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THE HEREDITARY ENZYMOPENIC METHEMOGLOBINEMIA PREVALENCE IN THE CHILDREN'S POPULATION OF SAKHA (YAKUTIA) REPUBLIC

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The hereditary methemoglobinemia I type is autosomal-recessive disease, endemic for Sakha (Yakutia) Republic. In this article methemoglobinemia registry data of Advisory polyclinic of Pediatric Center RH#1-NSM (Yakutsk) are presented.
Keywords: methemoglobinemia, Yakutia, registry data.

Introduction

The hereditary methemoglobinemia I type is autosomal-recessive disease which is characterized by sharp decrease of activity of the solvable form of enzyme NADH-cytochrome-b5-reductase in erythrocytes (less than 10 %) and moderated - in other bloody and tissue cells (20-60 %). According to the world literature the molecular-genetic cause of hereditary methemoglobinemia I – II types' development are changes in gene *DIA1* NADH-cytochrome-b5-reductase coding ferment (diaphorase-1). Gene *DIA1* is localized on the 22nd chromosome [4, 5] has length of 31 kb, contains 9 exons and 8 nitrons [9]. Two forms of enzyme, membrane connected and solvable, are produced from this gene by an alternative splicing, using different promoters [3, 7]. At present there is an assumption that at the 1st type methemoglobinemia there is a loss of enzyme stability, and at the 2nd one - its inactivation. The 1st type basically is associated with aminoacid substitutions, the 2nd one, behind some exception, with nonsense mutations and deletions in a gene [6].

In the world hereditary methemoglobinemia has wide prevalence in terrain of Alaska among Eskimos and Indians of an Ingalik tribe, who are the Atapask people, living in valleys of the rivers Kuskokwim and Yukon [8]. Single instances of the disease are revealed in populations of the various countries, thus some mutations are described in populations of China and Japan.

The Sakha (Yakutia) Republic is the endemial locus of the 1st type hereditary methemoglobinemia cases. The first works on clinical-laboratory indexes of disease are made by E.S. Banshchikova (2002). In the laboratory of molecular genetics of the RH #1-NCM molecular - genetical research is made by means of direct DNA-testing, the mutation of hereditary recessive methemoglobinemia Pro269Leu in gene DIA by PCR method, the RFLP -analysis and the subsequent electrophoresis in 2 % agarose gel is revealed. Heterozygous carrying frequency of the mutation is nearby 1 % in population, and among Yakuts is considerably higher - 7 %.

Research objective

To represent prevalence and clinical-laboratory characteristics of hereditary enzymopenic methemoglobinemia in children of Sakha (Yakutia) Republic.

Methods

On the basis of Advisory polyclinic of Pediatric centre RH#1-NSM by the hematologist children with hereditary enzymopenic methemoglobinemia (HEM) are registered.

Results and discussion

Since 2005, 43 children are registered, from them 17 - elder 18 years. 65 % of sick children are boys, girls make up 35 %. Allocation of children on age has shown that the greatest number of children is registered from 7 years (37 children). Probably, it is connected with late diagnostics

and registration. 98 % of sick children are children Yakuts and 2 % of children are Evenks. In Maksimova N.R. work (2008) the disease is revealed in Yakuts with frequency 14, 9 in 100 thousand people while in the world – 1 case in 100 thousand people.

In table 1 the data of the places of residence of children is presented. The greatest quantity of children with HEM is registered in Viliy region (15 cases – 47,0 in 100 000 of children's population), then in the central areas (11 – 33,3 in 100 000 of children's population) and areas over the river (10 – 12,7 in 100 000 of children's population) (Table 2).

Clinically sick children complain of a short wind at an exercise stress, fatigability, the headaches bound to a hypoxia. Since a birth cyanosis of cutaneous covering and visible mucosa is observed, especially appreciable in the field of lips, nose, lobes of ears, nail plates, oral cavity. The colouring spectrum depends in basic on MetHb level in blood, the higher MetHb level, the most evident is cyanosis. As a result of MetHb accumulation in erythrocytes, at early children's age, when the central nervous and muscular systems continue to develop, in tissues deficiency of oxygen is formed. Children with HEM are backward in physical development - 14 (31, 8 %), in psychomotor development - 10 (22,7 %). Level of MetHb in blood from the general hemoglobin at observable children has in average - 25,2 %, (min - 4,2 %, max - 46,2 %). As consequence of adaptable reaction of organism to hypoxia, the quantity of erythrocytes and hemoglobin in blood unit should be raised. At observable children under analyses of blood it is revealed only in 17 (39, 5 %), in them hemoglobin level is raised in 1,1 - 1,3 times, and the quantity of erythrocytes is raised in 1,1 - 1,28 times. In 11 (25, 6 %) signs of hypoferric anemia of the 1 degree are revealed that aggravates disease course.

At inspection of children with HEM, following concomitant diseases are revealed: tooth caries - 39 (90, 7 %), small anomalies of heart - 23 (53, 4 %), a chronic tonsillitis - 10 (23, 3 %), in one patient - a congenital heart disease, a valve stenosis of the pulmonary fulcrum, the operated congenital heart disease (ASD), juvenile rheumatoid arthritis, stomach ulcer, epilepsy with dementia, benign tumor of temporal department of brain.

Conclusions

Most often hereditary enzymopenic methemoglobinemia is revealed in children from Verhnevilyuisky and Ust-Aldan areas. In a clinical pattern congenital cyanosis of cutaneous covering and oral cavity mucosa prevails, MetHb level exceeds norm on the average in 12,6 times, level of hemoglobin and erythrocytes only in 17 (39,5 %) patients are raised compensatorily , in 11 (25,6 %) patients signs of hypoferric anemia of the 1st degree are revealed that aggravates a clinical course.

Thus, the carried out analysis of the methemoglobinemia register confirms endemicity of the disease for our Republic, especially for over the river and Vilyui areas and demands working out and introduction of screening methods of research of indigenous population for revealing of carriers of the given gene.

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THE FACTORS OF A RICK OF THE FORMING OF CEREBRAL ISCHEMIA IN NEW-BORN CHILDREN OF TUVA REPUBLIC

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RESUME

150 women of the native nationality of Tuva Republic and their new-born children were examined with the aim of discovering of the risk factors of cerebral ischemia in new-born children. Analysis of the statistic meaning of the distinctions of the qualitative signs was made with the help of the criterion x^2 with Yeits correction. The index of ratio of the chances with 95% confidence interval was used for risk calculation.

The discovered signs of pre-natal hypoxia during pregnancy increase a risk of acute ischemia of brain in 4,85 times in period of new-borning. Risk of the ischemic injury of central nervous system of a new- born child is increased in 2,92 times at a presence of the urogenital infection in a mother and twice - at a presence of anemia in a pregnant woman and a risk of misbirth.

Keywords: new-born children, cerebral ischemia, risk factors, prognosis.

Cerebral ischemia (CI) with hypoxia take a leading place, achieving 38,4-67,5 [1] in the structure of the perinatal sickness and mortality. Cerebral ischemia / hypoxia has got long-term (many years') consequence, and modern demographic situation demands constant perfection of aid to pregnant women and new-born children with the aim of decrease of perinatal sickness, mortality and prophylaxis of disablement since childhood. [2,4]. At the same time it's well