The prevalence of ADH1B and OPRM1 predisposing alleles for alcohol consumption are increased in the Hungarian psoriasis population

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INTRODUCTION

Psoriasis vulgaris (PsV) is a common systemic inflammatory disease with numerous genetic and environmental factors in the background. Although alcohol consumption is a key environmental factor affecting in great the symptoms and life of PsV patients, its genetic association with PsV remains to be elucidated.

AIMS

The objective of our study was to investigate the association of psoriasis with several established alcohol consumption and dependence related gene variants.

RESULTS

Differences between the psoriatic and Hungarian General population remained significant only for one SNP (rs1229984) after multiple test correction. Comparing the allele frequency distribution of SNP rs1229984 in the gene coding alcohol dehydrogenase 1B (ADH1B) significantly higher prevalence of effect allele `C` was found in the psoriatic population compared to the HG population (94.46% vs. 92.04%, p<0.001, respectively). Significant differences were observed between study groups in the association analysis according to the additive (OR=1.58, 95%CI=1.23-2.03, p<0.001) and the recessive model (OR=1.58, 95%CI=1.22-2.04, p=0.001) but not the dominant model (OR=4.29, 95%CI=0.55-33.08, p=0.163)

Table 1. Effect allele frequency distribution in rs1229984

SNP	effect allele	effect allele frequency among psoriasis patients N=	effect allele frequency in general population	p	modell	OR* (95% CI)	p
rs1229984	C	0.946	0.9204	0.001	ADD	1.58 (1.23-2.03)	0.00037
					DOM	4.29 (0.55-33.08)	0.163
					REC	1.58 (1.22-2.04)	0.001

By comparing the psoriasis subgroups several strata of psoriatic patients were defined, such as familial aggregation vs. sporadic case, early-onset of disease (≤40 years) vs. late-onset (≥ 40years) and PASI score (≤ 10, ≥ 10). Significant results were found only in case of one SNP rs1799971 (μ-opioid receptor gene, OPRM1) when familial cases were compared to sporadic cases. The effect allele G increased the risk of familial psoriasis by two fold compared to sporadic cases both in additive and in dominant models (ORadditive=1.99, ORdominant=2.01; p<0.001).

Table 2. Association of rs 1799971 with psoriasis vulgaris analyzed by subphenotype stratification

Phenotype groups	additive (GG vs. AA)	p-value	recessive (GG vs. GA+AA)	p-value	dominant (GG+GA vs. AA)	p-value
	OR(95%)		OR(95%)		OR(95%)	
early-onset psoriasis(≤40yrs) vs. late-onset (>40yrs)	0.66 (0.44-1.006)	0.0537	1.17(0.17-7.85)	0.8711	0.62 (0.39-0.97)	0.035
familial psoriasis v. sporadic psoriasis	1.993 (1.36-2.91)	0.0003	4.53(0.77-26.4)	0.092	2.01 (1.35-3.01)	0.0006
severe psoriasis (PASI≥10) vs. mild psoriasis (PASI<10)	0.97 (0.65-1.45)	0.8997	0.79(0.13-4.85)	0.8076	1.05 (0.68-1.59)	0.8291

MATERIALS AND METHODS

A population based case-control study including 3743 subjects (776 PsV cases and 2967 controls from the general Hungarian population) was conducted. Genotyping of 23 single nucleotide polymorphisms (SNPs) were determined using Mass Array platform with iPLEX Gold Chemistry (Sequenom). Differences in genotype and allele distributions were investigated. Multiple logistic regression analyses were also implemented.

Statistical analyses

The data were analyzed using STATA 12.0 Statistical software (StataCorp LP, College Station, TX, USA). The Mann–Whitney U and χ2 tests were used to compare the mean age and sex distribution of the two study groups. The existence of Hardy–Weinberg equilibrium (HWE) and significant differences in the allele and genotype frequencies between the two populations were examined with the χ2 test. After adjusting for multiple comparisons (Bonferroni correction), a p-threshold of 0.002 was applied; otherwise the threshold for significance was 0.05.

DISCUSSION

In this study we evaluated the relationship between 23 SNPs related to increased alcohol intake and dependence in a psoriasis group from Hungary. We found that the frequency of the genetic variant rs1229984 (ADH1B gene) increased in the whole psoriasis group, while the prevalence of genetic variant rs1799971 (OPRM1 gene) showed higher prevalence in the familial form of psoriasis patients. Importantly, the psoriasis risk related to these variants increased further in the subgroup of psoriatic patients with history of early onset and familial aggregation.

ADH1B is a key enzyme in the metabolism of ethanol to acetaldehyde and subsequent oxidation to acetate. The allele G with a detected increased prevalence in the psoriasis population leads to an increased enzyme activity, thus to decreased levels of the harmful acetaldehyde following the alcohol ingestion.

OPRM1 encodes the μ-opioid receptor, which upon activation by its ligands, such as opioids and analgesic agents like beta-endorphin, modulates the dopamine system [1]. It is implicated in complex behavior patterns such as alcohol dependence in Caucasian, native American tribes as well as in a study group of Asian descends [2-5] in alcohol dependence associated impulsivity [6] just as in a reduced response to rewarding stimuli [7, 8]. Out of the alleles, 118G has the major susceptible effect. In individuals carrying 118G stimulation, sedation, and positive mood levels after alcohol intake were significantly higher than in controls [8].

In conclusion, our data suggests that genetically defined high-risk individuals for alcohol consumption are more common among psoriasis patients than in the general population in Hungary, which highlights the importance to integrate the genetic determinants of health behavior into our current thinking of psoriasis diagnosis and treatment. These findings therefore also set the basis and the need for novel implications, besides focusing only on the role of non-genetic factors, in planning and delivering effective preventive interventions targeted for psoriatic patients.

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