Epidemiological Studies on Epilepsy in Siberia

The research observes epidemiology of epilepsy and epileptic syndromes and risk factors at the population of the middle Siberia (Krasnoyarsk region and the Tuva Republic, Russian Federation). The analysis concludes that Siberia (on example the Krasnoyarsk region and the Tuva Republic) is region with high prevalence of epilepsy (comparable with the occurrence of epilepsy in the Europe countries). Though it s lower when comparing the epilepsy prevalence in developing countries. Prevalence of all forms of epilepsy was higher at children and teenagers. High prevalence of idiopathic epilepsy was in childhood populations in the Krasnoyarsk region and the Tuva Republic. Post-stroke epilepsy dominated in structure epilepsy with late onset in Krasnoyarsk region, including Krasnoyarsk city.

Keywords: Epilepsy, Epidemiology, Siberia, Russian Federation.

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Introduction

Epilepsy is a neurological disorder that affects people in every country throughout the world. Epilepsy is also one of the oldest conditions known to mankind. It is characterized by a tendency to recurrent seizures and it defined by two or more unprovoked seizures. The clinical manifestations of seizures will therefore vary and depend on where in the brain the disturbance first starts and how far it spreads. Transient symptoms can occur, such as loss of awareness or consciousness and disturbances of movement, sensation (including vision, hearing and taste), mood or mental function.

Localization-related epilepsies, sometimes termed partial or focal epilepsies, arise from an epileptic focus, a small portion of the brain that serves as the irritant driving the epileptic response. Generalized epilepsies, in contrast, arise from many independent foci (multifocal epilepsies) or from epileptic circuits that involve the whole brain. Epilepsies of unknown localization remain unclear whether they arise from a portion of the brain or from circuits that are more widespread. Epilepsy syndromes are further divided by presumptive cause: idiopathic, symptomatic, and cryptogenic. Idiopathic epilepsies are generally thought to arise from genetic abnormalities that lead to alteration of basic neuronal regulation. Symptomatic epilepsies arise from the effects of an epileptic lesion, whether that lesion is focal, such as a tumor, or a defect in metabolism causing widespread injury to the brain. Cryptogenic epilepsies involve a presumptive lesion that is otherwise difficult or impossible to uncover during evaluation (ILAE, 1993).

The risk factors and epileptogenic mechanisms for the different types of epilepsy have been correlated with their prognosis, thus making it possible to establish therapeutic strategies based on pharmacological agents or surgical procedures. Nevertheless, in 30-40% of cases, epilepsy is not satisfactorily controlled by the available remedies, and a non-negligible proportion has a poor prognosis in terms of both the severity of the epilepsy and its psychosocial outcome.

There are different causes of epilepsy that are common in certain age groups. During the neonatal period and early infancy the most common causes include hypoxic-ischemic encephalopathy, infections of central neural system (CNS), trauma, congenital CNS abnormalities, and metabolic disorders. During late infancy and early childhood, febrile seizures are fairly common. These may be caused by many different things, some thought to be things such as CNS infections and trauma. During childhood, well-defined epilepsy syndromes are generally seen. During adolescence and adulthood, the causes are more
likely to be secondary to any CNS lesion. Further, idiopathic epilepsy is less common. Other causes associated with these age groups are stress, trauma, CNS infections, brain tumors, drug use and alcohol withdrawal. In older adults, cerebrovascular disease is a very common cause. Other causes are CNS tumors, head trauma, and other degenerative diseases which are common in the older age group, such as dementia (Harrison's Principles of Medicine. 15th edition).

Epidemiology is the medical discipline which studies the dynamics of a medical condition in the general population. It is concerned about the numbers of people with the condition, who are at risk and what is the outcome of the condition. It allows for the rational planning of health delivery. It is very important because around 50 million people in the world have epilepsy at any one time. The lifetime prevalence of epilepsy (i.e. the number of people presently in the world who have epilepsy now or have had it in the past or will experience it in the future) is approximately 100 million people (WHO, 2001). The researchers who are engaged in epilepsy in the countries of the Europe and the USA have come to a conclusion that 7-10 % of all population at least time transfer to lives afebrile paroxysm, and febrile spasms are marked at 3-5 % of the population of Europe (Hopkins and Shorvon, 1995).

