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ПИСЬМА В РЕДАКЦИЮ

COMMENT ON JOURDAIN ET AL. ARTICLE "IS EXPOSURE TO IONIZING RADIATION ASSOCIATED WITH CHILDHOOD CARDIAC ARRHYTHMIA IN THE RUSSIAN TERRITORIES CONTAMINATED BY THE CHERNOBYL FALLOUT? A CROSS-SECTIONAL POPULATION-BASED STUDY"[1]

© 2020 г. R. I. Goncharova*

Institute of Genetics and Cytology of the National Academy of Sciences of Belarus, Minsk, Republic of Belarus

**E-mail: R.Goncharova@igc.by*

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The aim of the article of Jourdain et al., was "to investigate childhood cardiac arrhythmia (CA) and chronic exposure to caesium-137 (^{137}Cs) resulting from the Chernobyl accident" in order to reply to question "Is exposure to ionizing radiation associated with childhood cardiac arrhythmia in the Russian territories contaminated by the Chernobyl fallout?".

Jourdain et al. conducted a prospective cross-sectional study which provided data on the entire population under study, namely a total of 17 697 children living in the Bryansk area since May 2009 to May 2013.

Analysis of cross–sectional data usually consists of comparing the differences between the subgroups (representative subsets) at a definite point of time, namely "exposed" children (8816 children living in heavily contaminated territories, 4 regions with ^{137}Cs deposition levels >555 kBq/m^2 or 15 Ci/km^2) and "unexposed" children (8881 children living in weakly contaminated, so called control, territories, 6 regions with ^{137}Cs deposition levels <37 kBq/m^2 or 1Ci/km^2). So, children were selected for this study on the basis of ^{137}Cs soil deposition of the Bryansk area.

For comparing the differences among representative subsets one usually use the odds ratio (OR) and logistic regression. OR is defined as the ratio of the odds of A (cardiac arrhythmia) in the presence of B (heavily contaminated territories) and the odds of A (cardiac arrhythmia) without the presence of B (weakly contaminated territories). For estimation of probability of CA occurrence depending on radiation contamination, the OR and logistic regression were used by Jourdain et al. OR is a measure of strength of association between CA and variable factor (heavily or weekly contaminated territories).

CA was diagnosed in 2526 children of entire population, including 1172 children living in heavily contaminated territories (13.3%) and 1354 children living in so called control territories (15.2%). The difference is statistically significant. So, the CA frequency in heavily contaminated territory was significantly lower than those in weakly contaminated one.

OR for dichotomous variables (heavily and weakly contaminated territories) = 0.85 (95% CI is 0.78 to 0.93, $p < 0.01$), table 2 of the article. Multivariate logistic regression model gives OR = 0.90 (95% CI is 0.81 to 1.00, $p = 0.06$), table 3 of the article. On this bases, Jourdain et al. make conclusion: "This study does not observe an association between CA and ^{137}Cs deposition levels in the Bryansk region exposed to the Chernobyl fallout".

But it is necessary to take into account that only 1891 children have detectable ^{137}Cs whole-body burden (21.45%) among 8816 children living in heavily contaminated territories while only 1214 children have detectable ^{137}Cs whole-body burden (13.67%) among 8881 children living in weakly contaminated territories. So, majority of children (75.5–86.3%) has not ^{137}Cs burden. That is why children living in heavily contaminated territories cannot be considered as "exposed" children and children living in weakly contaminated territories cannot be considered as "unexposed" children. ***Only children having*** ^{137}***Cs burden can be considered as radiation-exposed individuals.*** Furthermore, CA was diagnosed in children with/ without detectable ^{137}Cs whole-body burden, irrespective on the residence region. Consequently, ***to reveal the association between CA and radiation exposure, it is necessary to calculate OR for children diagnosed with CA among children with detectable*** ^{137}***Cs burden who live in both highly/weakly contaminated territories.***

Jourdain et al. did not fulfil this essential condition and, as a consequence, the conclusion "This study does not observe an association between CA and ^{137}Cs deposition levels in the Bryansk region exposed to Chernobyl fallout" is not considered as valid inference for assessment of link of radiation exposure with CA.

[1] BMJ OPEN. 2018.8. E019031. DOI:10.1136/BMJOPEN-2017-019031.

