



# Placebo effect in chronic migraine prevention. A systematic review

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### Background

The preventive management of headaches has different routes of administration (Oral, Subcutaneous, Intravenous, and Application to the head). Placebo effect is a powerful determinant of health outcomes in several disorders, Meta-analysis of clinical trials in pain conditions such as fibromyalgia and osteoarthritis shows placebo effect can contribute to up to 75% of the overall treatment effect. The placebo effect on different routes of administration is poorly described. Thus, we seek to analyze in this meta-analysis the difference between the routes of administration in the placebo effect in the management of chronic migraine.

### Methods

We conducted a meta-analysis with 8 randomized, double blind, Placebo Clinical trials, with 2498 persons. Men and Women over 18 who suffer from chronic migraine (over 15 migraine episodes per month for 3 months) without associated comorbidities. We compared those who received placebo-administered agent for preventive treatment of chronic migraine SC, EV or oral against those who received placebo-administered head injection. The primary outcome was reduction in the number of days with migraine in the month assessed at 12 weeks of treatment compared with baseline.

### Results

Our study showed that placebo responses were greater when botulinum toxin type A was applied in the head, followed by intravenous injection of an anti-CGRP monoclonal antibody eptinezumab. Oral topiramate and subcutaneous Mabs had no difference, being inferior to other routes of administration. Also, our analysis shows that much of the effect of drugs in the treatment of migraine is still due to the high placebo effect, which contributes about 80% of the therapeutic gain.

### Conclusions

Administration route affects placebo responses in CM preventive treatment but not therapeutic gain as much. Elucidating the underlying mechanisms that mediate placebo effect in migraine treatment is beneficial to clinical practice and drug development.

**Keywords:** Chronic migraine, Placebo effect, Randomized clinical trials