WHAM evidence summary: Lymphatic filariasis: Prevention

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CLINICAL QUESTION

What is the best available evidence on preventing the spread of filariasis?

SUMMARY

Lymphatic filariasis is a parasitic infection spread by mosquito in tropical countries. The disease course is primarily asymptomatic but includes episodic acute disease that can become chronic.[1-15] Prevention of disease is the most effective management strategy. Vector control strategies (e.g. mosquito netting) are highly recommended in geographic regions where filariasis is present[1] (*Level 3*). Preventive chemotherapy (albendazole plus either diethylcarbamazine [DEC] or ivermectin)[2] (*Level 1*) at an individual and/or population level is also highly recommended to prevent the spread of disease.

CLINICAL PRACTICE RECOMMENDATIONS

All recommendations should be applied with consideration to the wound, the person, the health professional and the clinical context.

In geographic regions with filariasis, implement vector control strategies including mosquito netting, mosquito repellent and covering the skin (Grade A).

In geographic regions with filariasis, an annual dose of combination therapy (albendazole plus either diethylcarbamazine or ivermectin) or six to twelve months of diethylcarbamazine-medicated salt should be implemented to reduce the spread of disease (Grade A).

SOURCES OF EVIDENCE

This summary was conducted using methods published by the Joanna Briggs Institute (JBI). This evidence summary is based on a structured database search using the search terms lymphoedoema, filariasis, lymphatic filariasis and Bancroftian filariasis. The evidence sources are described in Table 1.

BACKGROUND

Epidemiology

Lymphatic filariasis is a parasitic infection of threadlike worms that is spread by female mosquito bite. Mosquitoes become infected after feeding on blood from people infected with microfilariae (juvenile worms). When the mosquito moves to another person and feeds, the microfilariae enter the skin and migrate to the lymphatic system were they develop into microfilariae (mature worms) and

Table 1: Sources of evidence and the level

Level 1 Evidence	Level 2 Evidence	Level 3 Evidence	Level 4 Evidence	Level 5 Evidence
Experimental Designs	**Quasi-experimental Designs**	**Observational – Analytic Designs**	**Observational – Descriptive Studies**	**Expert Opinion/ Bench Research**
1.a Systematic review of RCTs[2] 1.b A systematic review including trials of various methodologies[15] 1.c RCTs[8-13]		3.e Observational study without a control group[1]	4.c case series[5]	5.c Expert opinion[3, 4, 6, 7, 14]

continue breeding. The resulting microfilariae then return to the bloodstream. The time frame from infection to production of microfilariae in the blood steam is six to twelve months.[2, 3] Three different roundworms are implicated in lymphatic filariasis,

Wuchereria bancrofti (found in tropical regions of Africa, Asia, China and Pacific Islands), *Brugia timori* (Asia) and *Brugia malayi* (Indonesia).[2]

Lymphatic filariasis is endemic in 58 countries, but 80% of people who are at risk of exposure live in one of the following ten countries: Bangladesh, Côte d'Ivoire, Democratic Republic of Congo, India, Indonesia, Myanmar, Nigeria, Nepal, Philippines and the United Republic of Tanzania.[4]

Clinical presentation

Clinical course of lymphatic filariasis falls into three broad categories: asymptomatic disease, acute phase and chronic disease.

Filariasis is primarily asymptomatic; however, even people without clinical symptoms can experience pathological changes to the lymphatic system with the widening of lymphatic vessels (lymphangiectasia).[2] In the acute phase, patients experience sudden, episodic onset of signs and symptoms including fever, enlarged inguinal and axillary lymph nodes (adenolymphangitis), and lymphoedema, with skin exfoliation often occurring at the resolution of an acute episode.[4-6] Repeated episodes of acute bacterial adenolymphangitis (ADL) are associated with progression of the severity of lymphatic filariasis.[5] Chronic lymphatic filariasis is characterised by chronic and irreversible lymphoedema and elephantiasis of the limbs, scrotum and breasts.[2, 4, 6]

Diagnostic methods include:[6]

- establishing history of exposure,
- antigen detection assay to detect adult worms and, most reliably,
- microfilariae detection using venous blood smears, usually done at night when the microfilariae are most active in the bloodstream.

CLINICAL EVIDENCE

Management of lymphatic filariasis aims to reduce the spread of microfilariae at the community level include mass drug administration programs (preventive chemotherapy) and vector control programs.[2, 4]

Vector control

Preventing initial infection by avoiding mosquito bite is the most effective way to prevent lymphatic filariasis. Prevention strategies include:

- Sleeping under a mosquito net[3, 4] (*Level 5*).
- Covering the skin with clothing (long sleeves and trousers)[3] (*Level 5*).
- Application of personal mosquito repellent, especially between dusk and dawn[3] (*Level 5*).
- Indoor residual spraying of repellent[4] (*Level 5*).

Additional evidence is provided by a cross sectional study conducted in Tanzania. Insecticide treated netting was used in conjunction with a population level DEC program (monthly low dose for 12 months) in three villages. Individuals who used insecticide treated netting for the longest period had significantly lower risk of microfilariae prevalence (odds ratio [OR] 0.681, 95% confidence interval [CI] 0.50 to 0.94). The risk of new infections was also reduced by 58.8% (95% CI 30.3 to 5.4)[1] (*Level 4)*. It is unclear if there is increased protection associated with insecticide treatment of netting compared with regular mosquito netting.

