ISSN: 0975-766X
CODEN: IJPTFI
Available Online through ***Research Article***
www.ijptonline.com

MULTIPURPOSE EPIDEMIOLOGICAL SURVEY OF MULTIPLE PRIMARY MALIGNANCIES AT THE TERRITORIES AFFECTED BY CHERNOBYL DISASTER

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Received on 03-06-2016 *Accepted on 27-06-2016*

Abstract:

The analysis of multiple primary malignancies was carried out during a time period spanning 30-years (from 1981-2010) in the population of the Belgorod region, which is one of the administrative territories of Russia. This region was officially designated as “less” affected by the radiations from the Chernobyl radiation disaster that occurred in 1986. The main peculiarity that was observed in the multiple primary malignant neoplasms found within the population of the Belgorod region was an explicit reduction (of approximately 5-10 years) in the development of second and subsequent metachronous tumors after treatment of the first tumor. A predominating number of synchronous tumors that were composed of multiple primary malignancies were noticeable during the so-called "rejuvenation" period of the disease even after the passage of 15 years after the devastating incident. It was assumed that these malignancies were caused due to a reduction in the biological latency of the tumors, regardless of their location, as a long-term repercussion of the “promoter” effect of the low doses of radiation due to the Chernobyl accident.

Keywords: multiple primary malignancies; Belgorod region; metachronous tumors; synchronous tumors; Chernobyl accident; low doses of radiation.

Introduction:

The problem of multiple primary malignancies (MPM) is particularly emphasized upon during the study of clinical oncology. It has been the extensively discussed in the literature throughout the history of the study of this condition (Privalov, Vazhenin, 2004; Chissov etal, 2012; Neglia, 1991). The apparent rise in the number of patients with MPM accompanied by the insufficient study and analysis of its etiology and clinical manifestations determine the urgency of this problem. A sharply increasing rate of incidence of the disease has also been reported everywhere. It rises

simultaneously with an increase in the total cancer incidence, as well as an increase in the life expectancy of patients with malignant tumors after treatment (Parshkov etal, 2011; Shimizu etal, 2003; Trivedi etal, 1999; Kazubskaya, 2007; Kovalenko etal, 2014). The growth in the morbidity of MPM is most often recorded in old aged patients (Golivets, 2012; Ionizing radiation. Source and Biological Effects, 1982).

Parallelism between the development of post-radiation complications and MPM has been traced in multiple literary sources (Spondylitis, 1999; Chissov etal, 2000; Sobin etal, 2002; Aprin etal, 2014; Parshkov etal, 2010). According to published data, the radiation does not cause visible effects in the early stages of functional and morphological changes but instead in a long-term period, which may lead to the development of malignant tumors. Moreover, according to the authors, the implementation of carcinogenic effects comes after a long period of time (5-17 years) (Sobin, Wittekind, 2002).

As per the official data sources, the latent period for certain tumors could be as long as 20 years or even more. However, the average duration is considered to be 25 years (Parshkov etal, 2009). Thus, it doesn't lose relevance and requires a detailed study of the long-term consequences of radiogenic factors in the population. Investigation of the dynamics, structure, age and gender laws on the formation of MPM affected by radiation incidents is not only an actual scientific problem but also of great interest for practical health care (Popov etal, 2011; Merabishvili etal, 2000; Davydov etal, 2011).

It is vital for a complete assessment. Efficient systematization of epidemiological indicators is required for the investigation of the issue and solving practical problems. Early detection of recurrent tumors and MPMs should particularly focus on the level of prevalence in the region and the spread and structure of tumors. The accident at the Chernobyl Nuclear Power Plant (CNPP), has created unique opportunities for the study of population-level health effects of exposure to ionizing radiations. It is clearly defined in terms of time and space of external factors such as small doses of ionizing radiation (Popov etal, 2011). Belgorod region is one of the 14 territories of Russia which were officially isolated in 1986 from the adverse radiation effects among the victims of the Chernobyl radiation disaster.

