

Evidence Assessment: Summary of a Systematic Review

Who is this summary for?

For Doctors and Health Personal, Administrators and Managers of health facilities, Community Health Workers and the partners involved in the control of onchocerciasis.

Doxycycline plus ivermectin versus ivermectin alone for treatment of patients with onchocerciasis

Key findings

- Two trials reported no differences in adverse events between treatment groups.
- One study reported that adverse treatment effects, including itching, fever, headache, body pain, and vertigo, occurred in 12% of study participants.
- One study reported that one (1.3%) person had bloody diarrhea after starting treatment with doxycycline plus ivermectin, which stopped when treatment was withdrawn.

Background

Onchocerciasis, also known as “river blindness,” is a parasitic disease that is caused by infection from the filarial nematode (roundworm), *Onchocerca volvulus*. River Blindness (RB) is treated with ivermectin, which targets the tiny, young worms. It does not kill the large, adult worms. Adult worms need a certain type of bacteria (*Wolbachia*) to live. Doxycycline is an antibiotic. If doxycycline is able to kill this type of bacteria in the body, adult worms cannot live. The purpose of this review is to find out if combining the antibiotic doxycycline with ivermectin might provide additional benefit in preventing and treating RB.

Questions

- What is the effectiveness of doxycycline plus ivermectin versus ivermectin alone for prevention and treatment of onchocerciasis?
- What is the effectiveness of doxycycline plus ivermectin versus ivermectin alone for prevention and treatment of onchocercal ocular lesions in communities co-endemic for onchocerciasis and *Loa loa* (loiasis) infection?

Doxycycline plus ivermectin versus ivermectin alone for treatment of patients with onchocerciasis in Cameroon: Onchocerciasis - or "river blindness" is an endemic disease in Cameroon. According to statistics from the World Health Organization, 6 million people are infected in Cameroon. The use of doxycycline associated with ivermectin has been tested in two health districts. This combination may be more effective particularly in areas of loiasis co-endemicity with onchocerciasis.

| Table 1: Summary of the systematic review | | |
|---|--|---|
| | What the review authors searched for | What the review authors found |
| Studies | Randomized controlled trials | Three randomized controlled trials met the inclusion criteria |
| Participants | Participants resided in communities endemic for onchocerciasis. The authors include participants with skin (e.g. itchiness, skin depigmentation) and ocular signs (e.g. inflammation) of onchocerciasis that was diagnosed with positive skin snip for microfilariae, with presence of onchocercal nodules and characteristic ocular signs of onchocerciasis noted on slit lamp examination | All studies recruited participants normally residing in endemic onchocercal communities. |
| Interventions | The authors included trials comparing treatment with doxycycline plus ivermectin versus ivermectin alone. Treatment in the intervention arm was defined according to the recommended dose of doxycycline, 100 milligrams daily for six weeks, plus ivermectin, 150 micrograms per kilogram of body weight, taken orally as a single dose annually or semi-annually, or as given in an individual study. | All studies compared doxycycline plus ivermectin versus ivermectin alone in at least two treatment groups. All three studies used the same dose for ivermectin (single dose of 0.15 mg/kg); however, the timing of ivermectin administration and the dose and frequency of doxycycline varied among studies |
| Controls | Treatment in the control arm was defined as 150 micrograms of ivermectin per kilogram of body weight annually or semi-annually, or as given in the study. | Treatment in the control arm was defined as 150 micrograms of ivermectin per kilogram of body weight annually or semi-annually, or as given in the study. |
| Outcomes | <p>Primary outcomes</p> <ul style="list-style-type: none"> • Visual field: risk of visual field deterioration (unilateral or bilateral) during a follow-up period of one year. • Visual acuity: risk of visual acuity loss (unilateral or bilateral) during a follow-up period of one year. <p>Secondary outcomes</p> <ul style="list-style-type: none"> • Parasitological: mean count of microfilariae or proportion of participants with a count of microfilariae greater than one in: <ul style="list-style-type: none"> ◦ Cornea; ◦ Anterior chamber; or ◦ Skin. • Clinical: proportion of participants with incident cases or progression of any of the following: <ul style="list-style-type: none"> ◦ Optic nerve disease; ◦ Chorioretinitis; ◦ Iridocyclitis; ◦ Sclerosing keratitis; or ◦ Punctate keratitis. | <ul style="list-style-type: none"> • Improvement of vision • Optic atrophy, chorioretinitis, iridocyclitis, sclerosing keratitis, and punctate keratitis • The number of microfilarial loads per skin snip • Occurrences of adverse events in participants |
| Date of the most recent search: 15 July 2015. | | |
| Limitations: This is a high quality systematic review, AMSTAR =11/11 | | |
| Citation: Abegunde AT, Ahuja RM, Okafor NJ. Doxycycline plus ivermectin versus ivermectin alone for treatment of patients with onchocerciasis. Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD011146. DOI: 10.1002/14651858.CD011146.pub2. | | |

Table 2: Summary of findings

| Doxycycline plus ivermectin compared with ivermectin alone for onchocerciasis | | | |
|--|---------------------------------|-------------------------------------|--|
| Population: People residing in communities endemic for onchocerciasis | | | |
| Setting: Community-based | | | |
| Intervention: Doxycycline plus ivermectin | | | |
| Comparison: Ivermectin alone | | | |
| Outcomes | Relative effect (95% CI) | No of Participants (studies) | Quality of the evidence (GRADE) |
| Improvement in visual impairment at 6 months | 1.06 [0.80-1.39] | 240 (1) | Very low |
| Clinical outcomes: improvement in iridocyclitis at 6 months | 1.24 [0.69-2.22] | 240 (1) | Very low |
| Clinical outcomes: improvement in punctate keratitis at 6 months | 1.43 [1.02-2.00] | 240 (1) | Very low |

Applicability

The trials were conducted in Cameroon, Ghana, and Liberia. These interventions may be applied in other low resources settings such as Cameroon.

Conclusions

There is very low quality evidence on the effectiveness of doxycycline plus ivermectin compared with ivermectin alone in preventing and treating onchocerciasis.

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