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MULTIPLE MYELOMA AMONG CHORNOBYL ACCIDENT CLEAN-UP WORKERS – STATE AND PERSPECTIVES OF ANALYTICAL STUDY

The objective of the study was to analyze the Multiple Myeloma (MM) incidence in clean-up workers preparing the information background for consequent analytical study with a dose-dependent risk estimates.

Materials and methods. The Cohort Database was linked to the Ukrainian National Cancer Registry to identify the MM cases in a cohort of 152 520 male clean-up workers.

Results. The 64 MM cases were identified in the studied Cohort for the 1987-2012 period. Fifty-eight of them were included to the preliminary incidence analysis accounting for the 10-years lag-period. According to the preliminary data analysis the MM incidence rate in studied clean-up workers Cohort did not exceed the corresponding rate in general population of Ukraine along the 21 years after the catastrophe.

Conclusions. Standardized incidence ratio for the 2008–2012 period, that is 22–26 years after the accident, demonstrated the significant excess of MM incidence among male clean-up workers in comparison with general population of Ukraine of corresponding age and gender (SIR 1.61, 95% CI 1.01;2.21).

Key words: Chernobyl accident, clean-up workers, multiple myeloma, incidence.

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Множинна мієлома серед учасників ліквідації наслідків Чорнобильської аварії. Стан і перспективи аналітичного дослідження

Мета: проаналізувати захворюваність на множинну мієлому (ММ) серед учасників ліквідації наслідків Чорнобильської катастрофи (УЛНА) та підготувати інформаційну основу для подальшого аналітичного дослідження дозозалежних ризиків цієї патології, враховуючи її потенційну радіаційну зумовленість.

Матеріали і методи. Для ідентифікації випадків ММ у досліджуваній когорті УЛНА чисельністю 152 520 осіб чоловічої статі був проведений лінкідж бази даних когорти з інформаційним масивом Національного канцер-реєстру України.

Результати. За досліджуваний період (1987–2012 рр.) було ідентифіковано 64 випадки, 58 з яких були включені до попереднього аналізу захворюваності, враховуючи 10-річний лаг-період. За результатами попереднього аналізу захворюваність на ММ у досліджуваній когорті УЛНА не перевищувала характерний для загального населення рівень протягом перших 21 років після аварії.

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Висновок. Розрахунок стандартизованого співвідношення захворюваності (SIR) за період 2008–2012 рр., тобто через 22–26 років після аварії, продемонстрував достовірне перевищення рівня серед УЛНА порівняно зі спонтанним популяційним рівнем для населення України чоловічої статі (SIR 1.61, 95% CI 1.01;2.21). Після проведення незалежної діагностичної експертизи всіх ідентифікованих випадків, реконструкції отриманої дози зовнішнього опромінення на червоний кістковий мозок за методом RADRUE будуть проаналізовані дозозалежні ризики виникнення ММ з урахуванням можливого модифікуючого впливу інших факторів.

Ключові слова: Чорнобильська аварія, ліквідатори, множинна мієлома, захворюваність.

Проблеми радіаційної медицини та радіобіології. 2013. Вип. 18. С. 169–172.

Multiple Myeloma (MM) is a cancer originating from terminally differentiated B lymphocytes with predominant presentation in male population and substantial incidence increase with aging.

The exact aetiology of MM remains unclear. Suggestions of an association between MM and exposure to radiation are controversial. No evidence of an excess risk for MM was observed among the Life Span Study cohort of atomic bomb survivors (1950–2001) [1]. However, the MM incidence was higher among nuclear industry workers than in the general population. Borderline significant association for MM is published as a result of the 15-Country Collaborative Study of Cancer Risk among Radiation Workers [2]. Also the study that was completed by IARC in 1995 and involved nuclear workers from facilities in the USA, UK and Canada found the statistically significant, though weak, dose-related association for MM [3]. Similar results were reported in the studies performed in separate countries among workers of the facilities with radiological hazards. A significant effect of age at exposure, with positive association between MM and low level doses of external irradiation received at older ages was shown among nuclear workers at US Department of Energy facilities [4]. Weak statistically significant association between internal uranium dose and MM risk was shown among workers at Oak Ridge Gaseous Diffusion Plant [5]. In French nuclear workers cohort an excess of borderline statistical significance for MM was observed [6].

At the same time several recent studies have shown contradictory results of no excess of Multiple Myeloma (a Case-Cohort Study in Czech Uranium Miners [7], a Study on risk of treatment-associated leukemia and multiple myeloma in patients treated with pelvic radiotherapy [8]).

Thus, we have the lack of evidence for increased risk of MM after irradiation, especially among those irradiated in young or middle age. It is not clear what is the influence of possible risk modifiers like time since exposure, age at exposure, and effects of combined exposure to negative factors other than radiation.

The aim of the study was to analyze MM incidence in a cohort of 152520 male clean-up workers in 1986–2012 preparing the information ground for consequent case-control study with a dose-dependent risk estimates.

MATERIALS AND METHODS

Forming of the Information base for MM risk assessment in Chernobyl clean-up workers was started in a framework of the Ukrainian-American case-control study on Leukemia and other hematological disorders in a cohort of 110 645 male clean-up workers resided one of 5 oblasts of Ukraine or Kiev city [9, 10]. The study covered the period of observation 1986–2006 and was aiming to assess leukemia risks after exposure to ionizing radiation during emergency and clean-up activities after the Chernobyl catastrophe in 1986–1990.