Aim of research

To study the dynamics, structure, age and gender peculiarities of the formation of multiple primary tumors in the population of the Belgorod region during the 30-years observation period (1981-2010), before and after the Chernobyl accident.

Materials required and methods

Archived data in the regional cancer registry of the Oncology Center of the Belgorod region were used for research. The analysis included 4,289 cases of morphologically verified MPMs, which were identified for the first time in a surveillance period of 30 years (1981-2010). Traditional criteria were adopted in oncology practice while registering MPMs (Grundmann, Meyer, 2012). MPMs are considered as two or more independent malignant tumors in the same patient. The prevalence and morphological structure of malignant tumors were evaluated in accordance with the sixth edited classification TNM (Nadyrov etal, 2010).

On the basis of the time of their detection an MPM is classified as synchronous (identified after an interval of at least 6 months) and metachronous (identified after an interval of more than 6 months) (Chissov etal, 2012). Primary multiple tumors recognized the "same" or "different" histological structures arising in various organs and tumors arising in the same body, but having a "different" histological structure.

The analysis of MPM incidence was based on a comparison of statistics for a five-year observation period (1981-1985; 1986-1990; 1991-1995; 1996-2000; 2001-2005; 2006-2010.) which was differentiated by gender. The incidences observed in males and females were studied separately.

The allocation of incidence rates by age groups was used as a method of calculating cumulative diseases. An analysis based on standard age groups is not entirely objective for the analysis of cancer incidence in populations. True incidence is reflected only in the age group of 0-4 years and in general for all generations (0-85 years of age and older). It was determined that each population age group has a certain number of sick persons. In fact, the distribution of cancer incidence in accordance with age groups of the population depends on the number of cases that are detected up to a certain age and, accordingly, the population that survived up to this age.

The incidence of MPMs is calculated on the basis of the number of cases of MPM that have accumulated in the population up to a certain age. Disease incidences are calculated in "gross" figures of approximately 100 thousand for the analysis of the accumulated in the population up to a certain age. Incidence rates in populations are also determined corresponding to the gender.

For example, during 2006-2010 in the Belgorod region among people of the age of 74 years or above, 290 cases of MPMs were identified in men and 374 cases in women. In this period total number of people upto 74 years of all age groups under the risk of illness amounted to 3,421,715 persons per year in males and 3,927,105 in women. Accordingly, the

"rough" indicator of cancer incidence in the age of 74 years was equal to 8.5 for men and 9.9 for women per 100,000. This indicator reflects the intensity of the disease that is accumulated to a certain age group of the population. In this case, the indicator accumulated in cancer incidence reflects the ratio of the number of detected cases of malignant neoplasms in the population that have been exposed to a potential risk to fall ill.

With such methods of calculating the missing diseases peaks in the individual age groups and are equally common in the elderly, which is normally observed while determining the relative incidence rates according to the standard procedure. Moreover, population morbidity is accumulated to a certain age and it can be considered as a possible biological latency. The number of individual tumors, thereby, provides an objective picture in the population of cancer incidence, particularly after the additional factors.

It has been concluded by study and analysis of cancer incidence in the population of territories contaminated with radionuclides due to the Chernobyl accident over the years (Popov etal, 2011; Vazhenin etal, 2003). Before the emergency period (1981-1985) this was included in the study of the spontaneous incidence. The differences between the intensive indicators were considered significant when the probability of error of the first series were less than 5% ($P < 0.05$).

Results

Over the observation period of 30 years (1981-2010) a total of 4,289 cases of MPM have been recorded in the population of the Belgorod region, out of which 2,052 cases were found in men and 2,237 cases in women. The highest incidence rates were registered in 1991-1995 and 1996-2000, (14.7 and 15.1 cases per 100 thousand). While in the pre emergency period (1981-1985) and in the first five years after the accident (1986-1990) the disease occurrences were merely 3.6 and 5.9 cases per hundred thousand, respectively.

