Diethylcarbamazine (DEC)-medicated salt for community-based control of lymphatic filariasis (Review)

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[Intervention Review]

Diethylcarbamazine (DEC)-medicated salt for community-based control of lymphatic filariasis

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ABSTRACT

Background

Mass treatment with diethylcarbamazine (DEC)-medicated salt has been used in a number of places as a control measure for lymphatic filariasis. We sought reliable evidence about its effect on lymphatic filariasis transmission.

Objectives

To evaluate the effects of DEC-medicated salt on infection with lymphatic nematodes in studies of individuals and communities.

Search strategy

In August 2006, we searched the Cochrane Infectious Disease Group Specialized Register, CENTRAL (*The Cochrane Library* 2006, Issue 3), MEDLINE, EMBASE, and LILACS. We also checked reference lists.

Selection criteria

Studies of DEC-medicated salt in endemic populations or microfilaraemic individuals that reported on some measure of human infection before and after the intervention.

Data collection and analysis

Two authors assessed study eligibility and methodological quality. We calculated the percentage change in microfilariae prevalence and density, adult worm prevalence, disease rates, and vector infection and infectivity. We carried out meta-regression to explore the variability in percentage reduction in microfilariae prevalence between studies.

Main results

Twenty-one studies were included; two compared DEC-medicated salt with other forms of DEC, five had some control group, and 14 were before-and-after studies. Five were efficacy and safety studies of individuals who were all microfilaraemic at baseline; the rest studied endemic communities.

Percentage reductions in microfilariae prevalence were large (43% to 100%) and consistent in most studies with high levels of coverage. Large reductions in microfilariae density were also observed, though most studies reported changes in microfilariae density only for

people with microfilaraemia at baseline. Vector infection and infectivity also declined, but the samples were usually small. Changes in disease prevalence were inconclusive as most studies were not powered for this outcome. Adverse events seemed mild.

Only two studies compared DEC-medicated salt with other forms of DEC (such as annual or standard 12-day dose), but in both performance of DEC-medicated salt was better.

A few studies included longer term follow up (two to 19 years). Reductions in microfilariae prevalence, density, and vector infectivity were maintained over time. The DEC concentration in the salt and the duration of intervention were significant factors influencing the percentage reduction in microfilariae prevalence in these studies.

Authors' conclusions

DEC-medicated salt is an effective intervention when maintained with levels of coverage of at least 90% for at least six months. Further studies are required to assess the effects of continuous low-dose, DEC-medicated salt on adult worms, disease prevalence, and development of drug resistance.

PLAIN LANGUAGE SUMMARY

High population coverage of DEC-medicated salt maintained over at least six months in a community is effective at reducing transmission of lymphatic filariasis and can, if maintained over a long enough period, completely interrupt transmission

Filariasis is a parasite infection of threadlike worms, affecting about 120 million people in more than 83 countries. The infection is transmitted by mosquitoes. Larval forms take up to a year to develop into adult worms, which mate and release thousands of microfilariae (mf) into the blood over the course of their lives. Mf are ingested by mosquitoes from the blood of an infected individual, completing the cycle. This infection may lead to severe disability in the form of lymphoedema and eventually elephantiasis of limbs, and hydrocoele. Though most infected people remain asymptomatic, the lymph vessels are often damaged. A drug, diethylcarbamazine (DEC) has been shown to kill mf, but repeated doses are needed before adult worms are killed or sterilized. This review looked at the effectiveness of giving entire communities DEC-medicated salt. The review of studies found evidence that DEC when given in a low dose over a period of months or years is effective in reducing the prevalence of filariasis in communities, with no recognized adverse events.

BACKGROUND

Life cycle

Lymphatic filariasis is caused by three species of nematodes: *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori.* These are long, threadlike worms that lodge in the lymphatic vessels of their human hosts. People become infected when bitten by mosquitoes carrying infective larvae, which migrate to the lymphatics where they mature into adult worms (macrofilariae). Once a pair of male and female worms mature and reproduce (a 'patent' infection), they release early-stage larvae called microfilariae (mf) that make their way to the bloodstream, from which they may be ingested by mosquitoes during blood meals. Mf mature within the mosquito to the stage infective to humans, completing the life cycle.
The most widespread infections are *W. bancrofti* and *B. malayi* (confined mainly to southern India, with smaller foci in other parts of Asia). *B. timori* is focally important in areas of the Timor Sea.

Infection and clinical disease

People infected with filarial worms may be microfilaraemic (mf in the blood) and asymptomatic, or they may develop acute or chronic manifestations. The adult worms lodge in the lymphatics and dilate the vessels. As fluid accumulates, damage to the skin occurs, allowing bacterial infection to invade the body. This is

thought to be the immediate cause of the painful acute attacks (Dreyer 2000). The range of clinical disease caused by lymphatic filariasis includes fever, inflammation of lymphatic vessels (lymphangitis), disease of the lymph nodes (lymphadenopathy), reversible and irreversible swelling (oedema), elephantiasis of limbs, genitals, and breasts, fluid in the scrotum (filarial hydrocoele), and a rarer tropical pulmonary eosinophilia syndrome characterized by wheezing and coughing at night, high counts of eosinophils, and lung nodules. Individuals with clinical disease can be treated symptomatically, and elimination of infection can prevent development of chronic disease, but those with more advanced conditions are unlikely to be restored to normal. Lymphatic filariasis can be a very a painful and profoundly disfiguring disease leading to temporary or permanent disability. It has a major social and economic impact on endemic countries as sufferers may be unable to work, marry, or have children. It has been estimated to be the second leading cause of disability worldwide (Mathers 2006).

