Re: Risk of Thyroid Cancer After Exposure to $^{131}$I in Childhood

Cardis et al. (1) carried out a population-based, case-control study of thyroid cancer in Belarus and the Russian Federation after exposure to radioactive iodine (mainly $^{131}$I) and other radionuclides released during the 1986 Chernobyl accident. A linear no-threshold dose–response relationship for relative risk (RR) [estimated via odds ratio] was stated to be found for radiation doses up to 1500–2000 mGy for persons younger than 15 years of age at the time of the accident. This correspondence provides reasons to doubt the reliability of this conclusion about the linear no-threshold dose–response relationship.

Relative risk was evaluated relative to a reference dose interval of 0–15 mGy. Thus, there was no true unexposed group! Also, because dose estimates have large errors (2), some doses listed as 0–15 mGy may be much larger. For the dose interval of 16–199 mGy, I calculated a crude odds ratio of 1.303 (95% confidence interval = 0.736 to 2.307) relative to the interval 0–15 mGy. The indicated odds ratio was not statistically significantly greater than 1 ($P = 0.439$) and its lower 95% confidence limit of 0.736 was consistent with the possibility of a hormetic response.

The implied excess relative risk function used by Cardis et al. (1) for doses up to 1500–2000 mGy was

$$RR_{LNT} = 1 + \beta d, \quad \text{for } d \geq 0, \quad [1]$$

where $RR_{LNT}$ is the relative risk based on the linear no-threshold model, $d$ is the absorbed radiation dose, and $\beta$ is the excess relative risk per unit dose. The study design used by the researchers did not allow them to distinguish between $RR_{LNT}$ and relative risk according to a new hormetic relative risk ($RR_{HRR}$) model (3), where

$$RR_{HRR} = 1, \quad \text{for } d = 0, \quad \text{and}$$

$$RR_{HRR} = (1 - PROFAC)RR_{LNT}, \quad \text{for } d > 0. \quad [2]$$

after low doses and dose rates, because there was no unexposed group. The protection factor (PROFAC) takes on values from 0 to 1, depending on the proportion of cancer cases prevented due to radiation hormesis. The standard incidence ratio introduced by Ivanov et al. (4) in characterizing a hormetic dose–response curve for the incidence of solid cancers among nuclear workers (liquidators) who participated in recovery operations after the Chernobyl accident corresponds to (1 – PROFAC). A similar hormetic curve was reported for cancer mortality among Chernobyl accident emergency workers (5). From the study design of Cardis et al. (1), both $RR_{LNT}$ and $RR_{HRR}$ would be found to be consistent with the data. Thus, the data used did not confirm a linear no-threshold dose–response relationship over the indicated dose interval.

There is also a problem with the way Cardis et al. (1) implemented their nonlinear modeling that involved the term $\gamma d^2$ both in linear and exponential forms. Unfortunately, $d$ in these models cannot simply be replaced with $E(d)$ when evaluating $E(RR)$. The notation $E(\cdot)$ represents a dose group–specific average. Thus, $E(d)$ and $E(RR)$ are dose group–specific averages of $d$ and $RR$, respectively. For the linear form, one has to replace $d^2$ with $E(d^2)$ not $E(d)^2$ as was used. For the exponential form, the solution is more complicated. Thus, conclusions that were based on their nonlinear modeling may also not be valid.

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REFERENCES


NOTES

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