EPISODIC AND CHRONIC MIGRAINE DIFFER IN 1911A>G POLYMORPHISM OF *TRPV1* GENE: A POSSIBLE BIOMARKER OF MIGRAINE CHRONIFICATION?

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Introduction

- Migraine subdivides under the International classification of headache disorders 3rd edition on episodic and chronic subtypes depending on attack frequency and pain intensity [1].
- According to the current view, one of the key roles in migraine pathogenesis belongs to expressed in trigeminal nociceptive neurons transient receptor potential vanilloid type 1 (TRPV1) receptors [2,3], what reveals in their activation and further release of the main migraine pain mediator CGRP [4].
- Due to implication in generation of pain the *TRPV1* gene is one of the primary candidates for investigation in light of migraine.
- Genetic studies have showed that single nucleotide polymorphism (SNP) 1911A>G (rs8065080), leading to amino acid substitution Ile585Val in the *TRPV1* gene, affects functional activity of TRPV1 receptors and is involved in different pain conditions [5,6].
- *TRPV1* 1911A>G SNP has not been tested in migraine patients.

Aim

Here was evaluated the genotype frequency distribution of 1911A>G in the *TRPV1* gene in healthy individuals and patients with episodic and chronic migraine to test the influence of the SNP on susceptibility to these forms of migraine.

Materials and methods

- The study included 56 patients diagnosed with migraine (32 episodic and 24 chronic) and 50 healthy individuals as a control group. The diagnosis of episodic and chronic migraine was established according to the ICHD-3.
- DNA from peripheral blood was used to test *TRPV1* SNP by allele-specific PCR combined with gel electrophoresis (Fig.1).
- Samples were genotyped in a randomized order and all labtecnical procedures were performed blind to any phenotype information.
- Differences between the groups in genotype distributions were analyzed using Fisher's exact test. A *p*-value smaller than 0.05 was considered as significant.

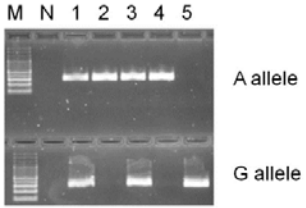

Fig.1. Allele-specific PCR analysis of 1911A>G genotypes. Column M – the 100 bp marker DNA ladder; column N – negative control; columns 1 and 3 – a sample heterozygote AG; columns 2 and 4 – a sample homozygote AA; column 5 – a sample homozygote of GG

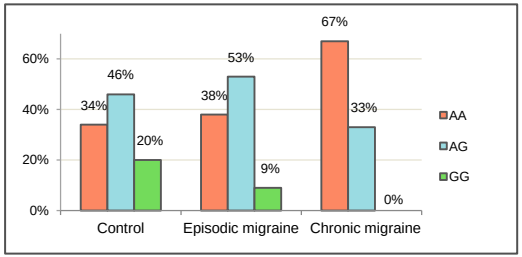

Fig. 2. TRPV1 rs8065080 SNP distribution in control, episodic and chronic migraine groups

Tab 1. *TRPV1* 1911A>G genotypes and alleles distribution in the control group, episodic and chronic migraine patients

Genotype	Control group % (n)	Episodic migraine % (n)	Chronic migraine % (n)
AA	34 (17)	38 (12)	67 (16)
AG	46 (23)	53(17)	33 (8)
GG	20 (10)	9 (3)	0 (0)

Results

- The genotype frequency distribution in chronic migraine differed significantly from episodic migraine and control groups (p=0.049 and p=0.012, respectively) due to nearly double increase of AA genotype frequency and **complete absence of the GG genotype** (Fig.2, Tab.1). Chronic migraine patients revealed only AA and AG variants, what is in accordance with data on higher pain sensitivity and activity of TRPV1 receptors at these genotype carriers [5,6].
- Episodic migraine patients statistically did not differ from the control group (p=0.467) but the contribution of still presenting GG variant was relatively reduced.
- The distribution of investigated genotypes was in Hardy-Weinberg equilibrium**.**
- Obtained results show the decrease of GG genotype frequency with acceleration of migraine attacks in trend of its chronification.

Conclusions

Earlier we have already presented a pilot study on a distinctive genotype frequency distribution of *TRPV1* 1911A>G in chronic migraine [7]. Current sample has been strengthened and obtained results are in good agreement with that previous study, underpinning and expanding our conclusions drawn:

- There is a different genetic determinism of episodic and chronic forms of migraine based on differences in TRPV1 1911A>G genotype distribution, i.e. the role of TRPV1 receptors in the heterogenity of migraine may be assumed.
- Since the prevailing view suggests that chronic migraine is a progression of episodic migraine [8], the complete absence of the GG variant in chronic migraine cohort could be interpreted as this genotype's association with adaptive protective mechanism against migraine chronification.
- Our data confirm a different predisposition to chronic pain in migraine and give a prerequisite for a new look at the nature of chronification of migraine pain, proposing that the absence of GG genotype may indicate a potential risk of migraine progression from episodic to chronic.
- If proved in the larger patients sample, absence of GG genotype possibly may serve as a biomarker of migraine chronification risk, so SNP TRPV1 1911A>G genotyping may be used for predicting severity of migraine and choosing a treatment strategy.

References

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