The prevalence of epilepsy is the proportion of a population with that disorder at a given point in time. From many studies around the world it has been estimated that the mean prevalence of active epilepsy (i.e. continuing seizures or the need for treatment) is approximately 8.2 per 1000 of the general population of the Europe. However, this may be an underestimate as some studies in developing countries suggest a prevalence of more than 10 per 1000 (WHO, 2007).

The incidence of epilepsy is the number of new cases at a given time. Studies in developed countries suggest an annual incidence of epilepsy of approximately 50 per 100000 of the general population. However, studies in developing countries suggest that this figure is nearly double that at 100 per 100000 (WHO, 2007). Incidence data are particularly limited, especially from low and lower middle income countries. They are usually divided into those of recurrent unprovoked seizures and those that include first seizures, acute symptomatic seizures or isolated seizures.

Morbidity of epilepsy in the different countries of the world varies from 20 to 120 cases in a year on 100000 at population.

Better understanding of the epidemiology of epilepsy is a prerequisite for improving epilepsy care. However, the epidemiological study of epilepsy remains difficult for a number of reasons. When suspected, epilepsy is not always easy to diagnose. Many epidemiological studies on epilepsy have been published, but the lack of rigorous definitions of the disease, differences in the methods of case ascertainment, classifications of seizures or epileptic syndromes and evaluation of risk factors hamper meaningful comparisons. The incidence rates of epilepsy in the Europe vary between 28.9 and 47 per 100000 (ILAE, 2005).

The age distribution of the incidence of epileptic seizures and epilepsy is bimodal, with two peaks of frequency: in childhood and in the elderly.

Data on prevalence are available from the Russian Federation although differences in methodology and study populations make comparisons difficult. An epidemiological study of active epilepsy in people over 14 years is being performed in eight European and (Asian) sites of the Russian Federation in people over 14 years. It has been completed in the Moscow and in the Irkutsk city and the Ulan-Ude city in the eastern Siberia (Kabakov and Shprakh, 2002). The crude prevalence rate of epilepsy increased from the western to the eastern regions, from 2.2 in the Moscow to 4.2 per 1000 in the Irkutsk. The prevalence was relatively consistent within the European part (2.2-3.4 per 1000) and within Asian (4.1-5.0 per 1000). Late-onset epilepsy was more frequent in the European than in the Asian region (Guelyt et al., 1999; Guekht, 2005).
The age-adjusted incidence rates of first epileptic seizures or newly diagnosed epileptic seizures in Europe range from 18.9 to 69.5 per 100000 (ILAE, 2005). The crude incidence rates for adolescents and adults (aged > 14 years) in several areas of the eastern Siberia, the Russian Federation, were similar: 25-30 per 100 000 (Kabakov and Shprakh, 2002; Guekht et al., 2004).

However, before our studies epidemiology of epilepsy in big territory of the middle Siberia (the Krasnoyarsk region and the Tuva Republic) was not studied.

The Krasnoyarsk region (Russian: Krasnoyarsky kray) is second largest federal subject of Russia, occupying an area of 2,339,700 km² (903,400 sq mi), which is 13% of the country's total territory of Russia (for example, the size of Algeria). The Krasnoyarsk region lies in the middle of Siberia, and belongs to the Siberian Federal District, stretching 3,000 km from the Sayan Mountains on the south along the Yenisei River to the Taymyr Peninsula in the north. Over 95% of the cities, a majority of the industrial enterprises, and all of the agriculture are concentrated in the south of the region including Krasnoyarsk city. Population (Census, 2002) was 3,023,525 (including Taymyr and Evenk Autonomous Okrugs). Population of Krasnoyarsk region mostly consists of Russians (88.38%), and some other peoples of the former Soviet Union. The indigenous Siberian peoples make up no more than 1% of the population. Krasnoyarsk is a city and the administrative center of Krasnoyarsk region It is the third largest city in Siberia, with population of 948,500 (2009 est.). BUT Zheleznogorsk is a closed administrative territory of Krasnoyarsk region Population of BUT Zheleznogorsk mostly consists of Russians. Population of Zhelesnogorsk town was 93,875 (Census, 2002), population of BUT Zheleznogorsk - more 110,000 (Sadikova et al., 2010).