The highest percentages in the structure of MPM within the total cancer incidence were registered among women in 1991-1995 (5.3%) and men in 1996-2000 (5.2%). However, the percentage of contribution of MPM to the structure of total cancer incidence among women and men was only 1.8 and 1.1% in 2001-2005.

Despite an improvement in the accounting system of external testing, the specific weightage of MPM in the total number of malignant neoplasms decreased to 2.3%. Moreover, in the female cohort the figure was only 1.9%, and in men - 2.8%.

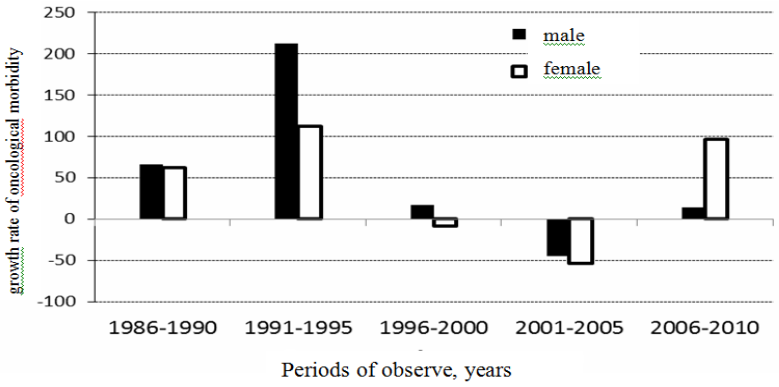

Fig. 1. The growth rate of MPM diseases in cohort of men and women of Belgorod region in dynamic during five years observation (1986-2010).

Indicators of growth rate diseases concerning MPM demonstrate wave-like dynamics of their development in the population of Belgorod region throughout the disaster period. The increased incidence of 1986-1995 is clearly visible in Fig. 1. The rate of morbidity, however, declined in 1996-2005. A new wave of growth in the diseases was observed in 2006-2010.

It is also important to note that during 1981-2000, MPMs were identified mainly with metachronous development. However, for the period 2001-2010, that is, after 15-20 years after the Chernobyl accident, MPMs were characterized by the predominance of synchronous tumors. During this period in a cohort of men were diagnosed 371 cases of MPM with simultaneous development (synchronous) and 342 cases of metachronous development. Among the women 454 and 294 cases of synchronous and metachronous developments were registered respectively. For example, the percentage of tumors with synchronous and metachronous MPM development in men in the years 1981-1985 were found to be 4.5% and 95.5% respectively (meaning more incidences in favor of metachronous cancer); and in 1986-1990 - 89.5% and 10.5% cases were registered, respectively. Amongst women who were registered on the MPM in these periods the share of metachronous tumors against synchronous was respectively: 88.9% and 11.1%, and 92.9% and 7.1%.

In 2001-2005 and 2006-2010 the ratio has changed diametrically and a remarkable increase was observed in cases with synchronous development. The percentage of synchronous tumors specified in this period it amounted to 51.8% for men and 52.2% respectively compared to 48.2% and 47.8% of tumors with metachronous development. Similarly, among women, synchronous tumors were detected more frequently in terms of the number of cases reported and the weightage of synchronous tumors as a percentage of all MPM amounted to 54.4 and 63.9%, and the development of metachronous tumors development was 45.6 and 36.1%.

We cannot fix the fact that during the period before the disaster (1981-1985), the majority of secondary tumors had arisen after treatment of the first tumor registered after 10 years or more. However, the picture changed in 1991-1995 as a vast number of metachronous tumors were detected during the first 5 years after treatment of the first tumor (Merabishvili etal, 2000).

In 2001-2005 and 2006-2010, almost all cases of metachronous polyneoplasia were identified within 5 years after treatment of the first cancer localization: 332 and 338 cases in a cohort of 250 men and 498 women, respectively were specified during the period. It is suggested that this pattern of accelerated development of polyneoplasia, regardless of their location, was due to the reduction of spontaneous biological latency of tumors due to the promoter effect of low doses of radiation. It is believed that it is a result of precisely small doses of radiation that took place during the early clinical manifestations of secondary tumors (mostly 5 years after treatment of the first tumor) that are consistent with the existing opinions of radiation-induced tumor development (Selchuk, 1994; Vazhenin etal, 2003; Ferbeyre etal, 2002).

