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LETTER TO THE EDITOR

Acceptability of 8 atropine concentrations for myopia control in children: a network meta-analysis

Ahnul Ha · Seong-Joon Kim · Young Kook Kim · Jae Ho Jung

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Dear Editor

Myopia has been of increasing worldwide health concern over the past few decades [1]. Recent studies have demonstrated that atropine is one of the most effective treatments for slowing down childhood myopia progression [2, 3]. However, premature treatment termination (i.e., dropout) is a significant hindrance limiting the effectiveness of atropine. Certainly, when long-term management is required, acceptability is an important part of treatment success additional to efficacy and lack of adverse effects. Thus, the aim of this study was to compare dropout rates among various atropine concentrations using a network meta-analysis (NMA).

The study protocol was prospectively registered at PROSPERO (CRD42021248957). We systematically searched the Cochrane Register of Controlled Trials in The Cochrane Library, PubMed, and EMBASE on May 31, 2022. The keywords included were *myopia* and *atropine*. Two investigators independently selected randomized controlled trials (RCTs) according to the following criteria: (1) participants younger than 18 years, (2) atropine treatment duration of at least 12 months, and (3) reporting of proportion of all-cause discontinuation (i.e., dropout rate). An NMA was performed using the R package "netmeta". We aggregated the dichotomous outcomes based on relative risk (RR). Arm-based analyses were performed to estimate the RR and 95% confidence interval (CI). Heterogeneity was quantified using the (within-design) Q statistic, the between-study variance τ^2, and the heterogeneity statistic I^2 [4]. We used local and global approaches for consistency testing [5]. We ranked the atropine concentrations by P-score. Publication bias was assessed by Egger test.

Online Resource, Fig. 1 shows a flowchart of the study analysis. Among the 16 trials (4,298 participants), 8 different concentrations of atropine were involved: 1, 0.5, 0.25, 0.1, 0.05, 0.025, 0.02, and 0.01% (Fig. 1A and Online Resource, Table 1).

As indicated in Fig. 1B, 0.05% atropine showed the lowest dropout rate (0.47; 95% CI = 0.16–1.44) and was estimated to be the best concentration

Young Kook Kim and Jae Ho Jung are the authors contributed equally to the study as co-corresponding authors.

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A. Ha
Department of Ophthalmology, Jeju National University School of Medicine, Jeju-Si, Korea

S.-J. Kim · Y. K. Kim (✉) · J. H. Jung (✉)
Department of Ophthalmology, Seoul National University College of Medicine, 101 Daehak-Ro, Jongno-Gu, Seoul 03080, Republic of Korea
e-mail: md092@naver.com

J. H. Jung
e-mail: jaeho.jung@snu.ac.kr

(*P*-score = 0.857). However, there were no statistically significant differences among the various concentrations of atropine and the control in terms of the RR of dropout, which ranged from 0.47 (95% CI = 0.16–1.44 for 0.05%) to 1.57 (95% CI = 0.90–2.73 for 1%).

Our NMA showed moderate cross-study heterogeneity ($I^2 = 50.6\%$), and between-design inconsistency was not significant ($Q = 5.71$; $\tau^2 = 0.32$; $P = 0.46$). There was no disagreement between the direct and indirect estimates (all Ps ≥ 0.05) and no significant risk of publication bias ($P = 0.45$).

The overall dropout rate across all RCTs included in the NMA was 11.8% (range: 2.0–30.9%). Although 0.05% atropine showed the lowest dropout rate, there were no significant dropout rate differences among the various concentrations of atropine. Our previous NMA revealed that efficacy was not proportional to dose (0.05%, comparable to high-dose atropine) but that adverse effects were dose-related [2]. Interestingly, the current study also found that dropout rate was not dose dependent. Adverse effects could be one of the major factors in premature termination of treatment. Even though 0.05% is a higher dose than 0.01, 0.02 or 0.025%, its adverse effects did not increase the dropout rate.