It is now known that, contrary to an earlier belief based on blood smears, filarial infection is common in childhood. As many as one-third of children under five may already have acquired adult worms in endemic areas (Witt 2001). Although childhood infections are largely asymptomatic, there is also growing evidence that subclinical damage to the lymphatic system starts early (Dreyer 2000).

Diagnosis

Most individuals with filarial infections are asymptomatic during much or all of the time they are infected, so clinical signs are not helpful in determining who is infected. Until recently, the only definitive diagnostic test for infection was a blood smear to look for mf. This had to be done at night in most places, as this is when mf are circulating. There are now antigen tests for adult worms that can be performed at any time and which detect adult worm infections whether or not mf are being produced. This and other immunologic tests will undoubtedly be used in monitoring programmes and studies in the future, but most of the studies included in this review were carried out before these tests were available.

Chemotherapy of filarial infections

Diethylcarbamazine (DEC) was, from the late 1940s until the 1990s, the only really useful drug for community filariasis control. It has since been joined by ivermectin and by albendazole-DEC and albendazole-ivermectin combinations, but it still retains its importance as a major element of filariasis control. DEC is remarkably effective at killing mf. It also eventually kills many adult worms, but apparently only after repeated doses over a long period of time. Ivermectin, which also is a remarkably effective microfilaricide, does not appear to kill adult worms, but it may have a lasting sterilizing effect on them (Dreyer 1996). When any one of these drugs is given as a single dose or as a single regimen (eg once a day for 12 days), microfilaraemia invariably returns over time in some of those initially microfilaraemic, though not until many months after treatment (Pani 1991a). To achieve long-term control, which implies killing or sterilizing macrofilariae, multiple doses over time are needed. DEC has been shown to be effective in the treatment of both Malayan (Panicker 1991) and Bancroftian filariasis (Pani 1991b).

DEC causes no known long-term adverse drug effects, a necessary characteristic for a drug to be given community wide. It can have direct pharmacologic effects (eg nausea) and leads to severe adverse reactions like fever and weakness immediately after treatment in some people who are microfilaraemic, even if they had been completely asymptomatic. The effect is thought to be an immunologic reaction to dying mf or the release of endosymbiotic *Wolbachia* bacteria and its related antigens (Taylor 2001), or both. It can be severe, sometimes lasting several days. Although some adult worms appear refractory to use of DEC (Dreyer 1996), no confirmed resistance to DEC has been reported despite its long history of widespread use.

Control strategies

Within communities, filariasis is a stable infection. Endemic areas around the world remain so, in general, without some intervention. Changes resulting from, for example, improved living conditions, mosquito control, or urbanization, occur only gradually. Control programs themselves must be protracted, because, as discussed earlier, the available drugs do not appear to kill adult worms, and mf reappear after some period of time. For these reasons, the unit of treatment for definitive filariasis control is the community because transmission can only be stopped when mf are eliminated from the population, or brought down to levels below which transmission is negligible (but there is no agreement on exactly what this level is). The goal of virtually all filariasis control attempts has been to eliminate disease from the community by reducing or stopping transmission. Because there are no known animal reservoirs (animals that harbour the parasites, and also act as sources of transmission) for the important filarial nematodes, it should be possible to eradicate the disease.

An ideal type of community treatment for lymphatic filariasis would be a single dose of drug that could be given to everyone infected, would kill the circulating mf as well as the adult worms, and prevent reinfection from already-infected mosquitoes (until that mosquito generation dies). But, as discussed above, no single-agent regimens exist, so longer term strategies are needed. Some strategies involve biannual or annual doses to all members of the community for several years. Another approach is the addition of low concentrations of DEC to common salt, which has been used for periods of months to a year or so.

The World Health Organization sponsored Global Programme to Eliminate Lymphatic Filariasis advocates two strategies: an an-

nual single-dose two-drug regimen (albendazole plus either DEC or ivermectin) or six months to a year of DEC-medicated salt (Ottesen 2000). This review assesses the evidence for the latter strategy.

DEC-medicated salt

The first reported use of DEC-medicated salt was in Brazil in 1967, by Hawking, the man who first identified DEC as a filaricidal agent in the 1940s (Gelband 1994). Since then, it has been used sporadically in India, Africa, and Asia. Technically, it is relatively easy to add DEC to salt, ranging from simple village-level processes to more sophisticated manufacture. The simplest method involves adding powdered DEC to fine grain salt by hand or in a hand-turned drum. On a larger scale, it can be added at the same time and as part of the process of salt iodization (Houston 2000a). A range of low DEC concentrations has been used, from about 0.1% to 0.4% DEC by weight.

Introduction of DEC-medicated salt for filariasis control involves an array of social and economic issues, some of which are obvious. Adding a drug to the general food supply can be complicated; for example, it has not been possible to organize this centrally in India, while in other countries, such as Guyana, it has (see Houston 2000a for further discussion). Given the cost and logistic issues, being clear about the effectiveness of this intervention is important.

OBJECTIVES

To evaluate the effects of DEC-medicated salt on infection with lymphatic nematodes in studies of individuals and communities.

METHODS

Criteria for considering studies for this review

Types of studies

- Randomized controlled trials, other comparative trials (trials with a control group not receiving DEC-medicated salt, or receiving a different intervention), and before-and-after studies in single populations (ie no control group) of DEC-medicated salt in individuals or in filariasis-endemic populations.

- Studies comparing different DEC-salt regimens, such as different methods of salt distribution, different concentrations of DEC in salt, and different intervention periods.