The Tuva Republic is federal subject of Russia also. The republic is situated in the far south of the middle Siberia. The capital city is Kyzyl. Area is 170,427 km² (66,802 sq mi) (for example, territories of 2 x Austria or 1 x Florida). The area of the Tuva Republic is a mountain basin, ca. 600 m high, encircled by the Sayan and Tannu-Ola ranges. Mountains and hills cover over 80% of the republic's territory. Population was 305.510 (Census, 2002). Childhood population was 105.547 in 2007 (Sharavii, 2010). Tuvans, a Turks people, make up 77.0% of the republic's population. Other groups include Russians (20.1%), Khakas (0.4%), and a host of smaller groups, each accounting for less than 0.5% of the total population of the Tuva Republic. During the period 1959-2002 there has been more than a doubling of ethnic Tuvans. The Russian population growth slowed by the 1980s and has now begun to shrink.

The purpose of the research is studying of epidemiology of epilepsy and epileptic syndromes and its risk factors in population the middle Siberia (the Krasnoyarsk region and the Tuva Republic)

Material and methods

Work is executed within the limits of complex theme of federal scientific project “Epidemiological, clinical and genetics aspects of diseases of central, peripheral and autonomic neural systems and preventive health care” (the supervisor of the studies - Prof. Natalia Shnayder). The Register of epilepsy and epileptic syndromes which has been introduced in practical public health services on the basis of Krasnoyarsk region’s clinics and Tuva Republic clinics is created (Shnayer et al., 2010).

All patients passed careful preliminary anamnestic and clinical selection. The research volume includes clinical neurologic inspection, research of the somatic status, psychological testing of higher cortical functions, neurophysiologic inspection (multiple parameter analysis computer electroencephalography (EEG), including three-dimensional localization «Brain Loc» of sources epileptiform activity, video-EEG-monitoring), laboratory techniques (clinical analysis of blood, blood biochemistry, analysis of the immune status), functional methods (electrocardiogram - ECG, echocardiography, Holter monitoring - under indications), neuroradiology methods (magnetic resonance imaging -
MRI, computer tomography - CT, magnetic resonance angiography - MRA or spiral computer cerebral angiography).

Selection of patients was carried out by a method of the stratified randomization with using of criteria of inclusion and an exception. Criteria of inclusion in the Register: inhabitants of the Krasnoyarsk, inhabitants of BUT Zheleznogorsk of the Krasnoyarsk region, inhabitants of the Tuva Republic, adults and children who suffer from epileptic attacks at the moment of the reference in polyclinic, at the moment of hospitalization or in the anamnesis. Criteria of an exception: inhabitants of other regions of the Russian Federation, non-epileptic attacks, psychogenic reactions, conversion attacks (hysteria).

Terms of carrying out of research are 2004-2009. Statistical data processing of the Register is spent with using the standard parametrical and nonparametrical methods of comparison. The parametrical data was represented in the form of average sizes with an average quadratic error and 95% a confidential interval (CI). Reliability of statistical distinctions was estimated with using of Student’s criteria, Uilkokson’s and the Mann-Witney’s criteria. Distinctions were considered authentic at a significance value not less than 95%. Statistical processing is made by means of a package of applied programs for processing of biomedical data STATISTICA v.7.0 (StatSoft, USA, 2001).

Results of research

The mean standardized prevalence of epilepsy in general population of the Krasnoyarsk region (on example BUT Zheleznogorsk) was 2.8 on 1000, including idiopathic epilepsy - 0.21 per 1000, symptomatic epilepsy - 1.24 per 1000 (post-stroke epilepsy - 0.47 per 1000; posttraumatic epilepsy - 0.24 per 1000; epilepsy from the effects of congenital CNS abnormalities - 0.21 per 1000; epilepsy from the effects of CNS tumors - 0.17 per 1000), cryptogenic epilepsy - 1.35 per 1000 population. The incidence of epilepsy in general population of Krasnoyarsk region increased from 31 per 100000 in 2006 to 59 in 2008 (during our research) (Figure 1).

