1,500/day which is as much, if not more, than any woman makes when breast milk is the exclusive source of nutrition. It is therefore not legitimate to assume, as Hedrick et al. have done, that the cumulative excretion of Dydek and Blue's patient could be estimated by extrapolating the activity concentration of 100 ml aliquots to a daily volume of 1,500 ml. One can criticize Dydek and Blue (and our own reanalysis) for the same thing. In effect, we are calculating a safe activity concentration for an hypothetical individual who

is making 1,500 ml of breast milk a day, and then estimating when this concentration would be reached based on the time-activity relationship of someone who is undoubtedly making significantly less milk. The rationale for this approach is to provide a conservative guideline for someone whose volume might be close to 1,500 ml/day but whose activity concentrations are unknown. Unfortunately, the latter cannot, at any given time, be assumed to be the same as those of an individual making less milk. However, the volume factor in the equation we are using can be adjusted so that the calculated safe activity concentration more accurately reflects the daily milk production of the particular women whose milk activity is actually being assessed. Dydek and Blue have done this for their patient using several assumed daily milk volumes and the dose factor suggested by Hedrick et al. (see Letters to the Editor in this issue of the Journal). It is notable that even if their patient produced only 100 ml/day, nursing should not resume for 7 days following a 30-μCi dose of $Na^{123}I$ containing 4.8% ^{124}I.

We thus concur with Dydek and Blue that our original recommendation for resuming nursing following radioiodine uptakes with $Na^{123}I$, was inappropriate. Our publication was primarily directed towards presenting a systematic and quantitative approach for the determination of the period of time during which nursing should be discontinued following the administration of various radiopharmaceuticals to the mother. Most of the discussion pertained to technetium-99m radiopharmaceuticals. For radioiodine, our recommendations were essentially based upon the administration of pure ^{123}I; the inclusion of ^{124}I activity necessitates a significant modification to the analyses and much longer delays. It is worth pointing out that an 8-day abstinence from nursing following 0.1 μCi of ^{131}I is itself rather inconvenient. In the final analysis, one has to wonder whether there is ever a need to perform radioiodine uptakes in this context. Hyperthyroidism and thyroiditis can be reliably diagnosed using pertechnetate imaging in combination with clinical criteria and plasma hormone levels. Although some would argue that a radioiodine uptake is necessary for quantitating the treatment dose of ^{131}I in cases of hyperthyroidism, the uptake dose and agent then become irrelevant because nursing will have to be discontinued in any case when treatment is administered. It is our conclusion, therefore, that radioiodine studies of the thyroid should not be performed in women who wish to continue breast feeding. When radionuclide evaluation of the thyroid is deemed essential, technetium-99m pertechnetate is the preferred agent.

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