Ideally, we would prefer to limit the review to controlled trials, preferably randomized controlled trials. Systematic reviews of many conditions would exclude before-and-after studies because in the absence of an unbiased comparison it is rare that one can make reliable inferences about the effectiveness of an intervention. However, it is accepted that randomized controlled trials of public health interventions covering entire communities can be very difficult to design (Petticrew 2003). No randomized controlled trials of this intervention have ever taken place, none are planned, and they are unlikely to be feasible in practice.

We therefore decided to include non-randomized studies, including controlled trials, and before-and-after studies. Such studies are more susceptible to bias, particularly confounding (Deeks 2003), and this needs to be considered when interpreting results. However, before-and-after studies of DEC-medicated salt may provide reliable evidence because the prevalence and distribution of filariasis in communities does not change dramatically in the absence of an intervention (see 'Background'). Adult worms live on average eight years (Plaisier 1999), so even fluctuating transmission levels due to temporal variation in mosquito populations would not have much effect on the community for at least several years. Change can take place in communities over a period of many years in response to improved living conditions or successful vector control programmes, but not over the course of months or a year or two. For example, the effect of an integrated vector control programme (for a period of five years) on transmission was evident only after five years (Subramanian 1989). Similarly, after six rounds of mass drug administration, the effect on the transmission could be seen only at the end of five years (Ramaiah 2002). This is because these interventions only prevent new infections (which are rare), and most of the mf in the community came from existing infections. Where these unusual conditions hold, we can attribute changes before and after the intervention, assuming no other effective interventions were present.

Types of participants

1. Studies of individuals:

People with definite filarial infection, based on microfilaraemia, antigen testing, or other diagnostic testing.

2. Community studies:

Whole or part of communities in filariasis-endemic areas.

Types of interventions

DEC-medicated salt at any concentration and for any period of time.

Types of outcome measures

1. Studies of individuals

Primary

- Change in infection status over the period of DEC-medicated salt intake measured as a change in microfilarial density or antigenic change consistent with a change in infection status.
- Change in infection status at intervals after the period of intake ends (measured as above).
- Change in status of live adult worms (as detected by ultrasound) during or after the period of DEC-medicated salt intake.

Adverse events

- Any adverse event that prevents daily activities or requires hospitalization.
- Systemic adverse events (eg headache, malaise, myalgia, haematuria).
- Local adverse events (eg localized pain and inflammation, tender nodules, lymphadenitis, or lymphangitis).

2. Community studies

Primary

- Change in mf prevalence or appropriate antigen change during or after the period of DEC-medicated salt intake.
- Change in mf density or appropriate antigen change during or after the period of DEC-medicated salt intake.
- Change in status of live adult worms (as detected by ultrasound) during or after the period of DEC-medicated salt intake.

Secondary

- Change in disease status. (Persons with chronic manifestations like lymphoedema of the limbs and hydrocoele were considered to have filarial disease).
- Change in vector infection and or infectivity rates. (Vector infection status: mosquitoes with any stage of filarial larvae (mf, L1, L2, or L3) are infected. Vector infectivity status: mosquitoes with L3 stage filarial larvae are infective

Adverse events

- Any adverse event that prevents daily activities or requires hospitalization.
- Systemic adverse events (eg headache, malaise, myalgia, haematuria).
- Local adverse events (eg localized pain and inflammation, tender nodules, lymphadenitis, or lymphangitis).

Search methods for identification of studies

We attempted to identify all relevant studies regardless of language or publication status (published, unpublished, in press, and in progress).

Databases

We searched the following databases using the search terms and strategy described in Appendix 1 : Cochrane Infectious Diseases Group Specialized Register (August 2006); Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (2006, Issue 3); MEDLINE (1966 to August 2006); EMBASE (1988 to August 2006) and LILACS (1982 to August 2006).

Conference proceedings

We searched the following conference proceedings for relevant reports: the 18^{th} International Congress of Lymphology, Genoa, Italy, 3 to 7 September 2001; the American Society of Lymphology 3^{rd} Annual Conference, Palm Springs, California, 11 to 13 November 2001; Proceedings of The Royal Society of Tropical Medicine & Tropical Hygiene's conference on The Elimination of Lymphatic Filariasis as a Public Health Problem, London, 20 January 2000; and the 16^{th} International Conference on Lymphatic Filariasis, James Cook University, Townsville, Australia, July 1997.

Reference lists

We also checked the reference lists of all studies identified by the above methods.

Data collection and analysis

Selection of studies

Two authors (AS and JC) independently scanned the results of the literature search for potentially relevant studies. We retrieved the full report for studies thought to be potentially relevant. We independently assessed the trials for inclusion using an eligibility form based on the inclusion criteria. We resolved any disagreements through discussion or by involving another person, such

as a third author or a Cochrane Infectious Diseases Group Editor. We scrutinized each of the study reports to ensure that each is included only once. We listed the potentially relevant studies not eligible for the review and have given the reason for excluding them in the 'Characteristics of excluded studies'.

Data extraction and management

We extracted the data independently using a pre-piloted data extraction form. Any disagreements were resolved by firstly referring to the trial report, then by discussion. We contacted the study authors in the case of missing or unclear information. We extracted the mean (overall) baseline and mean (overall) follow-up measurements for continuous outcomes in each study group for individual-based and community-based studies respectively. Since one of the outcomes follows a skewed distribution, we have attempted to extra or estimate geometric means where possible. For the dichotomous outcome measure, mf prevalence, we recorded the number of participants with mf at both baseline and follow up for each study. We also extracted the number of participants allocated to each study group. Percentage changes in mf prevalence or density with respect to baseline were also calculated.

We constructed a series of tables that included a measure of initial filarial infection, outcome measures reported at various intervals, information on the concentration of DEC in salt, the duration (in months) of the intervention, and an estimate of the average per capita consumption of DEC over the period of the intervention, changes in disease prevalence, changes in vector infection and infectivity, and adverse events.

