Associations between depression, anxiety and medication adherence among patients with arterial hypertension: Comparison between persons exposed and non-exposed to radiation from the Semipalatinsk Nuclear Test Site

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ABSTRACT

In this study, we investigated the association between depression, anxiety and medication adherence in patients with arterial hypertension living in East Kazakhstan region. The sample size included 795 patients, of whom 403 patients were exposed to radiation at the Semipalatinsk Nuclear Test Site from 1949 to 1989, while 395 patients were unexposed to radiation due to their very remote residence from the Site at the same period. Both exposed and unexposed patients showed no significant differences concerning body mass index, smoking habit, the presence of hypercholesterolemia, and hypertension grade. Patients with arterial hypertension previously exposed to radiation had significantly higher rates of low medication adherence, subclinical and clinical depression, situational anxiety of moderate and severe grade, and personal anxiety of moderate grade. A logistic regression analysis allowed us to identify the presence of significant positive association between medication adherence and anxiety in exposed patients (OR = 4041 (95%CI:1709–9556) p = 0.001) and marginal association (OR = 2998 (95%CI:1008–8915) p = 0.048) between the same parameters in unexposed patients. It might prove to be useful to introduce psychological and medical counseling with an emphasis on strengthening of medication adherence and to inform the local population about radiation effects and dosimetry data.

1. Introduction

Adherence to therapy is the term describing the degree to which a patient follows the doctor's advice, including medication compliance, dieting and/or lifestyle changes. Adherence to therapy is considered to be unsatisfactory in case if a patient takes ≤80% or ≥120% medication doses prescribed for a long period (Nwabuo et al., 2014; World Health Organization, 2002). The data from numerous published studies indicate that effectiveness of anti-hypertensive treatment depends not only on the correctness and authenticity of treatment prescriptions (medication choice, dosage, mode of administration, etc.) but also on following the doctor's recommendations, i.e., treatment adherence (World Health Organization, 2003). Despite the ample amount of available anti-hypertensive medications, the effective control of arterial hypertension remains an important task for the medical community of Kazakhstan. One of the ways to solve it is to improve the readiness of patients to comply with the recommendations of health care providers

and to follow medical prescriptions (AlGhurair et al., 2012).

Depression is one of the main causes of disability and is the fourth leading cause of disease burden all over the world. The World Mental Health Survey showed that depression rates in the developed countries are as high as 14.6% of the general population comparing to 11.1% in the developing countries (Bromet et al., 2011). Patients with arterial hypertension tend to have high rates of mental distress, which is manifested as anxiety and depression. Meanwhile, there is insufficient data to conclude about their influence on treatment adherence. At the same time, the prevalence of cardiovascular disease in the patients suffering from major depression is higher than in the general population. There are a number of pathways to explain this correlation – psychotic adverse effects of antihypertensive medications, unhealthy lifestyle, poor access to medical care, the influence of negative environmental factors and association with cardiovascular risk factors (Zheng et al., 1997; Colton and Manderscheid, 2006; Xu et al., 2017).

Following about forty years of nuclear weapons' tests (from 1949 to

1989), the territory of East Kazakhstan was contaminated with radioactive fallout, and large population groups were exposed to radiation in the range of low to moderate doses (Gordeev et al., 2006; Simon et al., 2006; Drozdovitch et al., 2011). Despite many efforts of the country's government to mitigate radiation effects for both population and territories (Law on the Social Protection, 1992), most of the local residents continue to consider radiation as one of the negative risk factors for their health and for the health of future generations. The increased socio-psychological tension stimulates the development of radiophobia and radiation exposure anxiety in certain categories of population (Jumazhanova et al., 2016; Bauer et al., 2013). As a matter of fact, long-lasting residence on the territories adjacent to the Semipalatinsk Nuclear Test Site could be considered as the additional psycho-traumatic factor for the population of East Kazakhstan region.

Very few surveys studied the associations between radiation, cardiovascular disease and psychological status of the exposed people. Several studies were reported investigating adverse effects of radiation on cardiovascular disease prevalence and mortality focus on the workers from the Mayak Production Association in the Southern Urals (Azizova et al., 2015; Simonetto et al., 2014), while the evaluation of psychological disorders was carried out on the sample of Chernobyl accident emergency workers – liquidators (Loganovsky and Vasilenko, 2013). There is only one study devoted to long-term radiation effects on cardiovascular disease mortality in the population residing on radiation-contaminated areas adjacent to the Semipalatinsk Nuclear Test Site (Grosche et al., 2011). The recently published research addressed the problem of the relationship between radiation exposure in the range of low to moderate doses and prevalence of arterial hypertension in the population of two Kazakhstani regions (Markabayeva et al., 2018).