![Figure 1. Incidence of epilepsy in general population of Krasnoyarsk region in 2006 - 2008](image)

Prevalence of epilepsy at children from newborn till 15 years in the Krasnoyarsk region (mean age of patients - 9.8 ± 1.1 [95 % CI: 8 - 13] years old; mean age of seizures onset - 6.1 ± 0.6 [95 % CI: 3 - 9] years old) was 5.04 per 1000, including idiopathic epilepsy - 0.65 per 1000, symptomatic epilepsy - 2.52 per 1000, cryptogenic epilepsy - 1.87 per 1000. The
epilepsies in childhood that remit in adolescence are benign myoclonic epilepsy in infancy, childhood absence epilepsy (pure), early onset occipital epilepsy (Panayiotopoulos syndrome), benign epilepsy with centrotemporal spikes, Landau-Kleffner syndrome, epilepsy with continuous spike and wave during slow sleep and some generalized and focal epilepsies.

Prevalence of epilepsy at teenagers from 15 till 18 years in the Krasnoyarsk region (mean age - 15.9±1.5 [95% CI: 15 - 17] years old, mean age of seizures onset - 11.5±1.1 [95 % CI: 9 - 15] years old) was 5.75 per 1000, including idiopathic epilepsy - 1.27 per 1000, symptomatic epilepsy - 2.21 per 1000, cryptogenic epilepsy - 2.7 per 1000. Epilepsies with onset in adolescence included juvenile absence epilepsy, juvenile myoclonic epilepsy, generalized tonic-clonic seizures on awakening, photosensitive epilepsy, mesial temporal lobe epilepsy, progressive myoclonic epilepsy and other partial or generalized epilepsies.

Prevalence of epilepsy at adults in the Krasnoyarsk region (mean age of patients - 44.5±4.6 [95% CI: 29 - 56] years old, mean age of seizures onset - 34.5±3.1 [95% CI: 18 - 50] years old) was 2.31 per 1000, including idiopathic epilepsy - 0.10 per 1000, symptomatic epilepsy - 1.0 per 1000, cryptogenic epilepsy - 1.21 per 1000 (Sadikova et al., 2010).

Prevalence of epilepsy among adult of the Krasnoyarsk city (mean age - 48.6±17.2 [95% CI: 35-60] years old; mean age of seizures onset - 43.69±20.7 [95% CI: 28-59] years old) was 0.44 per 1000, including idiopathic epilepsy - 0.017 per 1000, symptomatic epilepsy - 0.29 per 1000 (post-stroke epilepsy - 0.11 per 1000; posttraumatic epilepsy - 0.093 per 1000; epilepsy from the effects of CNS infections - 0.05 per 1000; epilepsy from the effects of congenital CNS abnormalities - 0.008 per 1000; epilepsy from the effects of hereditary diseases of CNS - 0.008 per 1000; epilepsy from the effects of CNS tumors - 0.025 per 1000); cryptogenic epilepsy - 0.13 per 1000 (Dmitrenko et al., 2007).

<table>
<thead>
<tr>
<th>Territories (Tuvans: kozhuuns)</th>
<th>Prevalence (per 1000)</th>
</tr>
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<tbody>
<tr>
<td>Tuva Republic</td>
<td>5.49</td>
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<tr>
<td>Kyzyl city</td>
<td>0.36</td>
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<tr>
<td>Tandinskij kozhuun</td>
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<tr>
<td>Chedi-Kholskij kozhuun</td>
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<tr>
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<tr>
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<td>Tere-Kholskij kozhuun</td>
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Source: Sharavii, 2010.

Prevalence of epilepsy with a late onset (mean age of patients - 59.1±10.47 [95% CI: 55 - 67] years old; mean age of seizures onset - 52.3±15.14 [95% CI: 43 - 65] years old) was 0.31 per 1000 among senior adults (age - more 40 years old), including idiopathic epilepsy - 0.008 per 1000; symptomatic epilepsy - 0.22 per 1000; cryptogenic epilepsy - 0.008 per 1000 (Dmitrenko et al., 2007). The clinical manifestations of epilepsy in the elderly are
different from those in younger adults and children. The most common seizure types in the elderly are complex partial seizures, which may be shorter and less impressionable than those seen in younger patients. However, the elderly often have more severe, prolonged postictal symptoms, including postictal confusion with disorientation, hyperactivity, wandering and incontinence can persist for up to one week.