Assessment of risk of bias in included studies

There are no empirically based or generally accepted lists of appropriate quality criteria for observational studies (Downs 1998; Deeks 2003). AS and JC independently assessed the quality using a variety of criteria that we considered important and had specified a priori. These included: high coverage of the community of interest (defined as at least 90% receiving the DEC-medicated salt intervention); presence of some type of comparison group who receive no intervention, a placebo, or a different form of treatment; and reporting of outcomes at the level of the whole community, rather than just for those who are initially mf positive. We also attempted to identify other control activities (such as mass DEC or vector control) that were carried out at the same time or just before the DEC-medicated salt intervention in the same area.

Data synthesis

We grouped the studies by design: studies comparing DEC-medicated salt with another form of DEC; studies with control groups for comparison; and before-and-after studies. Studies that compared with DEC-medicated salt with another form of DEC were considered to be most important from a policy perspective; it is well known that DEC is effective in clearing mf, but the optimal means of delivering DEC to communities is less clear. Filariasis is a relatively stable, endemic disease, but in some study areas vector control programmes or other interventions were already in place before DEC-medicated salt was introduced. For these reasons we considered studies that had some form of control (usually another village receiving ordinary salt) to be preferable to before-and-after studies.

Our main analyses are presenting the percentage reduction of each outcome from baseline for each study arm of each trial. There is no formal comparison (meta-analysis) between the percentage reductions in each group of trials because the studies are not randomized, are highly heterogeneous, and reporting of outcome measures was limited. However, we carried out a meta-regression to attempt to explain the variation in percentage reduction in mf prevalence observed between studies. Meta-regression examines heterogeneity by looking at the relationship between treatment effects and one or more study level characteristics. Accordingly, the variables included in the model were the proportion of the population covered by the intervention, baseline mf prevalence, concentration of DEC in salt, and duration of intervention. The significance of the regression model is tested using the F statistic of the ANOVA. Most studies were of short duration, but filariasis is a chronic infection and information on longer-term outcome of interventions is needed. We therefore reported separately on results from studies with longer periods of follow up (over two years). In these studies, the possible association between the DEC intake and the percentage reduction in the mf prevalence was tested by significance of the Pearson's correlation coefficient r, which measures the degree of association.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Eligibility

We identified 35 relevant articles; we included 21 studies (described in 30 of the articles) and excluded four studies (described in five articles). Reasons for exclusion are described in the 'Characteristics of excluded studies' and details of the included studies are in the 'Characteristics of included studies'.

Study locations

Ten studies were conducted in India (Raghavan 1968; Krishna Rao 1976; Katiyar 1977; Narasimham 1979; Rao 1981; Reddy 1986; Krishna Rao 1991; Kaul 1992; Panicker 1997; Shenoy 1998), six in China (PIPD 1976; FRG 1979; Ru 1984; Fan 1990a; Fan 1990b; Liu 1992), two in Tanzania (Davis 1969; Meyrowitsch 1998), and one each in Brazil (Hawking 1967), Haiti (Freeman 2001), and Papua New Guinea (Sapak 2000).

Study designs

We divided the studies into those conducted on individuals and communities, and then into one of three study designs: DEC-medicated salt versus other forms of DEC; DEC-medicated salt versus a control; and before-and-after study.

Studies of individuals

Four studies were carried out in adults who tested positive for microfilaraemia (Appendix 2). They were designed specifically to demonstrate the DEC-medicated salts efficacy (ability to clear mf under 'ideal' closely controlled conditions, eg hospital inpatients) and safety. Three were before-and-after studies (Hawking 1967; Davis 1969; Shenoy 1998) and one compared DEC-medicated salt with a placebo as a control (Panicker 1997). Panicker 1997 and Shenoy 1998 studied *B. malayi*, while Hawking 1967 and Davis 1969 studied *W. bancrofti*.

Studies of communities

The 17 community studies involved participants who were living in filariasis-endemic communities, irrespective of their mf status (Appendix 3). All included participants with *W. bancrofti*, except Kaul 1992, which included participants with *B. malayi*.

Two studies compared DEC-medicated salt with other forms of DEC. Sapak 2000 compared DEC-medicated salt (0.2%) for one year in six villages with a single annual dose of DEC in five villages. The initial mf prevalence was different in both groups (55% in the DEC-medicated salt group and 71% in the annual dose group). Neither per capita consumption of DEC-medicated salt nor the percentage coverage of the population were reported, and only those who agreed to give blood, receive treatment, and remain in the study area were followed up. Meyrowitsch 1998 assigned each of four communities with varying levels of mf prevalence to a different DEC regimen − standard 12-day course, semi-annual single dose, monthly single low dose for one year, or DEC-medicated salt (0.33%) for one year.

Four studies compared DEC-medicated salt with a control group, either untreated salt (Narasimham 1979; Krishna Rao 1991) or no salt (Krishna Rao 1976; Kaul 1992). Two communities in Krishna Rao 1976 used DEC-medicated salt (0.1%), one for 45 weeks and the other for 12 weeks. The proportion of population covered is not specified. Narasimham 1979 and Krishna Rao 1991 limited participation to a few randomly selected households with at least one mf-positive person, resulting in DEC-medicated salt coverage of 3.4% and 10% of the population, respectively. The reasons for this low coverage are not entirely clear, but it may be partly due to the random selection of treatment and the control households from the same village. However, within the selected treatment group of households, the coverage for DEC-medicated salt was 100%. Both studies used DEC-medicated salt (0.2% w/w) for six months. Three communities in Kaul 1992 received 0.23% DEC-medicated salt (100% coverage reported) for one year, and one community acted as the control.

