

# Childhood migraine chronification: is there a role for prophylactic treatment?

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**Introduction:** Chronic migraine (CM) is a very debilitating condition. In this study we investigated the effect of prophylactic therapy on childhood migraine chronification. We also evaluated predictive factors of chronification.

**Materials and methods:** We included 165 pediatric patients (age < 18 years) with migraine evaluated at Bambino Gesù Children's Hospital from May 2021 to May 2023. All had headache frequency > 4 per month (i.e. "high frequency"), anxiety (GAD-7) and depression (PHQ-9) screening, no ongoing preventive treatment at baseline visit (T0). Demographic and clinical data (headache onset, age of high frequency onset, neuropsychiatric comorbidities) were recorded at T0. Headache frequency, the use of attack and prophylactic treatment were recorded at follow-up T1 (approximately 4 months) and T2 (approximately 12 months). The sample was divided in two groups based on exposure or not to prophylaxis in order to compare the chronification frequency. Subsequently, we divided our cohort in two groups based on progression or not to CM to identify features associated to chronification.

**Results:** 123 (74.5%) patients were female and the median age of disease onset was 10 years (range 5-17). Ninety-three patients (56.3%) received prophylactic treatment (13 topiramate, 24 flunarizine, 19 amitriptyline, 26 palmitoylethanolamide, 11 tryptophan). Among this group, 57 (61.3%) had high frequency onset before 10 years of age. At T1, 43 patients (46%) stopped the treatment due to a monthly migraine attacks reduction, 25 (27%) continued the ongoing therapy and 25 changed treatment. At T2, 13 patients (14%) progressed to CM, of whom 6 overused analgesics and 10 (76.4%) had psychiatric comorbidities. The remaining eighty patients (86%) reported a lower attack frequency at T2. Seventy-two patients didn't receive preventive drugs. Twelve patients (16.7%) overused analgesics and 53 (73.6%) had psychiatric comorbidities. At T2, 64 patients (88.9%) progressed to CM, and 49 of them (76.6%) had psychiatric comorbidities. Chronification frequency was significantly lower in the treated group: 14% vs 88.9% (Odds-Ratio 0.023, 95% CI 0.0079-0.052, p < 0.001), suggesting a protective role of prophylaxis.

We divided our cohort in two groups based on progression or not to CM to identify features associated to chronification. We considered preventive treatment, sex, age of headache onset before and after 10 years, age of high frequency onset before and after 10 years, excessive use of analgesics and psychiatric comorbidities. At univariate analysis, the use of preventive treatment significantly reduced the risk of chronification. Female sex, age of headache onset after 10 years, age of high frequency onset after 10 years, excessive use of analgesics and psychiatric comorbidities were significantly associated to progression to CM. Nevertheless, on multivariate logistic regression analysis, we found that the independent variables significantly associated to progression to CM were excessive use of analgesics (p = 0.001) and psychiatric comorbidities (p = 0.005), while it was confirmed the protective role of preventive treatment (p < 0.001).

## Conclusion

- Chronification frequency is significantly higher in patients who have not received preventive treatment. The protective role of prophylaxis was further confirmed when we analyzed the features associated to chronification. This finding may suggest that clinicians should consider pharmacological treatment in children with increasing headache frequency to prevent CM.
- Female sex, age of migraine onset after 10 years and high frequency onset after 10 years were associated with chronification, but a stronger correlation was found with excessive analgesic use and neuropsychiatric comorbidities. Therefore, it may be beneficial to routinely screen children and adolescents with migraine for anxiety and depression and to educate the patient and parents on the correct use of analgesics.

Multivariate logistic regression analysis		
Independent variable	Dependent variable: chronification	
	OR [95%CI]	p
Psychiatric comorbidities	1.17 [1.05-1.30]	0.005
Preventive treatment	0.49 [0.44-0.54]	< 0.001
Female sex	1.04 [0.92-1.17]	0.5361
Headache onset > 10 y	1.07 [0.94-1.23]	0.313
High frequency onset > 10 y	1.02 [0.90-1.16]	0.714
Excessive use of analgesics	1.26 [1.10-1.44]	0.001

