

MEETING ABSTRACTS

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AL001

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

L. Carlsen

Rigshospitalet Glostrup, Neurology Department, Glostrup, Denmark
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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

T. de Vries, D. Schutter¹, R. Dammers², A. Vincent², A. H. J. Danser¹, A. Maassen van den Brink¹

¹Erasmus MC University Medical Center, Internal Medicine, Division of Pharmacology and Vascular Medicine, Rotterdam, Netherlands; ²Erasmus MC University Medical Center, Neurosurgery, Rotterdam, Netherlands

Correspondence: T. de Vries

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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.



Articles	Headache Frequency	Headache Intensity	Headache Duration	Medication Taken
	p-value			
	Intention to Treat Analysis			
Specific Music Therapy for Primary Headaches in Adolescents (Koenig et al., 2013)	0.00	0.48		
	Completers			
Smartphone Based Music Intervention for Episodic Migraine (Parlongue et al., 2021)	0.01	0.31	not significant*	
Binaural Stimulation in Migraine (Lovati et al., 2019)	0.009	0.02		0.02
	p(C) value			
	Intention to Treat Analysis			
	Post Treatment			
Butterbur Root and Music Therapy in Childhood Migraine (Oelkers-Ax et al., 2008)	0.042			
	Follow Up			
	0.076			
	Completers			
	Post Treatment			
	0.005	0.505		
	Follow Up			
	0.018	0.793		

* p-value was not stated in the article text

Fig. 1 (Abstract LP021). Summary of Significance Outcome

Article	Randomization	Similar Group	Equal Treatment	Accountability	Blinding	Levels of Evidence
Specific Music Therapy for Primary Headaches in Adolescents (Koenig et al., 2013)	+	+	+	+	+	Moderate
Smartphone Based Music Intervention for Episodic Migraine (Parlongue et al., 2021)	-	-	-	-	-	Low
Binaural Stimulation in Migraine (Lovati et al., 2019)	-	-	-	-	-	Low
Butterbur Root and Music Therapy in Childhood Migraine (Oelkers-Ax et al., 2008)	+	+	+	+	?	Moderate

+ = Stated clearly in the article
 - = Not stated
 ? = Unclear

Fig. 2 (Abstract LP021). Critical Appraisal of Articles Based on CEBM Oxford 2011

LP022

Galcanezumab in a 28-year old female with Myasthenia gravis and chronic migraine

V. Tischler-Strasser¹, K. Lehner¹, C. Lampl¹, A. Maassen van den Brink²
¹Saint John of God Hospital Linz, Neurology, Linz, Austria; ²Erasmus MC, Clinical Pharmacology, Rotterdam, Netherlands

Correspondence: V. Tischler-Strasser
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Objective: Myasthenia gravis (MG) is a neuromuscular, immune mediated disease, resulting in muscle weakness. Any medical treatment in individuals with Myasthenia gravis can lead to precarious clinical decisions, as various drugs can worsen the symptoms in patients with

Myasthenia gravis. This is especially true in patients suffering from other neurologic diseases like chronic migraine.

Methods: We present the case of a 28-year-old female suffering from Myasthenia gravis and chronic migraine at the same time. After a detailed risk-benefit assessment, which included extensive database research, the administration of Galcanezumab was initiated.

Results: The medication was well-tolerated, no further worsening of the symptoms of Myasthenia could be observed.

Conclusion: The treatment of chronic migraine with Galcanezumab in patients with MG seems to be possible. Although it seems to have an effect on the immune system, until now no hint for Galcanezumab triggered antibody-production of any kind (with exception from allergic reactions) could be observed.

To ensure safety for patients and medical professionals further research is needed. Not only should this aim on additional patient characteristics, that may indicate worsening, but also the possible influence of MG medication.

The patient gave their explicit informed consent to publish their information in an open access journal.

LP023

Migraine epidemic or policy effect? How reimbursement shaped diagnosis trends in Lithuania

G. Makarevičius, A. Dapkutė, K. Ryliškienė
 Vilnius University, Center of Neurology, Faculty of Medicine, Vilnius, Lithuania

Correspondence: A. Dapkutė
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Objective: We aimed to ascertain how reimbursement changes of novel monoclonal antibodies acting against calcitonin-gene related peptide or its receptor (anti-CGRP/R) (erenumab became reimbursed since 2020 June 01 and fremanezumab since 2021 January 28) has influenced the diagnostic rates of migraine and other headaches.

Methods: The annual numbers of people diagnosed with G43, G44 and G50 as defined by the ICD-10 were obtained from the Institute of Hygiene, Ministry of Health of the Republic of Lithuania. Medical sales (defined daily doses (DDD) and monthly doses sold) data was obtained from the State Medicines Control Agency of Lithuania. Number of diagnoses and sale data of migraine-specific acute and preventive medications before the implementation of reimbursement policies of anti-CGRP/R monoclonals (2017-2019) were compared with years after policy implementation (2021-2023). All statistical analyses were performed using R software.

Results: In post-reimbursement years, the number of total migraine diagnoses (G43) increased by 40.6% from 14088 cases in 2019 to 23705 in 2023. In 2021-2023, there were more yearly new migraine diagnoses than in 2017-2019 (3417.67 and 894.33 per year on average respectively, p=0.015). The rate of change for migraine statistically significantly increased post-reimbursement (p<0.001). Other headache disorders (ICD code G44) and trigeminal neuralgia (ICD code G50) did not face a significant change in new yearly diagnoses (p=0.116 and p=0.420, respectively). Sales of triptans increased by 54.02% from 954389 DDD sold in 2019 to 1469973 DDD in 2023. Sales of anti-CGRP/R monoclonals increased by 6483.8% from 462 monthly doses in 2019 to 30417 in 2023.

Conclusion: The reimbursement of anti-CGRP/R monoclonals by the National Health Insurance Fund under the Ministry of Health of Lithuania has significantly increased the number of migraine diagnoses. This trend underscores the importance of access to effective treatments in encouraging patients to seek medical care proactively.