Cancer Risk in HBRAs in Yangjiang, China, and in Karunagappally, India

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INTRODUCTION

There are several high-background radiation areas (HBRAs) in Yangjiang of Guangdong Province, China, and Karunagappally of Kerala State, India. In order to evaluate the health effects of high natural radiation, epidemiological studies have been conducted by local scientists. Currently, these studies are continued with the help of Japanese researchers. In this paper, their results will be reviewed.

In Yangjiang, China, there are two HBRAs, i.e., Tongyou and Dong-anling, located in the west and east of Yangjiang area, respectively. In the 1970s, Dr L.X. Wei and his colleagues started the cancer mortality study among the residents in those HBRAs and its neighboring control areas selected from two counties, Enping and Taishan (1). The major results obtained from their study were published in 1980 (1). In 1991, a collaborative study involving Chinese and Japanese research groups began. The study groups in the two countries are led by Drs. L.X. Wei and T. Sugahara, respectively (2). This international collaborative study has two new features. First, the study group established a fixed cohort whose members resided in the HBRA and the control areas as of 31 December 1986. Second, the control area was restricted to the one in Enping County, which shares its eastern border with Yangjiang City, the political and economic center of Yangjiang area. The study area excluded from the new study was the control area in Taishan, which is located to the east of Enping and is 300 kilometers away from Guangzhou City, the capital of Guangdong Province (3). Recently, they conducted a series of case-control studies in order to evaluate the confounding effects of life styles and other factors on the radiation-related risk estimation of leukemia, and cancer of the lung and nasopharynx. The results obtained from the study on nasopharyngeal cancer were published, recently (4).

In the south-western part of Indian subcontinent, there is an HBRA in Karunagappally Taluk of Kerala State, India. In view of radiation levels and population sizes, this area is one of the most important HBRAs in the world. The taluk, consisting of 12 districts or panchayat, has the population of about 400,000 or about 70,000 families according to 1991 census. The radiation levels are particularly high in the taluk's coastal area. In Karunagappally, the research group led by K Nair conducted an enormous work, including questionnaire survey of every resident in the taluk (5,6). One of the advantages of this area is the existence of tumor registry established in 1990. Cancer incidence obtained from the registry was published in the Cancer Incidence in the Five Continents (7). In 1999, a collaborative study involving Indian and Japanese research groups started.

MATERIALS AND METHODS

Yangjiang Study in China: In each hamlet, outdoor gamma exposure doses were measured in the roads, meeting places, farmland and so on. Indoor doses were also measured in randomly selected houses, accounting for one-third of all houses in a hamlet (8). Mortality data for 1970-1978 were collected in a retrospective survey and data for 1979-1986 were obtained by means of a prospective survey of a dynamic population. The data for 1987-95 were obtained by the follow-up study of a fixed cohort whose members resided in the HBRA and the control areas as of 31 December 1986. In mortality surveys, village doctors, selected by the Yangjiang study task group, collected demographic information for subjects in their own villages and filled out the Health Household Registry form for each subject. Yangjiang study task group, consisting of three physicians from the Guangdong Institute for Prevention and Treatment of Occupational Diseases, visited each village once a year to check the HHR records, interviewed family members of the deceased and village doctors to collect information about the cause of death. They also visited all county hospitals in the study areas and major hospitals in the province to extract relevant medical information from the records. On the basis of information collected in this way, they determined causes of death and coded them according to the ninth revision of the International Classification of Diseases and Injuries. In the mortality risk analysis, the study subjects in the HBRA were divided into three dose groups based on the environmental dose-rates per year, and relative risks (RRs) were calculated to compare cancer mortality between each of the three radiation dose areas in the HBRA and the control area, using Poisson regression models. The study group conducted case-control studies nested in their cohort in order to evaluate the confounding effects of life styles and other factors on the radiation-related risk estimates. In a matched case-control study of nasopharyngeal cancer for the period of 1987-1995, two controls were randomly selected for each case from those who died from causes other than malignancies and external causes (4). Cases and their controls were matched with respect to sex and the years of birth and death (±5 years). Four trained interviewers interviewed study subjects' next-of-kin using a standardized questionnaire and collected information on socioeconomic status, dietary habits, tobacco smoking and alcohol consumption, disease history, pesticide use, medical X-ray exposure, the family history of NPC and so on.

