

MEETING ABSTRACTS

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AL001

Overuse of analgesics can affect the fertility biomarker Anti-Müllerian hormone in females. A translational study

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Objective: Over-the-counter analgesics (OTC) have been associated with disrupted male endocrinology, while effects on female endocrinology remains nearly unknown. The aim was to understand the effect of long-term analgesic exposure in females with medication overuse headache (MOH) on Anti-Müllerian Hormone (AMH), a surrogate measure of female fertility.

Methods: Using a translational approach, an observational prospective clinical study was conducted to determine AMH-levels in females with MOH, in combination with pre-clinical investigation of primary granulosa cells (GC) to understand the effects of analgesics on GC-function.

Results: We included 21 females (mean-age 30.0 years; SD (7.3)) for AMH-measurement. AMH increased by 21% from baseline (mean 20.1 pmol/L; SD (8.7)) after withdrawal of analgesics ((mean 24.3pmol/L; SD (12.0)); $p=0.0023$). Exposing primary GCs to analgesics (acetaminophen (100 and 200 μ M, $n = 9-10$) and ibuprofen (150 and 200 μ M, $n = 12-13$)) did not reduce AMH-levels. In contrast, *de novo* DNA synthesis in GCs ($n=6$) exposed to acetaminophen was reduced with 78% ($p=0.0036$) compared to controls, suggesting that cellular proliferation was restricted.

Conclusion: Frequent use of OTC was associated with repressed AMH-levels likely through disruption of GC proliferation. Further research is crucial to investigate a potential effect of analgesics on adult female reproductive endocrinology.

AL002

Sex differences in RAMP1/RAMP2 expression in the human middle meningeal artery match functional response to CGRP

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Objective: CGRP induces vasodilation after binding to the CGRP receptor (CLR-RAMP1), but can activate the adrenomedullin receptor (CLR-RAMP2) as well. Previously, age-dependent sex differences were observed for CGRP-induced relaxation of human middle meningeal arteries¹. In addition, RAMP1 and RAMP2 mRNA expression was highly variable between patients². The current study aims to investigate whether RAMP1 and RAMP2 expression differs between men and women and varies throughout life.

Methods: RNA was isolated from homogenized human middle meningeal arteries (14 F, 12 M, age 51 ± 3 years) and qPCR was performed for RAMP1 and RAMP2 mRNA expression. The ratio between RAMP1 and RAMP2 expression with increasing age was investigated for men and women separately.

Results: The RAMP1/RAMP2 ratio significantly decreases with age in men, while a positive trend can be observed for women. These findings match the pattern of maximum relaxation to CGRP as observed in a previous study¹, with a significant decrease with age in men and a trend for increased maximum relaxation with age in women.

Conclusion: The current study suggests that the maximum effect of CGRP-induced relaxation of human middle meningeal arteries matches the ratio of RAMP1/RAMP2 expression, and changes in a sex-dependent manner with increasing age. Interestingly, migraine is generally most prevalent in pre-menopausal women. Here, these young women show a relatively high RAMP2 and low RAMP1 expression, suggesting predominance of the adrenomedullin receptor over the canonical CGRP receptor in this population. Possibly, increased exposure of CGRP in young women results in downregulation of RAMP1. Future research should investigate whether RAMP1 and RAMP2 expression is altered in migraine patients.