Preventive chemotherapy

The World Health Organisation recommend prevention of filariasis with an annual single dose of combination therapy (albendazole plus either DEC or ivermectin) or six to twelve months of DEC-medicated salt[7] (Level 5).

The three primary treatments for eradication of microfilariae and macrofilariae and prevention of their spread are albendazole, ivermectin and diethylcarbamazine (DEC), either alone or in combination with each other. Albendazole is used to treat adult worms, DEC is used to treat both adult worms and microfilariae and ivermectin treats microfilariae and may have a role in sterilising adult worms. Medications are generally given in a single dose (albendazole 400mg, DEC 6mg/kg body weight or ivermectin 150 to 200µg/kg body weight).[2, 8-14]

The evidence on effectiveness of these three chemical treatments has been reported in a comprehensive Cochrane review that included seven randomised controlled trials (RCTs). The trials were conducted in child

and adult populations with follow up varying from three months to two years.[2] The findings, which are presented in more detail below, suggest that there is no significant differences between various chemotherapy regimens in preventing the spread of microfilariae and the review authors indicate that further research is required, particularly on combination regimens that seek to eradicate filariae at both juvenile and adults stages.[2]

Diethylcarbamazine (DEC)-medicated salt is also used in some countries (e.g. Guyana, China and Tanzania) at a population level to manage spread of filariasis. Medication is generally added to salt at the point of iodisation at between 0.1% and 1% concentration.[15]

The evidence on effectiveness of DEC-medication salt been reported in a Cochrane review of studies of different methodologies, the findings of which are presented below. The studies included in this review achieved high levels of community coverage; however, the follow-up periods were generally short (one year or less). The findings indicated that the intervention is effective with coverage at 90% for at least six months.[15]

Albendazole

- A meta-analysis found no significant difference between albendazole (n=401) compared with placebo (n=382) for microfilariae prevalence in all participants (those who were both positive and negative at baseline) at three-to-four months (risk ratio [RR] 0.95, 95% CI 0.66 to 1.37, p=0.80).[2] (Level 1.a evidence). In one included RCT, there was also no significant difference between albendazole (n=256) compared with placebo (n=243) at six months (RR 1.00, 95% confidence interval [CI] 0.66 to 1.53, p=0.99)[10] (*Level 1*).

Diethylcarbamazine (DEC)

- One RCT found DEC (n=246) was more effective than albendazole (n=256) in reducing microfilariae prevalence in participants who were both positive and negative at baseline at six month follow-up (RR 1.74, 95% 1.05 to 2.88); however there was no significant differences seen at three-to-four month follow-up[10] (*Level 1*).
- When DEC was combined with albendazole, there was no significant difference compared with DEC alone in reducing microfilariae prevalence in participants who were both positive and negative at baseline (RR 0.62, 95% CI 0.32 to 1.21)[10] (*Level 1*).

Ivermectin

- One RCT found ivermectin (n=145) was not significant different from albendazole (n=145) for reducing microfilariae prevalence in participants who were both positive and negative at baseline at six month follow-up (RR 1.14, 95% 0.65 to 1.99)[8] (*Level 1*).

Diethylcarbamazine (DEC)-medicated salt

- In 21 studies (4 conducted at an individual level and 17 conducted at community level) percentage reduction of microfilariae ranged from 43% to 100%. There was a significant moderate correlation between per capita consumption and reduction in microfilariae prevalence after 12 months (Pearson's correlation coefficient r=0.642, p=0.003)[15] (*Level 1*).
- A multivariate regression analysis indicated that without DEC-medicated salt intervention the spread of filariasis would increase annually by 11.38%. For each unit increase in DEC concentration there is a 217.78% reduction in annual spread and for each unit of duration of treatment there is a 3.92% reduction in annual spread[15] *(Level 1*).

Chemotherapy adverse events

- Six RCTs found there was no serious adverse events associated with albendazole, ivermectin or DEC. In one RCT that used much higher doses of medications there was a high incidence of scrotal syndrome (scrotal pain, epididymis enlargement and fever) in participants with albendazole[2] (*Level 1*).
- When compared to no treatment, DEC-medicated salt was associated with increased mild symptoms (details not reported) in one study. In a before-and-after study DEC-medicated salt was associated with mild headache, nausea and lymphangistis. In nineteen other studies there was no adverse effects associated with DEC-medicated salts[15] (*Level 1*).

ABOUT WHAM EVIDENCE SUMMARIES

WHAM evidence summaries are consistent with methodology provided in detail in resources published by the Joanna Briggs Institute as cited in this evidence summary. WHAM evidence summaries undergo peer-review by an international review panel. More information on the website: http://WHAMwounds.com

WHAM evidence summaries provide a summary of the best available evidence on specific topics and make suggestions that can be used to inform clinical practice. Evidence contained within this summary should be evaluated by appropriately trained professionals with expertise in wound prevention and management, and the evidence should be considered in the context of the individual, the professional, the clinical setting and other relevant clinical information.

PUBLICATION

This evidence summary has been published in:

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