In the analysis of MPMs by gender and age it was found that there were several registrations of individual cases of the disease in persons of younger ages, even adolescents (15-19 years), which was recorded in 1991-1995 and 1996-2000. Evidence of these "rejuvenation" diseases required a more detailed analysis.

The analysis of MPM in the population of the Belgorod region by age and gender shows that during 30 years of follow-up period (1981-2010) there occurred significant changes in disease dynamics which were specific to certain periods of observation and, especially, in different age groups, and among male and female cohorts, and different growth rates as well as morbidity were observed.

The most significant were the following figures. Typically, a steady increase in MPM was recorded mostly after 30 years of age in a cohort of men and women. However, in the dynamics of post-accident period (1986-2010), there are registrations of cases of MPM in people under the age of 30 years. In the women's cohort 14 cases were diagnosed before 30 years of age, whereas just 13 cases were recorded during 1986-2000. Among them, 2 cases were reported in girls in the 15-19 age group, 6 cases in 20-24 years age group and 6 cases in 25-29 years age group. Among men, for the same period 13 cases of MPM were identified, however the largest number of cases was registered in 1996-2000 (7 cases). Of all cases of MPM identified in the post-accident period - 4 cases were found in boys in the age group of 15-19 years, 3 cases in the 20-24 years age group and 6 cases in 25-29 years age group.

However, the highest rates of cumulative MPMs amongst men were registered in the third post-accident period (1996-2000), while amongst women these were mainly registered in the second post-accident period (1991-1995). The disease was particularly diagnosed in the elderly, in the age group of 65-85 years and older. In these specific periods the numbers of cases registered were 12.9-17.5 per 100 thousand for men and 12.2-14.4 for women respectively. While in the 1981-1986 period the morbidity in these age groups of men and women were 2.9 and 4.5 cases per 100 thousand respectively. For the purpose of clarity, the results are presented graphically in Fig. 2 and 3.

In 2001-2005, there was lower incidence rate compared to the previous period (1996-2000) in almost all age groups of both male and female cohorts.

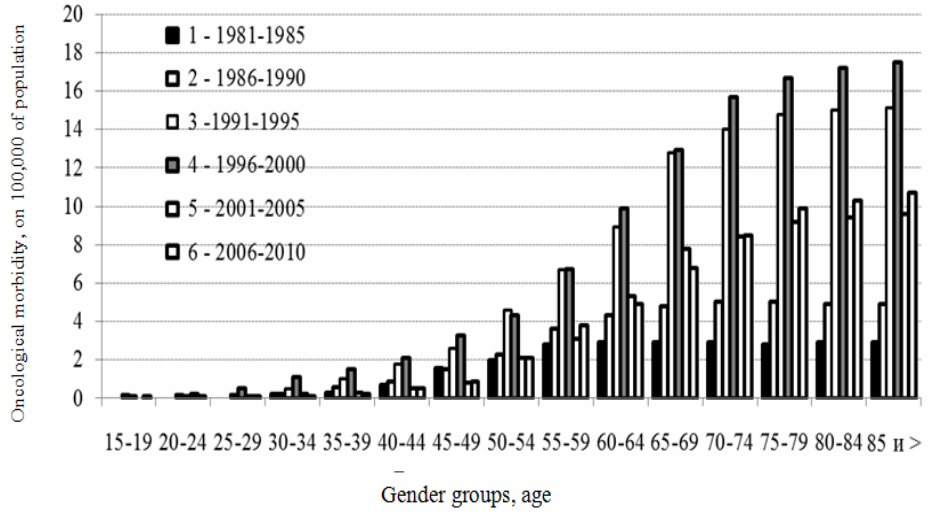

Fig. 2. The incidence of MPM in the different age groups of men at Belgorod region, with distribution by five-year observation periods (1981-2010).