The number of participants in each study ranged from 204 to 26,000. In the 11 before-and-after studies, DEC-medicated salt was distributed to whole communities, regardless of mf status. The concentration of DEC-medicated salt ranged from 0.1% to 0.26% in the four studies from India (Raghavan 1968; Katiyar 1977; Rao 1981; Reddy 1986), 0.1% to 1.0% for the six studies from China (PIPD 1976; FRG 1979; Ru 1984; Fan 1990a; Fan 1990b; Liu 1992), and 0.25% for the study from Haiti (Freeman 2001). The duration of the intervention ranged from 11 weeks to four years. We were unable to analyse the data for Fan 1990a because a programme of selective chemotherapy (5000 mg of DEC annually for three years) plus larviciding had been in place for three years before the study began, which made it impossible to determine the independent effect of DEC-medicated salt.

Outcome measures

Studies of individuals

All four studies reported on mf density, and Shenoy 1998 and Panicker 1997 also reported on adverse events.

Studies of communities

The two studies that compared DEC-medicated salt with other forms of DEC reported on mf prevalence; Meyrowitsch 1998 only measured mf densities for those participants who were both mf positive at baseline and completed the DEC regimens in different groups. Sapak 2000 also reported on antigen prevalence.

All four studies that compared DEC-medicated salt with untreated control groups measured mf prevalence, and most reported mf density only for those who were mf positive at baseline.

In the before-and-after studies, the outcome measures were measured at baseline (before the programme commenced) and after the programme was completed. A few studies continued the follow up for some period after completion. Ten of the 11 studies measured changes in mf prevalence (nine were of Bancroftian filariasis). Only nine studies reported on mf density, of which five reported mf density only among those who were mf positive at

baseline (Raghavan 1968; PIPD 1976; Katiyar 1977; FRG 1979; Liu 1992). The other four did not state clearly whether estimates of mf density applied to the whole community or just those mf positive (Rao 1981; Reddy 1986; Fan 1990a; Fan 1990b). Six studies provided data on changes in vector infection and infectivity rates (Raghavan 1968; FRG 1979; Rao 1981; Reddy 1986; Fan 1990b; Liu 1992). Two studies reported on changes in disease rates (Reddy 1986; Fan 1990b). Adverse events were only reported in seven of the studies.

Risk of bias in included studies

See Appendix 2 and Appendix 3.

Most studies (14) were before and after in design, only two compared DEC-medicated salt with another form of DEC, and five had some sort of control group (usually a separate village) that did not receive DEC-medicated salt.

The population coverage was very high (close to 100%) in nearly all of the community studies. In two studies, Narasimham 1979 and Rao 1981, control and the treatment households were selected from the same village (called a "Panchayat").

Some of the outcome measures, such as mf density, were poorly reported in many studies. Only two studies (Meyrowitsch 1998; Shenoy 1998) presented mf density as a geometric mean, which is the most appropriate measure as the distribution of mf in human blood is over dispersed (most infected people have very few or no mf, but a small number of people will have many mf in the blood). The other studies provided an arithmetic mean. It was not possible to calculate 95% confidence intervals for studies that reported arithmetic means only. Most studies reported mf density only for those mf positive, rather than for the whole community. Similarly, most studies reported disease prevalence only for those who were mf positive or symptomatic at baseline. Only one study reported on changes in outcomes like antigenaemia clearance rate, adult worm prevalence etc in addition to mf prevalence and density and therefore is described explicitly in this review (Freeman 2001).

One study from Kinmen Proper in China had used selective DEC chemotherapy plus larviciding for two years before the DEC-medicated salt intervention (Fan 1990a). It is therefore difficult to attribute the reduction in mf solely to the effects of DEC-medicated salt.

Effects of interventions

To ensure clarity and readability, we have presented the results under different headings. The primary headings are the different outcomes that were being studied, that is, mf prevalence, density, adverse reactions, vector infection or infectivity rates, and disease prevalence. Within each of these, the studies under different types of study (namely the DEC-medicated salt against other DEC strategies, DEC-medicated salt against control groups, and finally the before-and-after DEC-medicated salt group) are described.

1. Studies of individuals

All four studies reported complete clearance of mf and large reductions in mf density with DEC-medicated salt, but the sample sizes were small (Appendix 4). Adverse events were reported as being mild and manageable, but no further details were given.

2. Studies of communities

Mf prevalence (Appendix 5)

DEC-medicated salt versus other forms of DEC

Meyrowitsch 1998 reported that after one year of treatment mf prevalence had fallen in all four intervention groups. The greatest reduction was in the DEC-medicated salt group (92%) and the lowest was in the semi-annual single dose group (34%). Four years after the treatment period ended, there was no change in the corresponding reductions from baseline for the semi-annual single dose group (34%) and the monthly low dose group (54%), while it was slightly lower for the standard 12-day dose group (from 33% to 30%) and the DEC-medicated salt group (lowered to 60%).

Sapak 2000 reported a reduction in antigen prevalence six months after the start of the study (the DEC-medicated salt intervention lasted one year) in the DEC-medicated salt group (34%) and the DEC tablets group (7%). The antigen clearance rate (the change in the proportion of individuals who were positive for filarial antigenaemia before the treatment and subsequently became negative for antigenaemia after the treatment) for those positive at baseline was 43% in the DEC-medicated salt area and 13% in the village that received single-dose DEC.

DEC-medicated salt versus untreated control groups

Krishna Rao 1976 included three communities – two had DEC-medicated salt for either 45 weeks or 12 weeks, and the third was an untreated control area – and measured mf prevalence after one year and two or five years. There was a greater reduction in mf prevalence in the 45-week DEC-medicated salt community (86% at 1 year; 62% at 5 years) than the 12-week DEC-salt community (42% at one year; 40% at two years), but it increased in the control group (21% increase at one year; 13% increase at five years).

