Correlating alleles of genes LPH, CALCR, COL1A1, VDR with the indicators of bone tissue mineral density in female population of Eastern Kazakhstan

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Introduction

Reduced bone tissue mineral density (BTMD) is one of the leading causes of pathologies in people of different age groups in modern day environment (Benevolenskaya, 2003). Reduced BTMD is prevalent among females. Recent survey indicates that in the reproductive age around 30-40% of women are afflicted with osteopenia, 5% - with osteoporosis (Riggs and Melton, 1997). Moreover, pregnancy is currently believed to be an aggravating factor increasing the chances of reduced BTMD (Tzay-Shing et al., 1996).

To date, there is evidence of correlation between mineral density of bone tissue and a number of factors, among which genetic factors are most prominent. It has already been established that development of osteopenia and osteoporosis is directly dependent on the gene of lactase promoter (LPH), which is responsible for amino acid sequence coding between receptor and the calcitonin hormone (CALCR), 2046 G->T gene of collagen (COL1A1), as well as the vitamin D receptor gene (VDR) (Olds and Sibley, 2003).

It is also established that the occurrence of various alleles of these genes in populations varies (Grant et al., 1996). A number of research works on ethnical features in the osteoporosis genetics indicate that members of Asian ethnicities are positively more prone to having, in homozygous and heterozygous forms, genes associated with the elevated risk of reduced BTMD (Bandres et al., 2005). At the same time, findings of these research efforts are based mainly on the examination of women of Far Eastern populations. To date, there are almost no large-scale projects on identifying frequency of genetic markers affecting BTMD count and their correlation with real values of this indicator in the female populations of Turkic nationalities.

Ethnical and national features of Kazakhstan demographics allow to conduct thorough analysis of the frequency of genetic markers of high risk of BTMD reduction in European and Turkic populations living in equal socio-economic and ecologic conditions.
The purpose of research is to identify distribution of frequency of alleles of LPH, CALCR, COL1A1, VDR genes and correlation with indicators of BTMD in population of reproductive age females in the Eastern region of Kazakhstan.

**Materials and methods**

Genetic research has been conducted on 475 females exhibiting LPH, CALCR, COL1A1, VDR genes, presence of which, according to previous research, is due to confirmed increased risk of osteoporosis. Examined females were distributed by race: 213 women were of European descent, 262 - Asian.

Among European ethnic groups, it was revealed that majority of alleles were protective against osteopenia and osteoporosis (Table 1).

### Table 1. Frequency of identification of alleles of examined genes related to the higher risk of osteoporosis development, among women of European ethnicities

<table>
<thead>
<tr>
<th>Genes</th>
<th>Alleles identification frequency, n=213</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>allele</td>
</tr>
<tr>
<td>LPH gene</td>
<td>C/C</td>
</tr>
<tr>
<td>CALCR</td>
<td>C/C</td>
</tr>
<tr>
<td>COL1A1</td>
<td>T/T</td>
</tr>
<tr>
<td>VDR</td>
<td>BB</td>
</tr>
</tbody>
</table>

**TABLE 2. Frequency of sighting of alleles related to genes associated with higher risk of osteoporosis, among women of Asiatic nationalities**

<table>
<thead>
<tr>
<th>Genes</th>
<th>Частота выявления аллелей, n=262</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>allele</td>
</tr>
<tr>
<td>LPH gene</td>
<td>C/C</td>
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<td>CALCR</td>
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<td>VDR</td>
<td>BB</td>
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</tbody>
</table>

**Figure 1. Comparative frequency of genotypes associated with increased risk of osteoporosis in examined women in relation to their ethnicity**

As illustrated in Table 1, frequency of homozygous genotypes for alleles that define osteoporosis risk was lower than the examined population average. Thus, frequency of the C/C genotype for LPH gene is 13.6%, for CALCR gene -only 4.3%, T/T for COL1A1 -6.6% and BB for VDR gene is 12.7%.
Conversely, among women of Turkic nationalities there is a noted an increase in the frequency of alleles of the genes associated with reducing risk of BTMD (Table 2).

Thus, frequency of genotype C/C for LPH gene totals 22.9% which is 90% greater than in the European nationality women group, for CALCR gene -65.6% as opposed to 4.2%, over 15-fold excess; T/T for COL1A1 gene - 15.6% as opposed to 6.6%, 2.5-fold increase; and, finally, for VDR gene, BB genotype is 20.6% as opposed to 12.7% (1.5-fold increase). Graphical representation is available in Figure 1.

In general, acquired data indicate a higher degree of hereditary risk of developing reduced BTMD in the examined populace, which is mainly related to the presence of homozygous C/C genotypes for LPH and CALCR, T/T for COL1A1 and BB for VDR in women of Turkic (mainly Kazakh) descent.

The data on features of distribution of BTMD in relation to alleles of individual genes being studied.

In distribution of examination results on alleles of LPH gene it was discovered that absence of BTMD reduction in presence of C/C alleles presented only in 10.1% of cases. Women with this allele mostly exhibited osteopenia, rate of which totalled 77.5%, as opposed to osteoporosis occurring in 12.4% of cases.

Approximately equally common was absence of reduction of BTMD (52.7%) and osteopenia (44.7%), identified in case of the T/C allele presence. Rate of osteoporosis in this case totalled at just 2.7%.

Osteoporosis was not common for women presenting T/T allele - occurring only in 1.3% of cases. In this group, majority of cases exhibited adequate readings of BTMD (60.6%), while osteopenia occurred in 38.1% of cases.

Similar results of the analysis of occurrence of various degrees of BTMD in relation to the CALCR gene alleles indicate that osteopenia is also more common among women with C/C alleles (84.5%). Its rates in the T/C allele group totalled 34.9%, whereas T/T - only 8.5%. At the same time, osteoporosis rates did not largely differ, compared to the subgroups distinguished in relation to LPH gene alleles. It was 4.7%, 3.7% and 3.3% respectfully.

Distribution of cases of normal BTMD, osteopenia and osteoporosis for COL1A1 gene alleles indicates that only in case of T/T alleles presence it could be correlated with increase in number of osteopenia and especially osteoporosis cases, totalling at 58.2% and 12.7% respectively. Rates of osteopenia and osteoporosis in the T/G and G/G alleles groups were largely identical.

Distribution of osteopenia and osteoporosis by the VDR gene alleles indicates that, according to literature sources, reduced BTMD is characteristic feature of the B/B allele. This group presented osteopenia rate of 72.8%, and osteoporosis rate of 9.9%. In presence of B/B allele, respective indicators totalled 46.6% and 3.7%, whereas for B/B - only 40.9% and 2.0%.

As a result, our findings prove to be largely similar to those presented in the existing research literature, however we have also identified correlation of osteopenic syndrome with the presence of certain recessive alleles in heterozygous cases.

References