Table 1. Frequency of children with ^{137}Cs burden among patients diagnosed with cardiac arrhythmia depending on the residence region

Subgroups	Cardiac arrhythmia	Frequency of individuals with Cs		OR [95% CI]
	n	*n*	%	
heavily contaminated	383	100	26.11*	2.03[1.49–2.66]
lower contaminated	696	103	14.80	

* Significant at p-value = 9.8E-6 (Fisher's exact test)

Detectable ^{137}Cs whole-body burden is considered as real radiation exposure of children. OR calculated for dichotomous variables (not detectable ^{137}Cs burden and detectable ^{137}Cs burden (Bq/kg) was categorised into quartiles) varied in the range 0.84 to 1.37 (table 2 of the article) for heavily and weakly contaminated territories. Multivariate logistic regression model gives OR in the range from 0.96 to 1.07 (table 3 of the article). Since "for ^{137}Cs whole-body burden, the ORs close to 1 did not reach statistical significance" Jourdain et al. concluded that "there was no evidence of any association between the presence of CA and ^{137}Cs burden".

But it is necessary to take in mind that subgroup of 8816 children living in heavily contaminated territories consisted of 1891 persons with detectable ^{137}Cs burden and 7925 without ^{137}Cs burden, while subgroup of 8881 children living in weakly contaminated territories consisted of 1214 persons with detectable ^{137}Cs burden and 7667 children without ^{137}Cs burden. So, CA was diagnosed in children with/without ^{137}Cs burden of two studied subgroups. Important feature of the entire population as well as two subgroups of the population is following: occurrence of CA among children with and without detectable ^{137}Cs whole-body burden.

That is why for elucidation of an association between CA and the level of ^{137}Cs burden it is necessary to make following: to calculate the odds of A (cardiac arrhythmia) in the presence of B (detectable ^{137}Cs burden), to calculate the odds of A (cardiac arrhythmia) without the presence of B (not detectable ^{137}Cs burden) and then to calculate the ration of both odds.

Jourdain et al., did not fulfill this essential condition and, as consequence, the conclusion " there was no evidence of any association between the presence of CA and caesium burden" is not considered as valid inference for assessment of link of radiation exposure with CA in heavily and weakly contaminated territories. ***According to the principles of radiation biology, to elucidate the role (contribution) of ionising radiation in any biological alterations it is necessary to study these alterations in irradiated individuals.***

Unfortunately, the set of primary data concerning of ^{137}Cs burden and the presence of CA was not shown in the pdf version of article and the online supplementary index. It is possible to find such data only for subgroup of children with CA who had blood test (table B in the online supplementary index). CA were diagnosed in 383 children living in heavily contaminated territories (4.34% of 8861 children) and 696 children living in weakly contaminated territories (7.84% of 8881 children). The quantity of children with detectable ^{137}Cs burden was 100 (14 + 24 + 24 + 38) for heavily contaminated territories and 103 (45 + 28 + 17 + 13) for weakly contaminated territories.

The frequency of children with ^{137}Cs burden among patients diagnosed with cardiac arrhythmia is twice as high at the heavily contaminated territory as compared to weakly contaminated one (Table 1).

OR calculated indicate strong link between the occurrence of CA and frequency of children with caesium burden. Note, that mean value ^{137}Cs burden among children with detectable ^{137}Cs burden was 80.5 (20.1–814.0) and 44.6 (19.6 –121.5) Bq/kg in two residence regions respectively (table B in the online supplementary index).

But it is well known that cross-sectional data cannot be used to infer causality between cardiac arrhythmia, and variable factors (level of territory contamination or ^{137}Cs burden) because temporality is not known.

Additionally, primary data collected by Jourdain et al. gives possibility to determine causal link between radiation exposure due to ^{137}Cs burden and occurrence of CA. For this it is necessary to make analysis dose-response relationship for subgroup of 3105 radiation exposed children. Presence of dose-dependent increase of CA provides a demonstration of radiation-induced CA.

In accordance with the remarks above, it should be argued that conclusions of Jourdain et al. about the absence of an association between occurrence CA and ^{137}Cs deposition levels as well as between occurrence CA and ^{137}Cs burden in the Bryansk region exposed to the Chernobyl fallout are not sufficiently substantiated.