Karunagappally study in Kerala, India: Cancer incidence data were obtained by the tumor registry established in 1990. Indoor and outdoor radiation dosimetry data were obtained from all the houses in the taluk, numbering 74,478 using plastic scintillometer. Radon and thoron levels were also measured. A questionnaire survey was conducted to collect information on life styles of all the residents in the taluk (5,6). However, questions regarding medical exposure and details history of addresses were not included in the questionnaire.

RESULTS

Cancer mortality in the HBRA of Yangjiang was slightly lower than that in the control area during the period between 1970 and 1978 (1). In their recent analysis, the data for 1970-1978 were not used because they had not been computerized. The results of the cancer mortality study during the period 1979-1990 were presented at the 4th International Conference on High Levels of Natural Radiation held in Beijing in 1996. There was no difference in cancer mortality in the HBRA and the control areas (9). The relative risk comparing the HBRA and the control area was 1.00 (95% confidence interval, 0.86 to 1.15). The most recent report of the Yangjiang study, which observed 125,079 subjects, accumulated 1,698,316 person-years, and identified 1,003 cancer deaths during the period 1979-95, concluded cancer mortality in the HBRA was almost the same as that in the control area. Site-specific analyses did not find any cancer mortality differences in the HBRA and the control area (10). They also reported the excess relative risks per unit radiation dose of solid cancer for the period 1979-1995, assuming a linear dose-response relationship and using indirectly estimated individual dose (11). Their relative risk estimates might have been diluted by the effects of factors other than radiation since almost half of cancer deaths in their mortality data were cancers of the liver and nasopharynx, in which viral infection plays major etiological roles. The study group also evaluated potential confounding effects of various factors including life styles. Results obtained from a case-control study of nasopharyngeal cancer showed that the effects of life styles on radiation-related risk estimates were negligible (4).

Although the lifetime cumulative dose of children is low, childhood cancer mortality is of concern because children and fetuses are considered to be more sensitive to radiation than adults. During the period between 1979 and 1986, there were 10 and 3 leukemia deaths among the children aged under 15 living in the HBRA and the control area, respectively. On the other hand, there were 11 and 1 deaths from childhood cancer other than leukemia in the HBRA and the control area, respectively. The relative risk estimates obtained from Poisson regression analysis comparing the mortality risk in the HBRA and the control area were 1.1 (95% confidence interval=0.3-4.8), 3.4 (95% confidence interval: 0.7-62.9), and 1.7(95% confidence interval=0.6-5.7) for leukemia, cancer other than leukemia, and all cancer, respectively. None of them were statistically significant (12).

In Karunagappally study, extensive analysis is yet to be done. Their preliminary analysis showed no excess cancer incidence associated with high background radiation (6).

DISCUSSION

The average annual effective doses from the natural sources of external and internal exposures in the HBRA and the control areas were estimated to be 6.4 mSv, and 2.4 mSv, respectively (13). The chromosome aberration studies conducted by Jiang et al and Nakai et al in Yangjiang confirmed that the residents in the HBRAs were exposed to higher levels of radiation when compared to the residents in the control area (14, 15). Jiang et al examined 15 subjects from six families in the HBRA and 13 subjects from 4 families in the control area. They found that the frequency of unstable chromosome aberrations, dicentrics and rings, increased with the increase of lifetime cumulative radiation dose. They estimated that 15.4 unstable chromosome aberrations were yielded in every 1000 lymphocytes by the cumulative lifetime radiation dose of 1 Gy . Nakai et al examined 7 families including 31 members in the HBRA and 5 families including 22 family members in the control area and reported that the frequency of unstable chromosome aberrations increased by 16-18 folds for every sievert. On the other hand, as reviewed in this paper, there was no excess cancer mortality risk in the HBRA when compared to the control area. The 95% confidence interval for the prevalence of unstable chromosome aberrations associated with natural radiation does not overlap with the 95 % confidence interval for solid cancer risk associated with background radiation. These results strongly suggest that unstable chromosome aberrations do not necessarily result in elevated cancer risk.

