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Impact of coronavirus disease 2019 restrictions on the efficacy of atropine 0.01% eyedrops for myopia control – Findings from the Western Australia Atropine for the Treatment of Myopia study

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Abstract:

This study explored the impact of short-term coronavirus disease 2019 (COVID-19) restrictions on the efficacy of atropine 0.01% eyedrops on myopia control in a multiethnic cohort of Australian children. In the Western Australia Atropine for the Treatment of Myopia study, 104 and 49 children were randomized to receive atropine 0.01% eyedrops and a placebo, respectively. We compared the 1-year myopia progression and axial elongation following the 2-month lockdown in 2020 to the same months in 2019 and 2021, i.e., the 1-year myopia progression up to May 2019–October 2019 (non-COVID-19) versus the 1-year progression up to May 2020–October 2020 (COVID-19 period), and the 1-year progression up to May 2021–October 2021 (non-COVID-19) versus the 1-year progression up to the same months in 2020. After excluding participants who withdrew, completed their treatment phase prior May 2020, or those whose study visits did not fall between May 2020 and October 2020, 65 participants (mean age at baseline = 11.8 ± 2.5 years) were included in the final analysis (49 in the treatment group; 16 in the placebo group). After correcting for age, sex, and ethnicity, there was no significant main effect of the short-term lockdown on the rate of spherical equivalent or axial length change. However, there was a lockdown × treatment interaction effect on the rate of axial elongation ($P = 0.007$). This was such that in the treatment group, the 1-year axial elongation was faster during lockdown by 0.056 mm compared to the nonlockdown periods ($P = 0.009$), while the rate of axial elongation in those on the placebo eye drops was similar during lockdown and nonlockdown. Our findings suggest that there is a decreased efficacy of low-concentration atropine even with relatively lenient restrictions lasting for a few months.

Keywords:

Atropine, axial length, coronavirus disease 2019, myopia

Introduction

Before vaccines for severe acute respiratory syndrome coronavirus 2 became available, quarantine and lockdowns were the primary measures of containing novel coronavirus disease 2019 (COVID-19). While these measures are effective at containing disease outbreaks, eye care professionals feared that having children spend less time outdoors would accelerate myopia progression and the myopia epidemic.[1] Indeed, several studies have documented more rapid myopia progression in children during the COVID-19 lockdowns in comparison to the pre-COVID-19 era.[2-5] Low-concentration

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atropine treatment for myopia progression during periods of COVID-19 restriction has been reported to have reduced effectiveness;[6,7] however, efficacy relative to during non-COVID-19-impacted time frames have been difficult to explore as studies were not designed to address this issue.

The randomized controlled trial Myopia Outcome Study of Atropine in Children reported a decreased efficacy of atropine 0.01% eyedrops when the treatment period coincided with COVID-19 restrictions. In their study, the authors compared the efficacy of atropine 0.01% in 141 children whose treatment period fully coincided with their 2-month lockdown versus 63 children who entered the trial after restrictions. The investigators found that atropine 0.01% eyedrops were not effective in the highly COVID-19 restrictions impacted group but had significant myopia control effects in the low-impact group.

Here, we report myopia progression as measured using cycloplegic autorefraction and axial length in participants of the Western Australia Atropine for the Treatment of Myopia (WA-ATOM) study[8] before and following the COVID-19 lockdown in Western Australia.

Methods

The WA-ATOM study is a double-masked randomized controlled trial that aimed to determine the efficacy of atropine 0.01% eyedrops for myopia control compared to a placebo. The full protocol has been described previously.[9] Briefly, 153 children, 6–16 years old at baseline with spherical equivalent ≤−1.50 D and documented myopia progression of at least 0.50 D in the preceding 12 months, were randomized to receive either the treatment drops or placebo. Participants with anisometropia >1.00 D, astigmatism >1.50 DC, ocular or systemic comorbidities including amblyopia and strabismus, or who had previously used myopia control treatment were excluded from the trial.

This study was approved by the University of Western Australia Human Research Ethics Committee. Parents/guardians of the participating children read and signed an informed consent form before enrolment, while the children provided verbal assent. This trial complied with the Declaration of Helsinki and is registered on the Australia and New Zealand Clinical Trials Registry (number: ACTRN12617000598381). The use of the placebo and 0.01% atropine eyedrops was approved by the Therapeutic Goods Administration, Department of Health, Australia.

