

ROLE OF SPECIFIC MICRORNAS IN CLUSTER HEADACHE: ASSOCIATION WITH DISEASE PHENOTYPE AND NEUROPEPTIDE LEVELS

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Background. Increasing evidence supports the role of epigenetic mechanisms in primary headaches. microRNAs (miRNAs) may be involved in pain generation and migraine chronification, but their involvement in cluster headache (CH) is yet to be elucidated. This study evaluated the expression of selected miRNAs and pain-related neuropeptides in episodic cluster headache (eCH) during the active (AeCH) and remission (ReCH) phases, and in chronic cluster headache (cCH).

Methods. Fasting peripheral blood samples were collected to isolate peripheral blood mononuclear cells (PBMCs) and serum. Expression of miR-382-5p, miR-34a-5p, and miR-155 was assessed in PBMCs using Relative Quantification (RQ) normalized to the U6 housekeeping gene. We measured serum levels of alpha and beta calcitonin gene-related peptide (CGRPα, CGRPβ), pituitary adenylate cyclase-activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP) using validated ELISA kits in AeCH and cCH patients outside an acute attack.

Results. We enrolled 39 AeCH patients (age: 45.7±11.6 years, 31 males), 27 ReCH patients (age 47.4±11.6 years, 23 males), 19 cCH patients (age: 50.8±14.4 years, 16 males) and 23 healthy controls (HCs: age: 40.5±15.3 years, 15 males). No differences in miRNA expression were observed between CH participants and HCs. However, miR-155 expression was significantly lower in eCH compared to cCH (eCH: 0.18±0.12 RQ vs. cCH: 0.32±0.14 RQ, p=0.001), a finding confirmed when comparing AeCH with cCH (AeCH: 0.15±0.12 RQ vs. cCH: 0.32±0.14 RQ, p<0.001). CGRPα and PACAP levels were significantly higher in both AeCH and cCH groups compared to HCs. As regards CGRPα: AeCH 443.88±218.22, cCH 400.74± 201.67, HCs 214.35±114.89 (AeCH vs HCs p<0.001; cCH vs HCs, p =0.017). For PACAP: AeCH 50.57± 17.42; cCH 53.89±17.68; HCs: 35.93± 10.85 (AeCH vs HCs p<0.005; cCH vs HCs, p =0.03). No differences were found for CGRPβ or VIP levels.

Conclusions. Our data support the involvement of miR-155 and neuropeptides in CH pathophysiology. Our results confirm data from literature supporting a pro-inflammatory state in chronic CH, when considering that a higher miR-155 expression is consistent with an activation of the inflammatory pathway.