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Discontinuation of mass azithromycin distribution for trachoma: a systematic review

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ABSTRACT

The WHO recommends continuing azithromycin mass drug administration (MDA) for trachoma until endemic regions drop below 5% prevalence of active trachoma in children aged 1-9 years. Azithromycin targets the ocular strains of *Chlamydia trachomatis* that cause trachoma. Regions with low prevalence of active trachoma may have little if any ocular chlamydia, and thus may not benefit from azithromycin treatment. Understanding what happens to active trachoma and ocular chlamydia prevalence after mass distributions of azithromycin are discontinued may improve future treatment decisions. We systematically reviewed published evidence for community prevalence of both active trachoma and ocular chlamydia after cessation of azithromycin distribution. We included published studies from the peer-reviewed literature that included at least two post-discontinuation of mass azithromycin distribution surveys of ocular chlamydia and/or trachomatous inflammation—follicular (TF) prevalence. We assessed trends in the prevalence of both indicators over time after azithromycin discontinuation. We searched electronic databases for publications up through May 20, 2020. Of 140 identified studies, 21 met inclusion criteria and were used for qualitative synthesis. Although we found a gradual increase in ocular chlamydia infection prevalence over time post-discontinuation of azithromycin distribution, the TF prevalence generally gradually declined. Ocular chlamydia infection may return faster in communities compared to TF following discontinuation of treatment.

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Review questions

1 1. What is the prevalence of clinical trachoma (TF) and ocular chlamydia infection pre-MDA and post MDA?

2 2. Is there a correlation between pre-treatment trachoma prevalence and return of trachoma infection prevalence after discontinuing oral azithromycin treatment?

Search strategy

3 Search Items:
-Trachoma
-Azithromycin

4 Synonyms to be searched, if needed:
- Azithromycin: Zithromax

5 Search algorithm:
("Trachoma"[Mesh] OR trachoma) AND ("Azithromycin"[Mesh] OR azithromycin OR zithromax)·

6 Databases searched and search details:
o MEDLINE
Search bar:
("Trachoma"[Mesh] OR trachoma) AND ("Azithromycin"[Mesh] OR azithromycin OR zithromax)
Full search details:
("Trachoma"[Mesh] OR ("trachoma"[MeSH Terms] OR "trachoma"[All Fields])) AND ("Azithromycin"[Mesh] OR ("azithromycin"[MeSH Terms] OR "azithromycin"[All Fields]) OR ("azithromycin"[MeSH Terms] OR "azithromycin"[All Fields] OR "zithromax"[All Fields]))
o EMBASE
Search bar:
('trachoma'/exp OR trachoma) AND ('azithromycin'/exp OR azithromycin)
o Web of Science
Search bar (TOPIC):
("Trachoma"[Mesh] OR trachoma) AND ("Azithromycin"[Mesh] OR azithromycin OR zithromax)
o Cochrane Library
Search bar (Title, Abstract, Keywords):
Trachoma AND azithromycin

7 Other sources:
o Abstracts
Abstracts available online from the following conferences will be searched using the search terms outlined above:
· American Society of Tropical Medicine and Hygiene (ASTMH)
· Association for Research in Vision and Ophthalmology (ARVO)

Article eligibility criteria

8
Inclusion criteria:
o Primary, quantitative data
o Studies of community-wide oral azithromycin distribution for trachoma
o Includes measurement of prevalence of ocular chlamydia and/or clinical trachoma before and after azithromycin distribution
o Studies must include one pre-treatment time point and at least two post-treatment time points
o Dates of inclusion: All primary abstracts, reports, etc. published through May 2020

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9 Exclusion criteria:
- o Studies on mathematical modeling, surveillance reports, review articles
- o Studies without sufficient information on number of individuals/ villages tested
- o Studies without two distinct time points of pre- and post- azithromycin distribution
- o Studies on the use of azithromycin for purposes other than treatment of trachoma

We will not exclude studies that concurrently use topical tetracycline for trachoma treatment

Outcomes

10 Primary outcomes of interest:
- o Prevalence of clinical trachoma pre-MDA and post-MDA
- o Prevalence of ocular chlamydia infection pre-MDA and post-MDA

11 Secondary outcomes
- o Correlation between pre- and post-MDA prevalence of clinical trachoma if possible
- o Correlation between pre- and post-MDA prevalence of ocular chlamydia infection if possible

Data Extraction

12 Variables to extract:
- o Title
- o Authors
- o Journal
- o Year of publication
- o Study design
- o Geographic location of study
- o Sample size (numbers of communities, numbers of individuals)
- o Pre-MDA trachoma prevalence (ocular chlamydia infection and/or clinical trachoma/TF)
- o Post-MDA trachoma prevalence (ocular chlamydia infection and/or clinical trachoma/TF)
- o Frequency of MDA
- o Duration of MDA

Analysis

13 Strategy for data synthesis (qualitative, quantitative):
- o A qualitative synthesis of individual studies will be performed to discuss individual findings per the variables extracted.
- o For quantitative synthesis, a meta-analysis will be performed per the procedures outlined below

14 Meta-analysis (if data is not too heterogenic to allow):
- o Estimates of prevalence pre- and post-MDA will be pooled across studies using a DerSimonian and Laird random effects model for overall prevalence of each outcome (clinical trachoma and ocular chlamydia infection)

-Pre-MDA prevalence is predicting post-MDA prevalence
- o The I^2 statistic will be calculated as a measure of heterogeneity across studies. Sources of heterogeneity, including pre-MDA trachoma prevalence, country of origin, and year, will be evaluated using a random effects meta-regression model.

15 · Quality Assessment
- o Risk of bias will be assessed using the Cochrane risk of bias tool for randomized controlled trials and the ROBINS-I tool for non-randomized studies

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