Krishna Rao 1991 reported results after one and eight years in groups that received DEC-medicated salt for six months or a control. The 85% reduction in mf prevalence in the DEC-medicated salt group at the end of the six-month intervention changed to a 32% reduction after eight years, while the control group recorded

a 24% reduction at eight years (from 3% at six months). The proportion of individuals initially mf negative who became microfilaraemic was significantly lower in the DEC-medicated salt group (4.8%) than in the control group (12.3%). This high gain rate of infection could be due to the presence of reservoir of infection in the community.

Narasimham 1979 measured mf prevalence seven and 11 months after the start of the intervention in households using DEC-medicated salt or a control. It decreased in the households using DEC-medicated salt group (by 59% at seven months; 46% at 11 months) and did not change appreciably in the control households (mf prevalence at baseline: 18.1%, after seven months: 19.9%, and after 11 months: 23.5%).

Kaul 1992 studied Malayan filariasis in four villages: three villages were administered DEC-medicated salt for a period of one year and the control village did not receive any salt. In the three intervention villages, the mf prevalence was reduced to zero, from 8.1%, 2.7%, and 6.2% after one year, and it remained at zero after 10 years. In the control village, mf prevalence was not significantly different after 10 years.

Before-and-after studies

The percentage reduction in mf prevalence could be estimated for nine of the 11 studies; the other two studies did not report mf prevalence after DEC-medicated salt distribution (Raghavan 1968; Katiyar 1977).

Most studies reported a statistically significant reduction in mf prevalence even after three years; it remained extremely low in one study that was followed up for 20 years (Reddy 1986, unpublished data). The impact of DEC-medicated salt is evident from the 80% to 95% reduction after six months follow up in each study, irrespective of the initial mf prevalence. The intervention seems to be sustained over time: the mf prevalence did not reach the pre-study level even after eight years in most of the studies with this length of follow up. In the community study from Haiti (Freeman 2001), mf prevalence fell by 95% from 20.05% to 0.98%. Antigenaemia prevalence was 40.2% before treatment, and after one year of treatment about 95% (133/140) of those who were antigen positive had become negative.

In all these community studies, the coverage under the DEC medicated salt programme has been around 100% ranging between (98% to 100%). In those studies, where the treatment and the control households were selected from the same community, the coverage within the treatment group was 100%.

Mf density (Appendix 6)

DEC-medicated salt versus other forms of DEC

Meyrowitsch 1998, which compared DEC-medicated salt with a monthly low dose of DEC, standard 12-day dose, and a semi-annual single dose, reported changes in mf density one and four years after the intervention, but this was measured only for individuals positive at baseline and who completed all or most of their assigned intervention. This measurement is not synonymous with 'community mf density', which requires following those initially both positive and negative to account for individuals who may have become positive during the follow-up period. Reductions were greater than 90% even at four years after the treatment period, but because of the way the figures were calculated, they can only be taken as suggestive.

DEC-medicated salt versus untreated control groups

All four studies observed large reductions in mf density at the end of the intervention period, or after one year, and at later follow ups. Little reduction, or even an increase was seen in mf density in the control areas. In some studies the reductions seemed to be sustained over longer periods, particularly in Kaul 1992, but in one other study mf density had almost reached its pre-intervention value after eight years (Rao 1991). Most studies did not clearly state whether the mf density was estimated for the entire community or just those mf positive, or even the sample size on which the percentage reduction was based.

Before-and-after studies

Half of the 10 studies reported mf density only among those mf positive in baseline mf surveys. The other five did not state explicitly whether estimates were from the whole community or those mf positive only.

Freeman 2001 used DEC-medicated salt for one year and reported on both mf density and antigenaemia levels. There was a 99.5% reduction in mf density (from 8 to 0.01) one year from the start of treatment. Antigenaemia levels fell by 69% (from 740.9 to 279.6) and 57% (from 647.2 to 300.2) for those aged zero to 10 and greater than 10 years respectively after one year (data not shown). Other studies showed similarly large reductions in mf density, often maintained over six to 19 years of follow up.

Adult worm diagnosis or prevalence

One study, Freeman 2001, reported on the prevalence of adult worms based on ultrasound examination. Live adult nests were found among 12 of 15 men at baseline, and eight at the end of the study − a 37% reduction from baseline, though this was not statistically significant. The geometric mean number of adult worm nests per person also decreased by 44% (from 0.94 to 0.53), also not statistically significant. It is unclear why change in adult worm nests was presented as a geometric mean when the number of nests varied only between zero and two among the men at baseline.

Disease prevalence (Appendix 7)

DEC-medicated salt versus other forms of DEC

Meyrowitsch 1998 compared DEC-medicated salt with a monthly low dose DEC, standard 12-day dose, and a semi-annual single dose. Disease prevalence was measured by examining the prevalence of hydrocoele and elephantiasis for each group after one and four years. The greatest reductions in hydrocoele prevalence occurred in the monthly low-dose group (50%), those on the standard 12-day dose (29%), and those receiving the semi-annual single dose (26%); there was only a 5% reduction by the end of one year and 13% at the end of the fourth year in the community given DEC-medicated salt for one year.