Data on Multiple Myeloma cases were collected accounting for their potential radiosensitivity the same way as on Leukemia ones. Cases were identified with data linkage between the Cohort DB and the data pool of all incident cases in general male population of corresponding age and the oblasts of residency diagnosed and treated in the local and state hematological departments in 1986–2000. For the period 2001–2006 the Cohort DB was linked to the Ukrainian National Cancer Registry (NCRU) DB. Each of the identified cases went through the diagnosis verification procedure by the independent Diagnostic Review Panel of qualified hematologists and hematopathologists from the USA, France, United Kingdom and Ukraine [9, 11].

Clinical data for each case and biological material samples (peripheral blood, bone marrow or trepanobiopsy) for most of them were presented at the Review to confirm or clarify the diagnosis. The Panel's consensus opinion was the Review conclusion. 25 identified MM cases were sent for the review, 20 of them were confirmed. Diagnoses in 2 cases were considered to be doubtful only due to the lack of diagnostic material samples resulting from the distant period of diagnostics. This high confirmation rate was achieved due to the thorough preliminary diagnostic data search and review completed by local hematologists as well as the specialists of the National Research Center for Radiation Medicine.

Table 1
Distribution of the cohort members by region of registration in the State Chernobyl Registry

Region (oblast)	Cohort as of 01.01.2001 (subjects #)	Cohort as of 01.01.2007 (subjects #)
Dnipropetrovska	19 162	20 248
Donetska	–	22 334
Kyivska	21 114	26 303
Kharkivska	17 073	17 650
Cherkasska	11 546	12 801
Chernihivska	12 630	13 411
Kyiv city	29 120	39 764
Total	110 645	152 520

To estimate realized MM risks among clean-up workers, we had to know the doses of radiation exposure for all study subjects: the identified cases and selected controls matched by age and oblasts of residency. For retrospective dose reconstruction we used the time-and-motion RADRUE method which was developed for studies of the Chernobyl accident consequences by the international group of experts from Ukraine, Russia, and the USA [12]. This method uses the results of personal interviews of clean-up workers conducted with a special questionnaire collecting the data on history of their exposure (including place, period, duration of clean-up work and residence in the 70-km zone around the Chernobyl NPP). Combining these data with information on the radiation fields within a specialized computer code the expert-dosimetrist reconstructs the individual dose to red bone marrow (RBM) due to subject's external exposure. The questionnaire included questions about subject's exposure to negative factors other than radiation besides the dose related items. These data also were included in the analytical risk model.

Dose values were estimated for 17 of 20 cases with confirmed diagnoses. RBM dose due to external irradiation was in the range of 0.12–2920 mGy. Enormous range of individual doses makes risk analysis unreliable with respect to a low number of cases. Received MM risk estimates based on the 17 cases data and selected controls (matched by age and oblast of residency) were not stable and did not allow getting univocal conclusion on the value of MM risk excess in the

clean-up workers cohort if any existed. It initiated amendment of the study Cohort and extension of the observation period in order to get meaningful results.

The Cohort was extended accounting for late registered clean-up workers and for those resided Donetsk oblast. New Cohort composed 152520 persons in total (Table 1).

RESULTS AND DISCUSSION

To achieve the completeness of Multiple Myeloma cases diagnosed in the study Cohort a new linkage of the extended Cohort DB and the NCRU DB restricted to the males only was performed. Minimizing the potential losses we did not apply other criteria like the year of diagnosis and the year of registration, regardless of possible duplication or excessive information for the period 1986–2006. The correctness of the decision to perform a repeated linkage was confirmed by the obtained linkage results. Over the previously studied period 10 additional cases were identified. In the whole study period (1986–2012) the 64 MM cases were identified. 58 of them were included in the preliminary SIR analysis. Six cases were not included accounting for their occurrence during the lag period (10 years after the accident).

According to the preliminary data analysis MM incidence rate in the studied clean-up workers

Table 2
Standardized MM incidence ratio* in the Cohort of male clean-up workers in 1996–2012

Period of observation	Cases number		SIR (95 % CI)
	observed	expected#	
1996–2001	13	13.2	0.98 (0.45; 1.52)
2002–2007	17	15.7	1.08 (0.57; 1.60)
2008–2012	28	17.4	1.61 (1.01; 2.21)
1996–2012	58	46.3	1.25 (0.93; 1.58)

Note. * – age specific rates for the male population of Ukraine for each year of the study period used as a standard;

– sum of the expected cases for each year of the study period.

Cohort did not exceed the corresponding rate in general population of Ukraine along the 21 years after the catastrophe. Standardized incidence ratio for the period 2008–2012, that is 22–26 years after the accident, demonstrated the significant excess of the MM incidence among male clean-up workers in comparison with general population of Ukraine of corresponding age and gender (SIR 1.61, 95% CI 1.01; 2.21) (Table 2).

CONCLUSIONS

After the independent diagnostic review of the additionally identified cases, selection of the age and residency matched controls, the dose dependent MM risk analysis will be performed taking into account possible effect of factors other than radiation. There is a possibility of the certain corrections of the risk estimates after the additional extension of the study period

The planned amount of research will contribute to new knowledge about reliable values of the Multiple Myeloma risk under the prolonged exposure to low and medium doses of radiation.

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