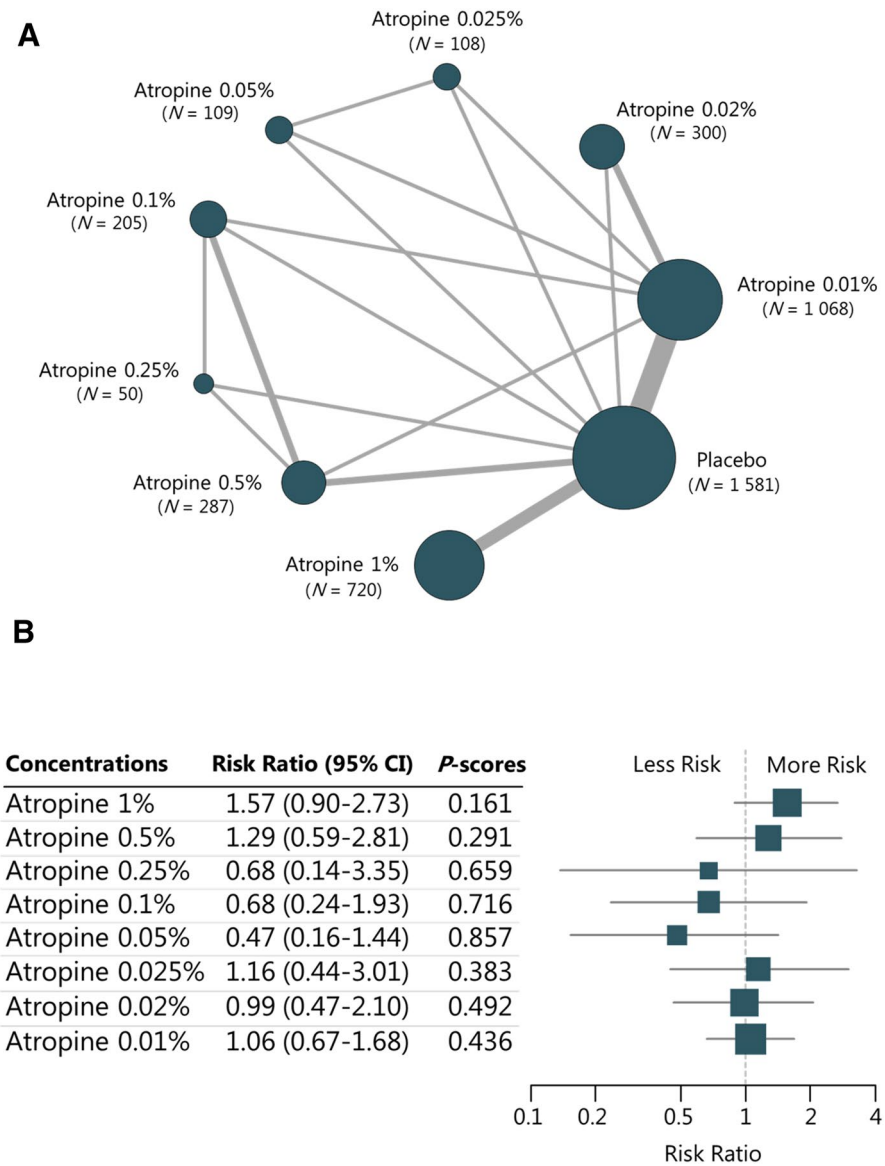

Fig. 1 **A** Network plot. The node size corresponds to the number of participants assigned to each treatment. Treatments with direct comparisons are linked with a line; line thickness corresponds to the number of trials evaluating the comparison. **B**. Forest plot of NMA comparing different doses of atropine for discontinuation risk. Each atropine concentration was compared with the control, which was the reference group. CI = confidence interval, RR = relative risk

Unfortunately, the majority of RCTs did not provide reasons for dropout, which fact hampered our ability to draw conclusions regarding the reasons for treatment cessation. Minimizing premature discontinuation of atropine treatment is a critical part of treatment success in slowing down myopia progression. Thus, we suggest that strategies for improving dropout problems should be investigated in order to encourage compliance in long-term atropine usage.

This NMA supports the contention that 0.05% atropine could be the primary dose for high efficacy, tolerable adverse effects, and a low dropout rate in slowing down myopia progression.

Author's contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by AH, SJK and YKK. The first draft of the manuscript was written by Jae Ho Jung and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability statement Derived data supporting the findings of this study are available from the corresponding author Young Kook Kim on request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval This work synthesized evidence from already published studies, and therefore, did not require any ethics review. The Seoul National University Hospital Institutional Review Board has confirmed that no ethical approval is required.

References

1. Dolgin E (2015) The myopia boom. Nature 519(7543):276. https://doi.org/10.1038/519276a
2. Ha A, Kim SJ, Shim SR, Kim YK, Jung JH (2022) Efficacy and safety of 8 atropine concentrations for myopia control in children: a network meta-analysis. Ophthalmology 129(3):322–333. https://doi.org/10.1016/j.ophtha.2021.10.016
3. Huang J, Wen D, Wang Q et al (2016) Efficacy comparison of 16 interventions for myopia control in children: a network meta-analysis. Ophthalmology 123(4):697–708. https://doi.org/10.1016/j.ophtha.2015.11.010
4. Higgins JP, Thompson SG, Deeks JJ, Altman DG et al (2003) Measuring inconsistency in meta-analyses. BMJ 327(7414):557–560. https://doi.org/10.1136/bmj.327.7414.557
5. Cipriani A, Higgins JP, Geddes JR, Salanti G (2013) Conceptual and technical challenges in network meta-analysis. Ann Intern Med 159(2):130–137. https://doi.org/10.7326/0003-4819-159-2-201307160-00008