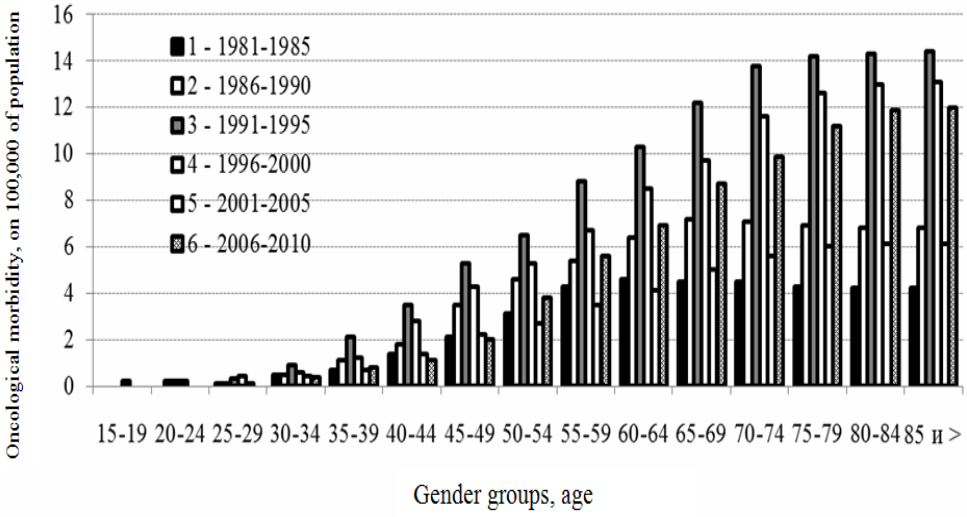

Fig. 3. Incidence of MPM in the different age groups of women at Belgorod Region, with distribution by five-year observation period (1981-2010).

The highest rates of MPM growth rate in the male cohort were observed in 1991-1995. The rates were highest in the 30-34 years age group (150%), then in the age groups of 65 years (166.7-196.0%) and especially in the 80-85 age and older (206.1-208.2%). In the next five years (1996-2000), the highest rate of growth pace was registered in the age group 25-29 years (150%). In 2001-2005, some growth was observed in the age group of 20-24, while virtually all other age groups incidence cohort experienced negative growth. In the years 2006-2010 of the disease positive growth occurred only in certain age groups, among the male cohort: 45-49 years (12.5%), 55-59 years (22.6%) and older than 70 years (1.2-11.5%). In women, the highest incidence rate of disease was observed in 1991-1995 among the age group of 25-29 years (200%) and 75-79 years and even up to a greater age, that is, 80-85 years of age and even older (105.8-111.8%). In the years of 1996-2000, and 2001-2005 a negative index growth rate was noticed for all age groups in the female cohorts. In the years 2006-2010 there was again a marked increase in the incidence rate in women, but only in the age group of 50 years and older.

Overall, these figures show a picture of rejuvenation of MPM in the population of the Belgorod region, especially the contrast which was expressed in a cohort of men throughout the 1991-2005 period, when changes of disease growth were recorded in the age groups younger than 35 years. An increased incidence of the disease was registered in the age group 25-29 years among women also, but it was fixed in 1991-1995.

Conclusion

Wave like dynamics of the MPM were identified in the population of the area during the post-Chernobyl period (1986-2010). Change to the polyneoplasia structure accompanied by a predominant development of synchronous tumors was registered in the 2001- 2010 period (15-20 years after the accident). Changes in incidences of the disease in the age groups younger than 30 years were observed along with the rapid increase in the incidence in older age group approximately 10-15 years after the accident. This was most likely due to the reduction of biological time latency of tumors in people with a genetic predisposition, as a result of the stimulating effect of small doses of radiation and also as a long-term consequence of the Chernobyl accident.

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