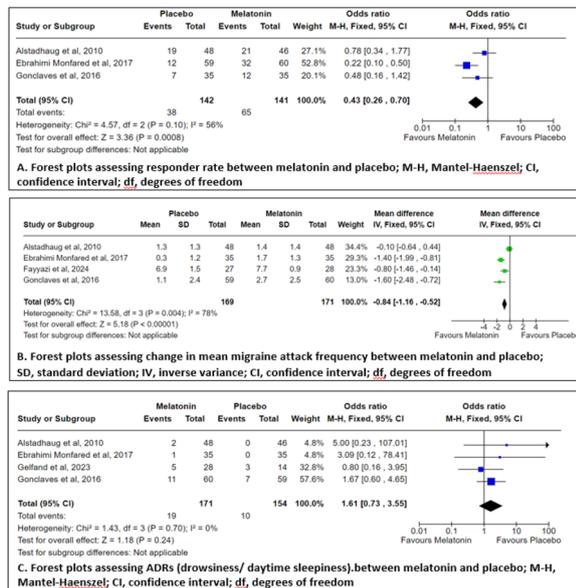


Fig. 1 (Abstract P319). See text for description

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Objective: In recent years many researches have focused on the investigation of migraine. In our observational study we aimed to evaluate the diagnostic value of transcranial doppler (TD) in migraine.

Methods: We included 1546 male patients (mean age 18 years) undergoing check-up in neurological department for military service eligibility. Migraine was diagnosed in 35 patients: 22 migraine without aura (M), 13 migraine with aura - (MA), 2 of them -sporadic hemiplegic migraine (HM). Diagnose were made according to ICHD –3 diagnostic criteria. All patients underwent TD as part of their check-up.

Results: Among the 22 M cases, 6 exhibited changes in linear blood flow velocity (LBFV) on TD, while 5 out of 13 MA cases showed similar changes. Decreased LBFV in the vertebral artery (VA) was observed in 10 out of 35 cases (6 M, 4 MA), and increased LBFV in both middle cerebral arteries (MCA) were noted in 3 cases (2 M, 1 MA). During the observation period, 4 patients developed spontaneous migraine attacks, during which TD was repeated (Table 1).

Table 1 (Abstract P320). LBFV on TD before and during attack

Interictally	During attack
Normal	decreased in MCA, and ACA from right side (side of pain).
increased in both MCA, decrease in right VA	Increase in both MCA > from right (side of pain), in VA no changes
Normal	Significant increase in right MCA (side of pain), decrease in left VA
Normal	Increase in LBFV in right MCA (side of pain)

ACA – anterior cerebral artery

As shown in Table 1, in 3 cases with normal interictal TD, changes were mainly observed in the MCA on the side of pain during a migraine attack.

Conclusion: Our findings suggest that changes in blood flow in the cerebral arteries (MCA and VA) detected by TD during different stages of migraine may have diagnostic value. Further detailed investigations with larger patient cohorts and comparisons with other primary headaches and healthy controls are necessary.

P321

Migraine and cognitive dysfunction: a narrative review

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Objective: The association between migraine and cognitive impairment has been studied, however, the relationship is not well established. Regarding the prevalence of migraine and the aging of the population, this topic has substantial public health implications. Thus, we aim to review the topic of cognition in migraine patients.

Methods: Based on non-systematic research in PubMed, we performed a narrative review of cognitive dysfunction and impairment in migraine. We included studies that reported cognitive symptoms or/and cognitive performance in the different migraine phases, subtypes, and their impact on migraine patients. All authors made both descriptive and interpretive analyses.

Results: Cognitive complaints are widespread in migraine patients, not only during the migraine episode but also in the inter-ictal phase. Cognitive dysfunction negatively affects the quality of life and daily functioning of migraine patients. Studies confirm that a reduction in cognitive performance occurs during the ictal phase and can persist in the post-ictal period. However, these cognitive impairments could be considered an epiphenomenon due to the ongoing pain processing. No consensus exists according to the phenotype with aura (MwA) and without aura (MwoA). Some studies reported that MwA patients have impaired attention and processing speed but findings are inconsistent. However, there is no significant difference in executive control network functional connectivity between MwA and MwoA. Functional neuroimaging studies captured brain changes according to migraine phases but only during attacks the existence of a neural basis for cognitive performance was found.

Conclusion: The fact that migraine presents as a paroxysmal disorder might affect the estimation of the association between migraine and cognitive outcomes. Although evidence suggests a reduction in cognitive performance throughout the migraine episode, it is not possible to conclude the presence of cognitive impairment during the pre-ictal and postictal phases.