



TIMOLOL EYEDROPS VERSUS PLACEBO FOR ACUTE MIGRAINE: SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVE: Oral beta-blockers like timolol are widely used for migraine prophylaxis but are not effective during attacks due to delayed serum levels and low bioavailability. Uncertainty remains about their efficacy via faster routes of administration. Thus, we conducted a systematic review with meta-analysis to evaluate the efficacy of timolol ophthalmic solution 0,5% versus placebo in acute migraine.

METHODS: We searched PubMed, Embase, Cochrane Central and Web of Science for randomized controlled trials comparing timolol ophthalmic solution with placebo in migraine attacks. The analyzed outcome was the effectiveness in controlling migraine attacks, defined as: attacks with a severity of none or mild 120 minutes after onset (Cossack, 2018), attacks with a reduction of 4 points in pain score (from 0 to 10) or its resolution after 20 minutes of pain onset (Kurian, 2020), and attacks with a decrease of $\geq 50\%$ in pain score (from 0 to 10) after 120 minutes of pain onset (Aggarwal, 2020). Statistical analysis was performed using RevMan 5.4.1. Heterogeneity was assessed with I^2 statistics. The PRISMA protocol was used for the selection of studies (Figure 1).

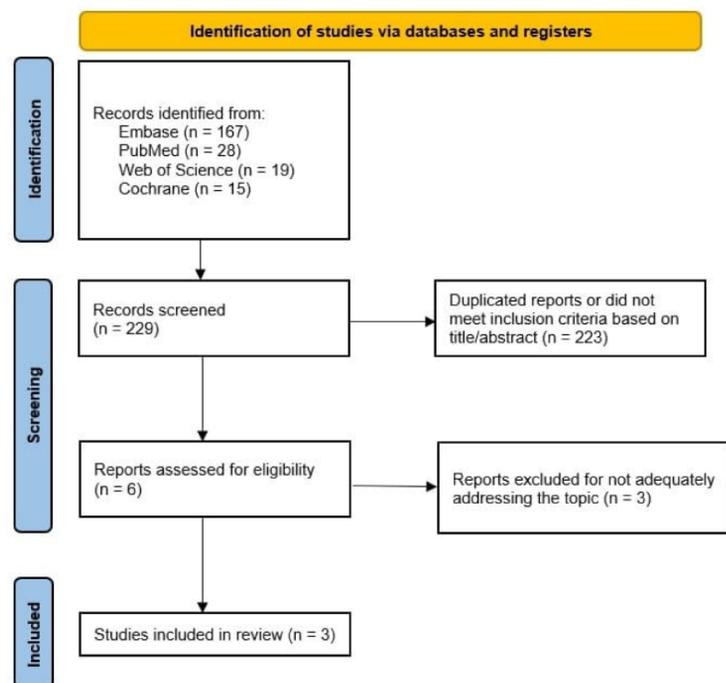


Figure 1. PRISMA flow diagram of study screening and selection.

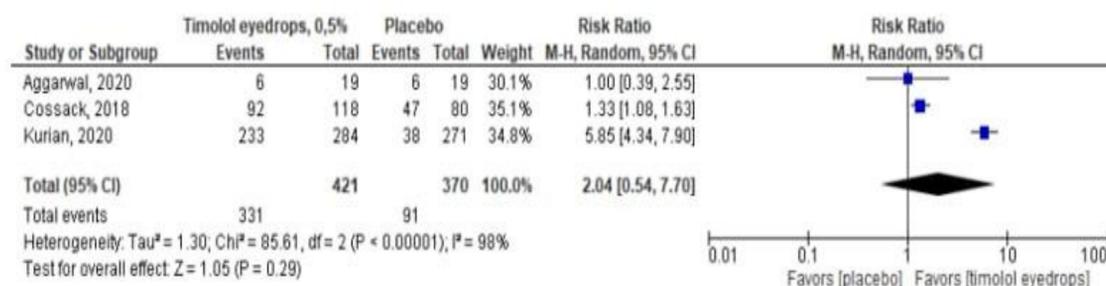


Figure 2. Forest plot of the effectiveness in controlling migraine attacks comparing timolol eye drops versus placebo.

RESULTS: The initial search yielded 229 results, of which 59 were removed due to duplication and 164 were excluded based on title/abstract screening. Of the remaining 6 studies, 3 did not adequately address the topic. We found only 3 crossover studies. Despite the methodological heterogeneity between them, we decided to include all the 72 patients which totaled 791 attacks analyzed. Timolol was used to treat 421 (53.2%) attacks. Effectiveness in controlling migraine attacks (RR 2.04; 95% CL 0,54-7.70; p=0.29; $I^2=98\%$) did not differ significantly from placebo.

CONCLUSION: In conclusion, timolol eye drops showed no statistically significant efficacy in acute migraine management versus placebo (Figure 2). However, further randomized studies are needed due to high heterogeneity in results and methods.

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