Participants were instructed to instilled the allocated eyedrops on a nightly basis for 2 years. Cycloplegic autorefraction (Nidek ARK-510A, NIDEK Co. Ltd, Japan) and ocular biometry (IOLMaster V5 [Carl Zeiss Meditec AG, Jena, Germany]) were conducted every 6 months. Cycloplegia was achieved by instilling 1–3 drops of cyclopentolate 1%. The 6-month change in myopia and axial length at each visit was determined by calculating the difference between that current and the previous visit.

Effect of short-term coronavirus disease 2019 lockdowns

In the state of Western Australia, the first school holiday in 2020 was planned for 10–27 April, but a "soft lockdown" for COVID-19 was implemented from March 29, 2020, to April 28, 2020 [Figure 1].[10] (Three "hard" lockdowns subsequently occurred, but each lasted for only 3–5 days.) During this 1-month period of COVID-19 restrictions, people were encouraged to stay home (although this was not mandatory), schools closed 1 week early for school holidays, all playgrounds were closed, and gatherings of more than 2 people from different households were banned.[10] Restrictions eased

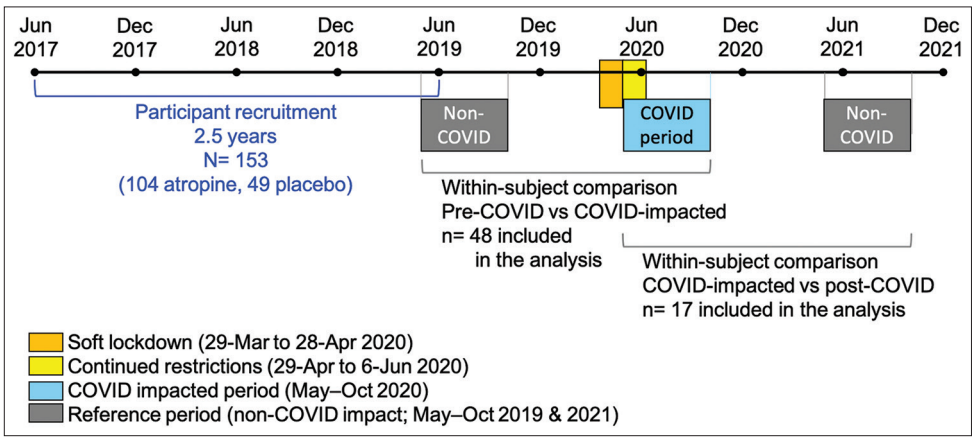

Figure 1: Timeline for participant recruitment, coronavirus disease 2019 (COVID-19), and reference period. The analysis includes 65 participants, after excluding withdrawals (*n* = 19), those who completed their treatment period before COVID-19 (*n* = 59), and those without scheduled visits between May 2020 and October 2020 (*n* = 10). COVID = Coronavirus disease

at the end of April but gatherings were still limited to 10 people and playgrounds remained closed until 6 June.[11]

During the 1-month soft lockdown, all scheduled study visits were postponed to May 2020 or later, thus the maximum delay in study visits was only 1 month.

Statistical analysis

The 1-year myopia progression and axial elongation as measured during May–October (late autumn to early spring in Australia) following the 2020 lockdown was compared to that in the same months in 2019 and 2021, i.e. the 1-year myopia progression up to May 2019–October 2019 (non-COVID-19) versus the 1-year progression up to May 2020–October 2020 (COVID-19 period), and the 1-year progression up to May 2021–October 2021 (non-COVID-19) versus the 1-year progression up to the same months in 2020 [COVID-19 period; Figure 1]. Linear mixed models were used to compare rates of myopia progression between COVID-19 and non-COVID-19 periods, adjusting for index age, sex, and ethnicity. Statistical significance was set at $P < 0.05$.

Results

A total of 104 and 49 children were randomized to receive atropine 0.01% eyedrops and a placebo, respectively. The baseline characteristics of participants in both groups have been described previously.[8]

Participant enrolment took place over 2.5 years; 19 participants withdrew and 59 participants completed their 2 years of study treatment before the 2020 COVID-19 lockdown. Another 10 participants did not have a study visit scheduled during the months of interest (May–October 2019, 2020, and 2021) and thus were not included in this analysis [Figure 1]. There was no difference in age, sex, or ethnicity between included or excluded participants ($P > 0.05$). Of the 65 participants (mean age at baseline = 11.8 ± 2.5 years) included in the analysis, 49 were in the treatment group and 16 in the placebo group. All 65 of these participants attended the study visit in May 2020–October 2020, which was compared to their non-COVID-19 period. The non-COVID-19 period took place in the same months either in 2021 ($n = 17$ participants) or in 2019 ($n = 48$).