The mean standardized prevalence of epilepsy at childhood population of the Tuva Republic with age from newborn till 18 years old (mean age of patients - 10.9±4.4 [95% CI: 7 - 14] years old, mean age of seizures onset - 4.9±0.4 [95% CI: 1.5 - 5.3] years old) was 3.19±0.3 [95% CI: 0.96 - 4.63] per 1000 (Table 1), including idiopathic epilepsy - 0.37 per 1000, symptomatic epilepsy - 1.25 per 1000 (epilepsy from the effects of CNS infections - 0.44 per 1000; epilepsy from the effects of hypoxic-ischemic encephalopathy - 0.35 per 1000, posttraumatic epilepsy - 0.33 per 1000, epilepsy from effects of congenital CNS abnormalities - 10.42 per 1000), cryptogenic epilepsy - 1.31 per 1000. Prevalence of epilepsy in Kyzyl city was 0.36 per 1000 at childhood population. The incidence of childhood epilepsy increased from 41 per 100000 in 2005 to 109 per 100000 in 2007 during our study (Figure 2) (Sharavii, 2010).

**Figure 2. The incidence of childhood epilepsy in the Tuva Republic in 2005 - 2007**

*Source: Sharavii, 2010.*

**Conclusion**

The studies had shown that the epidemiological characteristics of epilepsy in different region in the Russian Federation, including the middle Siberia, are similar. Our data has shown trends similar to those in eastern and western countries of Europe, although the studies in the European part of the Russian Federation, the western and middle Siberia indicated a lower prevalence than in the Europe. For instance, prevalence in the Krasnoyarsk region is 2.8 on 1000 in general population versus 8.2 (ranges from 3.5 to 10.7) per 1000 in general population of the Europe.

The rates are higher in rural areas compared to urban areas in different countries of world. Also, our studies had shown that prevalence of epilepsy in adults population in the Krasnoyarsk region (2.31 per 1000) was higher than prevalence in the Krasnoyarsk city (0.44 per 1000). It could be caused higher level diagnostic and medical aid, presence specialized epileptological centers and the early reference of patients with an epilepsy behind medical aid in the Krasnoyarsk. On contrary, in rural and remote territories of the Krasnoyarsk region diagnostic equipment (video-EEG-monitoring, MRI/CT and other
modern diagnostics methods of epilepsy) is absent, the specialized medical help (epileptologists) is absent also. Post-stroke epilepsy (Silverman et al., 2002) without gender distinctions dominated in structure epilepsy with late onset in the Krasnoyarsk region, including the Krasnoyarsk city (Figure 3). (Dmitrenko et al., 2007; Shnayder et al., 2010; Sadikova et al., 2010).

**Figure 3. Mean age of post-stroke epilepsy onset in adults in the Krasnoyarsk city**

The lifetime prevalence in children of the middle Siberia (5.04 per 1000 in the Krasnoyarsk region, 3.19 per 1000 in the Tuva Republic) correlated with lifetime prevalence in the European countries. For instance, the lifetime prevalence in the Norway (aged 0-15 years) was ranges from 4.4 to 6.8 (Forsgren et al., 2005), and in children of the Lithuania (aged 0-15 years) was 4.2 (3.4 when age-standardized) per 1000 (Endziniene et al., 1997).

Our studies had shown the prevalence of childhood epilepsy was higher in the Krasnoyarsk region (5.04 per 1000) versus in the Tuva Republic (3.19 per 1000). It could be caused difficulties of inspection of children during exit medical inspections of the children's population in remote mountain areas of republic where the message is possible by an air transport, and children from in deserted-steppe areas republic, where Tuvans have a nomadic way of life (cattle breeding).

Now, our epidemiological, genetics and clinical studies of epilepsy in the middle Siberia regions are continuing.

**Summary**

1. Our epidemiological studies suggest the middle Siberia (on example the Krasnoyarsk region and the Tuva Republic) is region with high prevalence of epilepsy (as prevalence of epilepsy in Europe countries). However, prevalence of epilepsy in the middle Siberia was lower, that in the European countries and in developing countries.
2. Prevalence of all forms of epilepsy in the middle Siberia was higher at children and teenagers. Prevalence of idiopathic epilepsy was high in childhood populations of the Krasnoyarsk region and the Tuva Republic.

References


