

MODULATION OF CEREBRAL HEMODYNAMICS BY ATOGEPANT IN EPISODIC MIGRAINE: A TRANSCRANIAL DOPPLER FOLLOW-UP STUDY

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Background. Migraine is characterized by dynamic neurovascular dysregulation, with endothelial dysfunction and impaired cerebrovascular reactivity (CVR) contributing to disease expression and progression. Calcitonin gene-related peptide (CGRP) plays a central role in both vascular modulation and trigeminovascular activation. However, the hemodynamic effects of CGRP receptor antagonism remain incompletely explored. Objective is to evaluate changes in cerebral hemodynamics and vasoreactivity in patients with episodic migraine treated with atogepant.

Methods. Twenty-three patients with episodic migraine underwent transcranial Doppler (TCD) examination at baseline (T1) and after 3 months of preventive treatment with atogepant (T2). Mean flow velocity (MFV), pulsatility index (PI), and breath-holding index (BHI) were assessed in the middle cerebral artery. A paired t-test was used for longitudinal comparisons. Patients were also assessed using the MIDAS scale.

Results. The study initially enrolled a population of 28 subjects, subsequently reduced to 23 evaluable patients (mean age approximately 41 years, predominantly female) following careful selection aimed at excluding potential cardiovascular confounding factors. The sample appeared clinically homogeneous, with a clear predominance of migraine without aura (96%).In the left hemisphere, a statistically significant reduction in the Breath-Holding Index (BHI) was observed, decreasing from 0.76 ± 0.26 to 0.61 ± 0.26 ($p = 0.011$). In parallel, the left side showed an increase in the Pulsatility Index (PI) ($p = 0.0027$) and a reduction in the baseline–post-apnea peak velocity variation (from 17.47 to 14.21 cm/s; $p = 0.026$), along with an increase in baseline velocity at T2, particularly on the left. Taken together, these parameters suggest a restoration of basal vascular tone and an increase in peripheral resistance in a vascular territory previously characterized by hemodynamic instability. In contrast, the right hemisphere exhibited less pronounced changes, confirming an asymmetric response to treatment.

Conclusions. The integration of the analyzed hemodynamic parameters (BHI, PI, and ΔV) supports an adaptive modulation of the cerebrovascular network induced by treatment with atogepant. After a three-month follow-up, a shift toward greater stability and reduced dynamic variability of flow is observed, particularly within the vascular territory of the dominant (left) hemisphere. This phenomenon is consistent with a restoration of homeostatic control of basal vascular tone.From a pathophysiological perspective, this hemodynamic pattern suggests a potential endothelial-protective effect of the molecule. Antagonism of the CGRP receptor appears to mitigate oxidative stress and neurovascular inflammatory processes, which are key elements in the migraine chronification. The more pronounced response observed in the left hemisphere reflects the known hemodynamic vulnerability of regions with higher synaptic density and elevated metabolic turnover, which in these patients benefit from a functional reorganization of flow regulation.In line with current theoretical models in the literature, the results indicate that atogepant acts by attenuating the hyper-reactivity of the trigeminovascular system to vasodilatory stimuli (such as hypercapnia). The reduction in the Breath-Holding Index (BHI) and ΔV, together with the increase in the Pulsatility Index (PI), should therefore not be interpreted as a depletion of hemodynamic reserve, but rather as a normalization of endothelial reactivity. In conclusion, the treatment promotes stabilization of cerebrovascular dynamics, optimizing autoregulatory efficiency and reducing susceptibility to dysfunctional hyperemic responses. CGRP receptor blockade with atogepant is associated with a favorable modulation of cerebral hemodynamics in episodic migraine. These findings support the vascular safety of gepants and suggest a potential indirect restoration of endothelial-dependent vasoreactivity.