

# MEASUREMENT OF PLASMA CGRP LEVEL IN PEDIATRIC MIGRAINE PATIENTS CHIOU & AL. 2019

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## CONTEXT

Migraine is a disorder characterized by recurring pulsating headaches with increased sensitivity to light, sound and head movement. It is one of the leading causes of disability.

Few studies have characterized the effect of anti-migraine medications on children. Since most young children cannot accurately describe their symptoms, finding biomarkers that can guide the choice of migraine treatment is crucial.

Calcitonin gene-related peptide (CGRP) has been shown to be a biomarker of migraine in adults. CGRP causes dilatation of both peripheral and cerebral blood vessels. Baseline plasma CGRP levels are significantly higher in migraine adult patients than in healthy controls. Additionally, during a migraine attack, the plasma CGRP levels of both adult and pediatric patients increase and strongly correlate with headache intensity.

In this study, the scientists explore whether CGRP could be a biomarker helping stratification of migrainous children, by studying the relation between plasma CGRP levels and the responses to anti-migraine therapies.

## MATERIALS

- CGRP (human) ELISA kit (Cat No. A05481, Bertin Bioreagent, France).
- Plasma samples stored at  $-80^{\circ}\text{C}$  between sampling and analysis





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### PROTOCOL

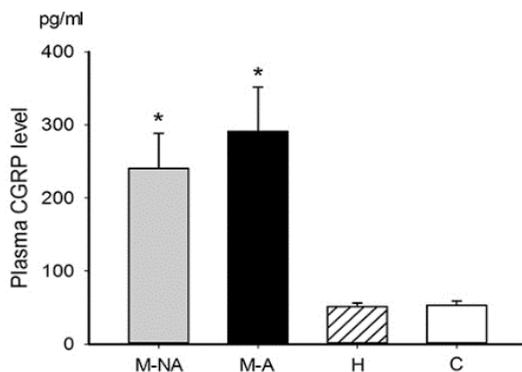
- 120 pediatric subjects were recruited, who never took anti-migraine drugs, including 68 patients with migraine (M), 30 with non-migraine headache (H), and 22 non-headache controls (C).
- Blood (3 ml) sampled from the cubital vein of each patient was put into a 5 ml Lavender tube (BD vacutainer™, Becton Dickenson, Plymouth, UK).
- Plasma samples were prepared by centrifugation (2,000 rpm for 15 min) of the whole blood and then stored at  $-80^{\circ}\text{C}$ .
- Plasma CGRP levels were measured using CGRP (human) ELISA kit (Cat No. A05481, Bertin Bioreagent, France). The person who conducted the CGRP measurement was blinded to the identity, attack status, and treatment of the study patients.
- Short-term therapeutic response to anti-migraine drugs was measured for at least 2 weeks after the start of therapy. Responders were defined with  $>50\%$  headache reduction.

### RESULTS

Mean plasma CGRP level is found higher in migraineurs compared to non-migraine headache patients and to non-headache patients. This higher plasma CGRP is observed during migraine attack as well as between attacks.

Topiramate responders had higher plasma CGRP levels than non-responders ( $437 \pm 131$  pg/ml,  $n = 14$  vs.  $67 \pm 19$  pg/ml,

$n = 6$ ,  $p = 0.021$ ). Survival curves of plasma CGRP levels also showed those with higher CGRP levels responded better to topiramate



*Plasma CGRP levels in different groups. The mean plasma CGRP levels in the migraineurs either during (group M-A) or between (group M-NA) attacks were higher than the non-migraine headache patients (group H) ( $p = 0.006$  and  $0.018$ , respectively) and non-headache controls (group C) ( $p = 0.016$  and  $0.045$ , respectively). The  $p$ -value among groups, analyzed by ANOVA test ( $p = 0.001$ ), followed by post-hoc Tukey HSD.  $*p < 0.05$*

Anti-migraine drug	CGRP in pg/ml (n)		p-value <sup>§</sup>
	Responders	Non-responders	
Cyproheptadine	191 ± 52 (4)	473 ± 188 (8)	0.45
Flunarizine	243 ± 77 (17)	466 ± 158 (13)	0.219
Topiramate	437 ± 131 (14)	67 ± 19 (6)	0.021*
Gabapentin	421 ± 253 (6)	352 ± 265 (6)	0.522

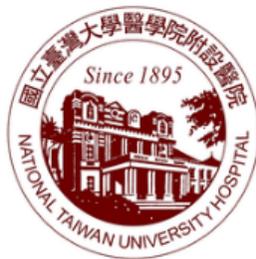
*Comparison of plasma CGRP levels between responder and non-responder to anti-migraine drugs. Data are mean ± SE with the n number in parentheses. The p-value between responder and non-responder groups, analyzed by Mann-Whitney test  $*p < 0.05$ .*



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## CONCLUSION

- This study suggests that the plasma CGRP could be a potential biomarker to help differentiating migraine from non-migraine headache condition in pediatric patients. In this study, the CGRP plasma levels were found considerably higher in topiramate-responsive children indicating that CGRP could also be investigated as an biomarker to categorize pediatric migraine patients. These findings are especially important for young children who cannot precisely describe their symptoms .
- The CGRP ELISA kit from Bertin Bioreagent allows accurate and reliable measurement of CGRP levels in human plasma samples.

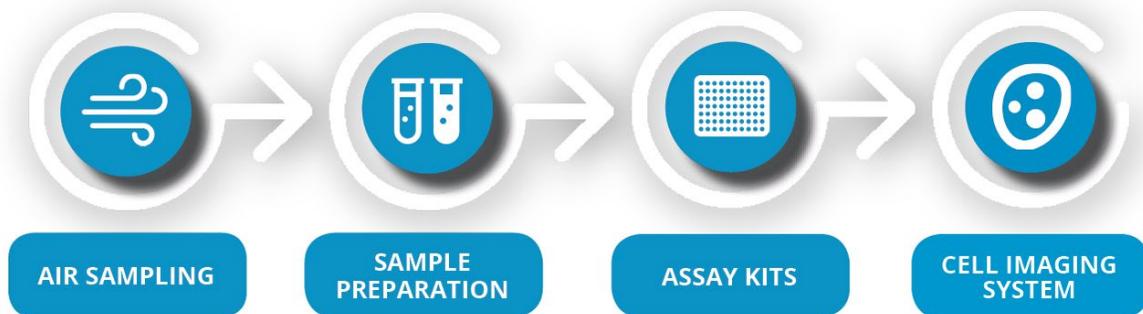


Fan PC, Kuo PH, Lee MT, Chang SH, Chiou LC.

Plasma Calcitonin Gene-Related Peptide: A Potential Biomarker for Diagnosis and Therapeutic Responses in Pediatric Migraine.

Front Neurol. 2019 Jan 24;10:10. doi:10.3389/fneur.2019.00010.

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