DEC-medicated salt versus untreated control groups

Three studies compared one or more DEC-medicated salt groups with a control group. Krishna Rao 1976, which had two DEC-medicated salt groups (one for 45 weeks and one for 12 weeks), reported a low pre-treatment disease rate in the community given DEC-medicated salt for 12 weeks, with no statistically significant change in disease prevalence after two years. However, in the community that received DEC-medicated salt for 45 weeks, a 53% reduction was observed in the disease rate after five years. Surprisingly, in the community that did not receive any salt there was also a statistically significant 60% reduction in the disease prevalence after five years. This study did not describe methods of clinical examination, criteria for diagnosis, or who carried out the examinations. Although statistically significant reductions in disease prevalence were observed in some groups, these should be interpreted with caution. Clinically, the possibility of recovery from advanced disease such as elephantiasis of leg due to semi-annual DEC treatment or in untreated control groups seems remote. Since prevalence rates are obtained through cross sectional surveys, one possible explanation is that investigators missed some cases detected in the earlier surveys.
Narasimham 1979 compared DEC-medicated salt with a control group. It was not clear how the study evaluated disease prevalence, but the prevalence at baseline was higher in the DEC-medicated salt group (6.5%) compared with the control group (11.6%). After 11 months of treatment, it had decreased by 8% (to 6.0%) in the DEC-medicated salt group and increased by 3% (to 11.9%) in the control group. Kaul 1992 compared the effects on Malayan filariasis of DEC-medicated salt for one year in three villages with no DEC-medicated salt. Two of the three villages showed statistically significant reductions in disease rates (measure not specified), while the disease rate remained stable in the control community. Statistical power may be too low to look for any statistically significant changes in the disease rates.

Before-and-after studies

Two studies measured disease prevalence at different times: both Reddy 1986 and Fan 1990b measured it at one year, and Reddy 1986 also at seven and 19 years. Disease rates for Reddy 1986 were obtained from routine surveys carried out by the National Filariasis Control Unit. The community disease prevalence after four years of DEC-medicated salt decreased over the 19 years from 0.39% at the start of the intervention to 0.05% after 19 years, a statistically significant decrease of 87%.
Fan 1990b described the change in disease status only among mf carriers detected in the pre-treatment survey in the Little Kinmen Islands of China and followed them for two years after the intervention. The disease rate was 26.2% among the 294 mf carriers before the trial started, and it fell to 18.3% after one year. Another group of 126 mf carriers with clinical manifestations such as lymph node enlargement, orchitis, epididymitis, funiculitis, chyluria, tropical pulmonary eosinophilia, and elephantiasis were followed up to two years. These symptoms disappeared completely in 66 (52%) mf carriers, showed significant improvement in 24 (19%), and did not change in 11 (8.7%). Most of this latter group had advanced chronic symptoms such as elephantiasis. Eleven (9%) participants who were disease free at start developed clinical manifestations.

Vector infection and or infectivity rates (Appendix 8)

DEC-medicated salt versus other forms of DEC

Neither Meyrowitsch 1998 nor Sapak 2000 reported on vector infection or infectivity.

DEC-medicated salt versus untreated control groups

Only two studies reported the impact of DEC-medicated salt on vector infection and infectivity rates. They remained low in the community receiving DEC-medicated salt for 45 weeks in Krishna Rao 1976 (56% fall in vector infection; 78% fall in vector infectivity), even after five years. The vector rates were statistically significantly higher in the community where DEC-medicated salt was given for 12 weeks (9% fall in vector infection; 36% fall in vector infectivity) and in the control area (57% fall in vector infection; 62% fall in vector infectivity).
Kaul 1992 reported vector infection and infectivity rates, but only in the villages that received DEC-medicated salt. These remained zero (it is unclear how many mosquitoes were sampled) after one and eight years.

Before-and-after studies

Seven studies reported details on vector infection rates (and/or infectivity rates), which ranged from 0.6% (0.1%) to 9.5% (3.4%)

before the start of DEC-medicated salt programmes. Two studies from China reported on vector infection only after the intervention (PIPD 1976; Ru 1984) and are therefore excluded from the results.

The percentage reduction following the programmes varied from 92% to 100% after one year, and in those studies where it had fallen to zero, vector infection or infectivity rates remained at zero for six (Fan 1990a) to 19 years (Reddy 1986). However, the measurements of vector infection and infectivity rates in many studies were imprecise, often based on inadequate sample sizes. In Freeman 2001 there was a statistically significant 61% decrease in the number of infected vectors after one year of treatment: from 3.1% to 1.2%. The vector infectivity rate also fell by 92% (from 2.4% to 0.2%) after one year of treatment.

Adverse events

DEC versus other forms of DEC

Neither Meyrowitsch 1998 nor Sapak 2000 reported on adverse events.

DEC-medicated salt versus untreated control groups

Two studies reported generally on adverse events. Krishna Rao 1976 reported "mild" adverse events only, with no further details. Krishna Rao 1991 recorded no adverse events in the communities given DEC-medicated salt or in those that did not receive salt.

Before-and-after studies

Four studies reported generally on adverse events (Raghavan 1968; PIPD 1976; Fan 1990b; Liu 1992), but with few details such as the number of events. No serious adverse events were recorded, and three reported no events. Where events occurred (Liu 1992), they seemed to be mild such as headache, nausea and lymphangitis, and associated with co-infection with intestinal helminths.

Multivariate analysis to explore heterogeneity between studies

The percentage reduction in mf prevalence varied greatly between studies, ranging from 43% to 100%. There was a significant correlation between the per capita consumption and the percentage reduction observed in the mf prevalence after one year (correlation coefficient r = 0.642; P = 0.003). This suggests that the reduction in the mf prevalence is influenced by the amount of DEC that has been consumed by the community.

