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Different Atropine Concentrations for Myopia Control in Chinese children and adolescents—A Systematic Review and Network Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Not have.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 August 2023 and was last updated on 06 August 2023.

INTRODUCTION

Review question / Objective To investigate the effects of different concentrations of atropine on delayed myopia progression in Chinese children and adolescents through a network meta-analysis.

Rationale Myopia is the most common refractive error in children and adolescents; it usually begins to develop in childhood and continues into adulthood and has become a public health problem worldwide. By 2050, the total number of cases of myopia worldwide is expected to reach 4.7 billion, whereas that of high myopia will reach 900 million. According to relevant data, the overall myopia rate among Chinese children and adolescents was 53.6% in 2018. In Taiwan and China, the number of children and adolescents aged 6–16 suffering from myopia is as high as 76%.

Myopia, especially high myopia, significantly increases the risk of ocular pathology and visual impairment, triggering physiological disorders such as glaucoma, retinal atrophy, retinal detachment, macular disease, and optic neuropathy. Visual impairment, especially uncorrected refractive error, is positively associated with anxiety and depression, which affect the mental health of children and adolescents. Therefore, there is an urgent need to slow down the progression of myopia among children and adolescents.

Myopia in children and adolescents can be treated through several methods. Some treatments that delay myopia progression in children and adolescents include increasing the time spent outdoors, changing close work habits, administration of topical medications, eye surgery, wearing corrective eyeglasses, and repetitive low red-light therapy. Among these, atropine eye drops and glasses to correct vision have been proven to be more effective methods for delaying progression relative to other methods, and atropine solution has been proven to be the most effective.

Although the efficacy of atropine solution has been recognized, adverse effects and the rebound phenomenon after its use remain a concern. The adverse effects of atropine eye drops are dose

dependent, though efficacy is not [11]. Ha et al., in 2021, explored the effects of eight different concentrations of atropine solutions on the progression of myopia in children and adolescents globally; however, differences in iris color in different regions of the country and in different races of the population may have different impacts on the efficacy of atropine solutions. Therefore, this study aimed to explore the optimal concentration of atropine solution for delaying myopia progression in children and adolescents in China and to lay the foundation for the determination of the optimal atropine solution for delaying myopia progression in different countries and races.

Condition being studied Myopia is a kind of Refractive error. When the eye is in a relaxed state of adjustment and parallel light enters the eye, it focuses before the retina, which leads to the inability to form a clear image on the retina, known as myopia. At this point, the examination of refraction will indicate the degree of myopia, for example, it is usually called 50 degrees myopia and recorded as "-0.50 D".
In a relaxed state of eye regulation, when parallel light from the outside enters the eye and its focus falls precisely on the retina, a clear image is formed, which is called emmetropia; If the focus cannot fall on the retina, it is called emmetropia, that is, Refractive error.

METHODS

Search strategy The PubMed, Web of Science, Cochrane Library, EMBASE and Clinicals.gov will be searched. The search time will be set from construction of the database to June 2023, and the search terms used will be the subject and free words. The corresponding Boolean logic operators will be used to construct the search formula, and the English search terms included “atropine,” “atropinol,” “atropine sulfate,” “sulfate,” “atropine,” “atropine sulfate anhydrous,” “anhydrous, atropine sulfate,” “anhydrous, atropine sulfate,” “sulfate anhydrous, atropine,” “atropen,” “atropine eugenol,” “augenöl, atropin,” “cholinergic antagonists,” “children,” “adolescents,” “adolescence,” “teens,” “teenagers,” “youths,” “adolescents, female,” “female adolescents,” “adolescents, male,” “male adolescents,” “juvenile,” “myopia,” “myopias,” and “night sightedness.” The language used will be limited to English.

Participant or population Study subjects: subjects aged ≤18 years and having a confirmed diagnosis of myopic refractive error.

Intervention Intervention group measures: treatment of the intervention group with atropine eye drops.

Comparator Control group measures: use of different concentrations of atropine eye drops or use of a blank placebo compared with the intervention group.

Study designs to be included The Cochrane Library, PubMed, Web of Science, EMBASE and Clinicals.gov will be systematically searched for relevant literature on the delayed progression of myopia with different concentrations of atropine solutions from the establishment of the database to June 2023. Data from the included literature will be extracted and evaluated for their quality, and a network meta-analysis will be subsequently performed using Stata version 14.0 software. Results will be plotted as graphs.

Eligibility criteria The inclusion criteria were as follows. 1) Study subjects: subjects aged ≤18 years and having a confirmed diagnosis of myopic refractive error; 2) intervention group measures: treatment of the intervention group with atropine eye drops; 3) control group measures: use of different concentrations of atropine eye drops or use of a blank placebo compared with the intervention group; 4) outcome observables: axial length of the eye and refractive error of the eye; 5) type of study: observational or randomized clinical trial study (RCT); and 6) study conducted in China.

Information sources A total of 1104 relevant papers will be retrieved, 356 duplicates will be screened, 613 papers unrelated to this study will be excluded after further reading the title and abstract,109 papers that will do not meet the requirements will be screened out after reading the full text according to the inclusion and exclusion criteria of the study, and 14 papers will be included in the reticulation meta-analysis. Of these studies,11 will be RCTs, and 3 will be retrospective cohort studies. The screening flowchart will be shown in Figure.

Main outcome(s) Axial length of the eye and refractive error of the eye.

Quality assessment / Risk of bias analysis The risk of bias assessment tool provided in the Cochrane Handbook for Systematic Evaluation 5.4 will be used to evaluate random sequence generation, allocation concealment, blinding of subjects and investigators, blinding of study results, completeness of results, selective reporting of results, and other sources of bias.

Strategy of data synthesis StataSE software (version 14.0) will be used to create a reticulation plot of direct and indirect comparisons between the results of different concentrations of atropine solutions. When there will be a closed loop in the evidence network, the consistency test will be performed using the node cut method. If the difference between the direct and indirect comparison results will be not statistically significant (P>0.05), the consistency model will be used for the reticulation meta-analysis; otherwise, the inconsistency model will be used. Thereafter, two-by-two comparisons between different atropine solutions will be performed, and a P-value <0.05 suggested that the differences will be statistically significant. Cumulative ranked probability plots (SUCRA) will be drawn using StataSE 14.0. A larger percentage of the area under the cumulative ranked probability curve indicated a more advanced ranking, which, in turn, indicated a better intervention effect. The ratio (OR) and 95% confidence interval (CI) will be used as indicators to analyze categorical variables. Funnel plots will be constructed to evaluate publication bias.

Subgroup analysis After extracting the basic characteristics of the literature, subgroup analyses can be performed for differences in age, region, etc.

Sensitivity analysis If the heterogeneity test found significant heterogeneity, sensitivity analysis was performed using Stata 14 software.

Language restriction English.

Country(ies) involved China.

Keywords Atropine; China; children and adolescents; myopia; network meta- analysis.

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