After correcting for age, sex, and ethnicity, there was no significant main effect of the short-term lockdown on the rate of spherical equivalent or axial length change. However, there was a trend of a lockdown × treatment interaction effect on the rate of axial elongation [$P = 0.007$; Table 1]. This was such that in the treatment group, the 1-year axial elongation was faster during lockdown by 0.056 mm compared to the nonlockdown periods ($P = 0.009$), while the rate of axial elongation in those on the placebo eye drops was similar during lockdown and nonlockdown [Table 1]. A similar interaction effect was noted for the spherical equivalent in the treatment group, although this was not significant [Table 1].

Discussion

Several studies have documented increased myopia progression rates or incidence in children following prolonged periods of COVID-19 lockdown.[2-5,12-14] In 14 children treated with atropine 0.01% eyedrops, a study in Israel reported that progression rates of spherical equivalent and axial length during 12 months of COVID-19 restrictions were up to twice that in the pre-COVID-19 era.[6] On the other hand, Yum *et al*.[7] did not find a significant effect of COVID-19 lockdowns on myopia control in 15 Korean children receiving atropine 0.01% eyedrops. However, children receiving atropine 0.025% or 0.05% eyedrops ($n = 88$) had significantly faster myopia and axial length progression by 24%–80% following 9 months of lockdowns. The study authors concluded that atropine eyedrop efficacy is reduced during periods of COVID-19 lockdowns. Notably, these retrospective reviews of clinical records[6,7] did not have a control group and thus it is possible that the atropine eyedrops were still having a similar impact on myopia control that would not have been apparent without an untreated group for comparison.

Our current study addressed this by exploring the interaction effects between COVID-19 lockdowns and

Table 1: One-year myopia progression during the coronavirus disease and noncoronavirus disease periods in each treatment group

	Non-COVID-19 period (95% CI)	COVID-19 period (95% CI)	EMM (95% CI)	P^a
Spherical equivalent (D)				
Placebo group (n=16)	−0.62 (−0.98–−0.26)	−0.72 (−1.04–−0.39)	−0.10 (−0.36–0.16)	0.88
0.01% atropine group (n=49)	−0.40 (−0.72–−0.08)	−0.58 (0.90–−0.26)	−0.18 (−0.33–−0.039)	0.062
Axial length (mm)				
Placebo group (n=16)	0.31 (0.20–0.41)	0.26 (0.16–0.36)	−0.04 (−0.11–0.12)	0.52
0.01% atropine group (n=49)	0.23 (0.12–0.33)	0.28 (0.18–0.39)	0.06 (0.02–0.09)	0.009*

*Difference between COVID-19 and non-COVID-19 periods statistically significant at P<0.01, [a]Difference in 1-year myopia progression in each group between the non-COVID-19 (2019 and 2021) and COVID-19- affected (2020) periods. CI=Confidence interval, EMM=Estimated marginal mean, COVID-19=Coronavirus disease 2019

treatment on myopia control and our findings indeed suggest a decrease in the efficacy of low-concentration atropine in controlling axial elongation during COVID-19 lockdown. However, the difference in elongation rate between the lockdown and nonlockdown periods was small. In addition, in contrast to previous reports of faster myopia progression in children who were not under any myopia treatment,[2-5,12-14] myopia progression was not faster in the placebo group after the COVID-19 lockdown compared to the non-COVID-19 periods. This is likely because of the short duration of the lockdown. Moreover, this short-term lockdown in WA was fairly lenient – limits were only placed on the number of household and outdoor gatherings while staying home and working from home was encouraged but not mandatory.[10] Our findings may reflect parents' preference to keep their children at home during the pandemic, resulting in an accelerated axial elongation as some have predicted.[1] Importantly, our findings suggest that there is a decreased efficacy of low-concentration atropine even with relatively lenient restrictions lasting for a few months. No significant effect of lockdown on axial elongation or spherical equivalent was found in the nontreatment group, although conclusions are limited by the small sample size of the control group. Thus, we should not rule out the possibility that the short-term lockdown has affected myopia progression in untreated children. Given the exploratory nature of our current analysis on the impact of COVID-19 restrictions on myopia control, further investigations are required to confirm this. Our current findings provide some pilot data for future studies.

Data availability statement

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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Conflicts of interest

Dr Lingham is employed by Ocumetra; Dr Mackey consults for Novartis.

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