Although the results of the Yangjiang study do not suggest any excess cancer risk associated with low-level radiation exposure, we can not totally deny the possibility of elevated cancer risk in the HBRAs that can be predicted on the basis of linear non-threshold response models. In such a circumstance, should we use the precautionary principle to avoid environmental risk and get rid of the sources of radiation exposure in the HBRAs? It may be right to do so if the exposure causes serious and irreversible health problems. Indeed, most of cancers cause fatal and irreversible health problems. However, the carcinogenic effect of radiation has a long latency period, which is 10-20 years. During a long latency period, cancer risk is affected by many factors other than radiation, including dietary habits and smoking. Actually, the effect of low-level radiation expected on the basis of a linear non-threshold response model is much lower than the risk associated with those factors, and, therefore, a small excess risk possibly inflicted by chronic low-level radiation exposure is easily compensated by healthier life styles. In that point of view, it is more cost efficient to make efforts in improving life styles of residents than in spending huge amount of money to eliminate the sources of low-level radiation exposure.

There are several major concerns regarding the epidemiological studies in the HBRAs in China and India. They are confounding effects of life styles and medical exposure, accuracy of diagnosis, migration of study subjects, and errors in individual radiation dose estimation.

1) Confounding factors: many radiation epidemiological studies ignored confounding effects of factors other than radiation, assuming that the distributions of potential confounding factors, including life styles, were not highly dependent on radiation levels. Since most of the residents in the HBRA and the control area in Yangjiang study were farmers, the Yangjiang study assumed that the socioeconomic status and life styles in the two areas did not differ greatly. Although there were no attempts to collect information on life styles from all the study subjects, the study group conducted three surveys to examine the distribution of those factors in the residents in the HBRA and the control areas. They did not find any distinct differences in life styles in the HBRA and the control area (16). According to a dosimetry survey conducted in 1986, the effective doses equivalent to inhabitants resulted from exposure to diagnostic X-rays in the HBRA and the control area were estimated to be 4.30 and 4.10 x10-5 Sv/person-year, respectively. One of the advantages of Karunagappally study in India is the fact that information on life styles of all the residents in the study area was already collected by the survey conducted in the 1990s. Unfortunately, however, information on medical exposure was not obtained in that survey.

2) Accuracy of diagnosis: in Yangjiang study, only less than a quarter of cancer diagnoses were made on the basis of pathological findings. However, we have the impression that the diagnosis of cancer itself seems reliable although the accuracy of primary cancer sites may be of concern. Further studies are necessary to validate our general impression. In Karunagappally, “death-reporting system is more or less complete” according to M K Nair et al (6). However, cause of death is unavailable in not a small number of cases. Their tumor registry will be the mainstay of cancer risk estimation. Death-certificate-only registration is 13% and the research group expects the rate to decrease over time (7).

3) Migration of study subjects: Yangjiang area is a rapidly developing area and, therefore, a sizable number of local farmers are working as temporal industrial workers in the areas other than the HBRA. That poses two major problems in the Yangjiang study, i.e., difficulties in radiation dose estimation and follow-up of study subjects. In other words, the study subjects living in the areas other than the HBRA are not exposed to high-background radiation and their exact addresses are difficult to identify.

4) Individual radiation dose estimation: in Chinese and Indian studies, individual doses of sampled subjects were measured using thermoluminescent dosimeters (TLD). However, it is practically impossible to directly measure all the residents in the study areas. Even if that is possible, it is impossible to measure a study subject’s lifetime cumulative dose. In Chinese study, the study group calculated cumulative doses for each subject based on hamlet-specific environmental doses and sex- and age-specific occupancy factors. Note here that their individual dose estimates did not take into account occupancy factors obtained from each individual or indoor doses specific for each household. They used the occupancy factors obtained from a survey of 5,291 subjects and hamlet-specific indoor and outdoor doses. In order to evaluate the errors involved in indirect dose estimation, they compared the individual doses estimated by this indirect method with those obtained from TLD measurements. The TLD-survey subjects numbered 5,204 in 88 hamlets, most of whom had also participated in the occupancy factor survey. Morishima et al (17) and Yuan et al (8) reported good correlation between the estimated and measure doses. Another drawback in their dose estimation is the fact that they used an internal radiation exposure dose common to all sex and age groups. In Indian study, individual dose estimation is also planned using a method similar to the Chinese approach.

Epidemiological studies of low-level radiation effects are complicated by the need for a large sample. For example, to detect a RR of 1.1 requires 2.36 million person-years for both the exposed and control groups (a= 5%, b= 20%). An approach to increase statistical power is to conduct pooled data analysis or meta-analysis using data from different studies. A collaborative study between Indian and Japanese research groups, started in 1999, improves the likelihood that such an approach may be possible using the Chinese and Indian data in the future.

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