Analysis of TRPV1 gene polymorphisms in episodic migraineurs and patients affected by medication overuse headache

S. Cargnin[1], M. Viana[2], G. Sances[2], C. Tassorelli[2], G. Nappi[2], PL. Canonico[1], A.A.Genazzani[1] & S. Terrazzino[1].

[1] Department of Pharmaceutical Sciences, Università degli Studi del Piemonte Orientale 'Amedeo Avogadro', Novara, Italy
[2] Headache Science Centre, National Neurological Institute C. Mondino, Pavia, Italy

Migraine is a disabling neurovascular disease that affects around 10% of the worldwide adult population, with a male to female ratio of 1:3[1]. Among the wide range of symptomatic drugs currently used in the clinical management of migraine, triptans are considered as the gold standard therapy for moderate or severe migraine[2]. The mechanisms of action of triptans are mediated by a high agonist affinity for 5-$HT1_{B/D}$ receptors and include i) vasoconstriction of painfully dilated cerebral blood vessels, ii) inhibition of nociceptive neurotransmission, and iii) blockage of the release of vasodilatatory and pro-inflammatory neuropeptides by trigeminal nerves, such are calcitonin gene-related peptide (CGRP), substance P and neurokinin A[3]. Besides these well-known triptans' effects, recent evidences indicate that sumatriptan may also block transient receptors potential vanilloid-1 (TRPV1s)[4]. TRPV1s are nonselective cation channels involved in the transmission and modulation of pain derived from injurious heat and inflammation. Intriguingly, TRPV1 and CGRP are colocalized in trigeminal neurons and the activation of TRPV1 has been reported to cause an increased neuronal release of CGRP, in turn resulting in neurogenic inflammation within the meninges, possibly initiating migraine attacks[5]. Furthermore, the observation that TRPV1 is more expressed in fibers innervating human scalp arteries of patients affected by chronic migraine compared to controls, supports the plausible role of this protein as a structural factor favouring migraine chronicization[6]. In the present study we hypothesized that genetic variations affecting structural domains of TRPV1 gene may have a role in modulating triptan response in migraineurs. In addition, we investigated the role of TRPV1 SNPs as susceptibility factors for medication overuse headache (MOH), a chronic daily headache caused by an excessive use of medication taken for symptomatic headache relief [7].

Adult migraineurs treated with triptans, MOH patients and control healthy subjects referring to the Headache Center of Mondino Institute of Pavia and the Headache Center of 'Maggiore della Carità' University Hospital of Novara, have been recruited. Genotyping of two functional SNPs of TRPV1 gene (rs222747 and rs8065080) was performed by real-time PCR using Applied Biosystems TaqMan Pre-Designed SNP Genotyping assays. The association between SNPs and studied outcomes (risk of poor response to triptans in migraineurs and risk of migraine chronicization to MOH) was assessed using logistic regression analysis adjusted by confounding clinical covariates, under a log-additive, dominant, or a recessive mode of inheritance.

Results of the present study, which will be presented at the Seminar, are expected to i) unravel subpopulations of migraineurs that, at present, are inadequately treated with triptans; and ii) better elucidate the role of TRPV1 as a key protein in triptans pharmacodynamics and migraine chronicization to MOH.

References

1. Jensen R, Stovner LJ. Lancet Neurol. 2008;7(4):354-61.
2. Sarchielli P, Granella F, Prudenzano MP et al. J Headache Pain. 2012;13 Suppl 2:S31-70.
3. Dussor G. Curr Opin Support Palliat Care. 2014;8(2):137-42.
4. Evans MS, Cheng X, Jeffry JA, et al. Headache. 2012;52:773–784.
5. Price TJ, Flores CM. J Pain. 2007;8(3):263-72.
6. Del Fiacco M, Quartu M, Boi M et al. J Neurol Neurosurg Psychiatry. 2015;86(4):393-7.
7. Diener HC, Limmroth V. Lancet Neurol. 2004;3(8):475-83.