The Occurrence of HIV-1 Resistance Biomarker Among Two Cohorts from Poland

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Abstract

Approximately 1% of the Caucasians shows resistance to HIV-1 infection conditioned by 32bp deletion in CCR5 gene. Homozygotes are almost totally resistant, but heterozygotes have delay the progression to AIDS. Due to the constantly increase of HIV infection in Poland we examined the incidence of del32 allele in two cohorts (south-western and south-eastern region of country) that remarkably differs in the incidence of HIV. Among the individuals from the south-western region, we detected 7 homozygotes (2.6%), in compare with individuals from the south-eastern area of Poland, where we found 1 homozygote (0.4%). The prevalence of CCR5del32 allele in the group from the south-western region was estimated at 11.6%, while in the group from the south-eastern region was assessed at 9.7%. Differences in the prevalence of genotypes and alleles between regions were not statistically significant. Our results were discussed in relation to the incidence of HIV infection in Poland. We conclude that occurrence of CCR5del32 biomarker does not reflect the incidence of HIV in the examined regions.

Introduction

In the aetiology of HIV-1 infection, some genetic factors may be important, for example the gene variants, which encode chemokine receptors: CCR5, CCR2 and CXCR4 - SDF-1 ligand receptor [1]. The human β-chemokine receptor is encoded by CCR5 gene located in the 3p21.3 locus. CCR5 consists of four exons and two introns; exon 4 contains ORF (open reading frame) and deletion of 32 bp in the ORF causes the formation of non-functional protein and protects homozygotes against HIV-1 R5 infection [2-5]. This alteration decreases, in heterozygotes, risk of infection [6] and delays progression into AIDS for about 2-3 years [3,5,7]. There are some evidence that the resistance of this type is related to the Caucasian due to spreading epidemics of diseases with similar pathogenesis to HIV infection. One hypothesis states that people with the deletion of 32 bp in CCR5 gene could have survived the epimenes, and allele with deletion could been inherited by progeny. Bubonic plague (1347 – 1351 year) [8] as well as smallpox could have also had a selective pressure on chemokine inherited by progeny. Bubonic plaque (1347 – 1351 year) [8] as well as smallpox (1347 – 1351 year) [8] could have survived the epimenes, and allele with deletion could have been conveyed by Vikings between 8th and 10th century [11]. Nowadays, the CCR5del32 biomarker occurs approximately in 1% of the Caucasian population [2].

The aim of our study was to examine the occurrence of CCR5del32 biomarker in two population groups from the south-western and south-eastern regions of Poland. Our results were compared with epidemiology data of HIV infection in this region.

Materials and Methods

The study involved 268 individuals from the south-western (dolnoslaskie) region of Poland and 252 individuals from the south-eastern (podkarpackie) region, altogether 520 subjects chosen randomly. The group was matched according to sex and age. The age of respondents was in the range between 20-29 years. DNA was obtained from peripheral blood lymphocytes (268 sample), buccal cells (125 samples) and hair follicle cells (13 samples). DNA from peripheral blood lymphocytes was isolated by fenol–chloroform extraction; from buccal cells and hair follicle cells by alkaline lysis according to Bella [12] and Klintshaar methods with minor modifications [13].

Molecular analysis of CCR5del32 (c.794-925del) variant was carried out with PCR technique, using primers described previously by Liu et al. [4]. The PCR reaction mixture in the total volume of 10 μl per tube contained: 0.2 mM dATP, dCTP, dGTP and dTTP, 0.5 U/μl OptiTaq DNA Polymerase (EURx, Poland), 1x Taq polymerase buffer; 1.5 mM MgCl₂, 0.5μM Fwd primer and 0.5μM Rev primer. PCR conditions were: 25 seconds at 95°C, 25 seconds at 62°C, 25 seconds at 72°C, 35 cycles. Results of PCR amplification were visualized on 2% agarose gel stained with SYBR Safe DNA gel stain (Invitrogen, Carlsbad, CA, USA). Band of about 182 bp was characteristic for wild type homozygotes (wt/wt), about 150 bp band was characteristic for homozygotes with 32 bp deletion (del32/del32), two bands (182 bp and 150 bp) were characteristic for heterozygote (wt/del32).

Analysis of the frequency of del32 variant in the CCR5 gene was assessed using the Pearson χ² test. Statistical analysis of data was performed using StatSoft, Inc. (2005) STATISTICA, version 7.0, http://www.statsoft.com. This study protocol was approved by the Ethics Committee of the Faculty of Medicine, University of Rzeszow, Poland.

Results

Among the individuals from the south – western region of Poland deletion was detected in 55 (20.5%) cases, including 7 homozygotes (2.6%). In individuals from the south - eastern region deletion was found in 48 (19%) subjects, including one homozygous case (0.4%). The prevalence of CCR5del32 was assessed at 11.6% and 9.7% (south-western and south-eastern region respectively, see Table 1). The differences in the prevalence of genotypes and alleles between regions were not statistically significant. Our results were discussed in relation to the incidence of HIV infection in Poland. We conclude that occurrence of CCR5del32 biomarker does not reflect the incidence of HIV in the examined regions.

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CCR5del32 variant is a modifying pathogenetic factor in type I diabetes and other diseases like diabetes. Moreover our data may be useful for planning prevention efforts.

References