The present study is the first attempt to establish associations between long-term radiation exposure in hypertensive patients, their anxiety and depression rates, and adherence to medical therapy. Since planning of medical treatment and rehabilitation measures for the patients with arterial hypertension previously exposed to radiation is an important task for health care system, the present study appears to be relevant. Knowledge of factors that influence treatment adherence in patients with arterial hypertension will allow reducing the rate of complications development, will improve the treatment effectiveness and patients' quality of life.

The aim of the present study was to clarify the associations between depression, anxiety and medication adherence among hypertensive patients, who were exposed or unexposed to radiation at the Semipalatinsk Nuclear Test Site, Kazakhstan.

2. Materials and methods

2.1. Characteristics of study population and study procedures

The overall sample size of this survey is composed of 798 patients with arterial hypertension and who live in the territory of East Kazakhstan region. Of these, 403 were exposed to radiation due to their permanent residency in the areas affected by the Semipalatinsk Nuclear Test Site's activity during the period of 1949–1989 and 395 patients were unexposed since they moved to East Kazakhstan region after 1991, when the Nuclear Test Site was closed by the Presidential Decree (Fig. 1 shows the area of interest). Information on radiation risk groups and individual effective radiation doses of the exposed patients was confirmed by the data of automated state medical registry (ASMR), which is the core database on the population exposed to radiation due to the Semipalatinsk Nuclear Test Site activity. Radiation exposure was verified through such legal document as "Polygonnoe udostoverenie" (Polygon certificate), issued in the 1990s, confirming residency in areas adjacent to the SNTS during its lifespan.

The Government of Kazakhstan adopted a state compensation program for the population exposed to radiation at the SNTS, which is being implemented from 1997 onwards, comprising screening

examinations of the population permanently living at the territories adjacent to the nuclear test site. This survey targeted 2232 patients with cardiovascular diseases including arterial hypertension, which was identified during the screenings disease carried out in 2016. From this screening list, 1000 adults (500 exposed and 500 unexposed) were randomly selected in 2016 and invited to participate in the study, of which 798 agreed, resulting in a response rate of 79.8%.

Each study participant gave written consent to participate after being informed about study objectives, benefits, medical items, and confidentiality of personal data. In accordance with ethics requirements, the study was approved by the Ethics Committee of Semey Medical University (Protocol No 4, October 14th, 2015). The exclusion criteria were pregnancy, malignant tumors, decompensated somatic disease, and mental disorders.

Before the survey beginning, all investigators attended training sessions covering all study procedures, i.e., study aim, how to administer the questionnaire and to take the standard measurements. All patients were interviewed personally. The study questionnaire covered passport data (patient's date and place of birth, parents' place of birth), radiation dose received education, body weight, and height, as well as smoking habits. Besides, the questionnaire was designed to obtain data on systolic and diastolic blood pressure, disease duration and clinical course, the presence of comorbidity, lipid profile, self-administered tests on adherence to therapy, anxiety, and depression.

2.2. Evaluation of clinical and laboratory tests

Medical examination included three blood pressure measurements taken after 5 min of resting using an Omron M4-I BP monitor, adopting the average of two last systolic and diastolic measurements in the analyses. Arterial hypertension was defined as systolic blood pressure 140 mm Hg or higher and/or average diastolic blood pressure 90 mm Hg or higher. The self-reported treatment with antihypertensive medication was also considered to be the case of arterial hypertension. Body mass index (BMI) was used to stratify patients by three body weight categories: < 25 (normal weight), 25–29.9 (overweight), and ≥ 30 (obese, in accordance with ICD-10: E66). The level of total cholesterol was measured in the laboratory of the Semey State Medical University by digital spectrophotometer PD-303S (APEL Japan) using BioSystems (Spain) reagents. Hypercholesterolemia was assessed over the total cholesterol level of 5 mmol/l and/or higher and by self-reported treatment with statin medication. All diagnoses were defined and coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Smoking was defined by self-reported habit and was classified as never smoking and ever smoking (past smoking and/or current smoking). All data obtained from the present study were verified for plausibility.

2.3. Evaluation of medication adherence, depression and anxiety

Evaluation of medication adherence in hypertensive patients was carried out with the help of the 4-item Morisky Medication Adherence Scale (MMAS-4), according to which medication adherers were identified with the score of 4 on the scale, medium adherers with a score of 3, and low adherers with a score of ≤ 2 (Morisky et al., 1986).

The Hospital Anxiety and Depression Scale (HADS) is a self-assessment scale that was developed for detecting states of depression and anxiety in the setting of a hospital medical outpatient clinics. Each item could be answered by a patient on a 4 point scale (0–3) so the possible scores for both anxiety and depression range from 0 to 21. According to this scale, a score of 0–7 could be regarded as being in the normal range, a score of 8–10 is suggestive of the presence of the respective state (anxiety or depression), while a score of 11 or higher indicating a probable presence of these mood disorders (Snaith and Zigmond, 1986).

The State-Trait Anxiety Inventory (STAI) is a valid and reliable self-