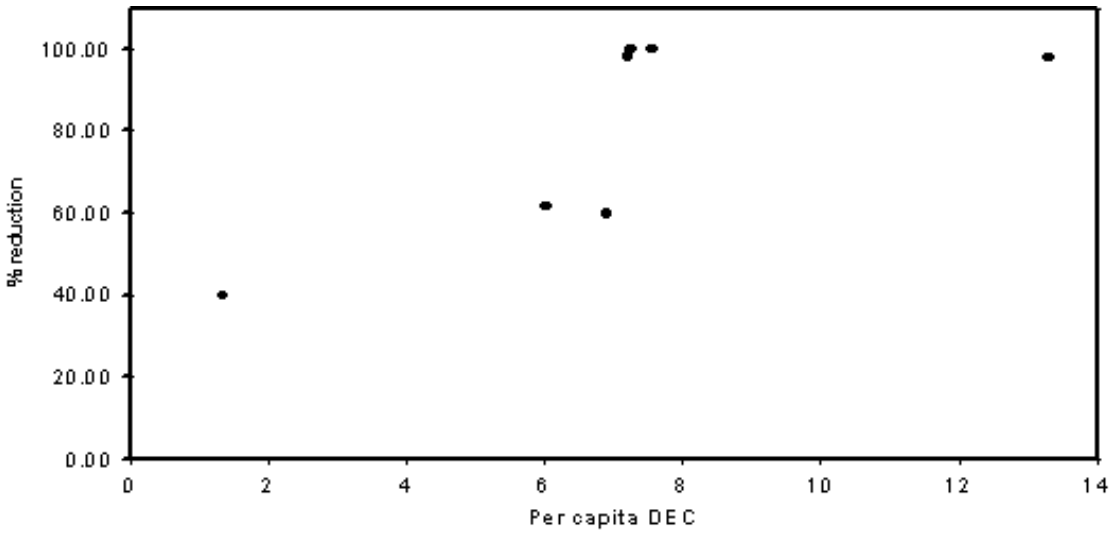
We therefore carried out a weighted meta-regression (using SPSS 13) to explore these differences in terms of the following study characteristics: concentration of DEC in salt; proportion of population covered in the study (though there is not much variability in this aspect between studies: range (98% to 100%); pre-treatment mf prevalence; and duration of the intervention. These variables were chosen as they were the only possible predictors clearly reported by the majority of studies. The inverse of the sum of sample sizes were used as weights. The percentage mf reduction one year after the start of treatment (available for most studies) was the independent variable. The first model included all the above mentioned predictors. At this stage only concentration of DEC in the salt emerged as a significant predictor and the model described 77% variation in the data. In the second model, of the three remaining variables, duration of intervention was found to be significant and was included in the model, which described 91% of the variation in the data (F = 96.85, P = 0.000). As there were no more significant predictors, the final model was based on the DEC concentration and duration of the intervention, the significant predictors of the reduction in the mf prevalence one year after the intervention. The regression model was as follows:

The percentage reduction after one year equals -11.138 + 217.78 * (DEC concentration in the salt) + 3.92 * (duration of intervention). This implies that when no DEC intervention is supplied, the mf prevalence is expected to increase by 11.38% after one year. For every unit increase in DEC concentration, the percentage reduction after one year will increase by 217.78%. Similarly, for every unit increase in duration, the percentage reduction after one year will increase by 3.92%.

The coefficient for DEC concentration is the highest, but the standardized coefficients showed that both contribute equally to the model. Standardized coefficients tell you how much change in the outcome there is for one standard deviation change in each independent variable, allowing direct comparisons of the importance of different variables. This is because it is often difficult to tell which independent variables (DEC salt concentration, duration of intervention) are most important in determining the magnitude of the outcome (reduction in mf prevalence) just from looking at the coefficients, as different variables are measured on different scales. Meta-regression was repeated excluding the before-and-after studies, but this did not greatly affect the results (data not shown).

Fifteen of the community studies reported results after one year of DEC-medicated salt. Reductions in mf appeared high except in those studies, which had both the control and the treatment group (of households) from the same community. Seven studies followed communities receiving DEC-medicated salt for two or more years (range two to 19 years). In most cases, the effects of DEC-medicated salt on mf prevalence appeared to be maintained over time and it was seen that in these communities the proportion covered was high. There appeared to be a relationship between per capita consumption of DEC-medicated salt and percentage reduction in mf prevalence (see Figure 1), though this reached only a borderline significance (the correlation coefficient, r = 0.68, P = 0.05).

Figure 1. Long-term effects of DEC-medicated salt



DISCUSSION

This review was undertaken to assess the short-term and long-term effects of DEC-medicated salt in the control of lymphatic filariasis, one of three interventions advocated by the Global Programme for the Elimination of Lymphatic Filariasis (the others are single annual dosing with DEC or a combination of antifilarial drugs). DEC-medicated salt may be an effective and safe way of increasing uptake in some endemic communities. Reviews of DEC-medicated salt published in 1994 and 2000 concluded that it was effective in reducing mf levels in communities, but many studies were of low quality (Gelband 1994; Houston 2000a; Houston 2000b). This Cochrane Review contains several new studies with control groups, strengthening results of the earlier review. Meta-regression also demonstrated that the duration of the intervention and DEC concentration were the most important variables explaining differences between study findings.

We included 21 studies. The primary outcome was to evaluate the effect of DEC-medicated salt on infection in humans (mf prevalence or density, and antigenaemia); secondary outcomes included other aspects such as potential for continued transmission (vector infection and infectivity rates), clinical disease, and adverse events.

Studies of individuals (efficacy studies, mostly on small numbers of hospitalized patients) showed that all the mf-positive individuals who were administered DEC-medicated salt had no detectable mf by the end of the trial. DEC-medicated salt can therefore be an effective tool for elimination.

Among communities, the percentage reduction in mf prevalence in communities receiving DEC-medicated salt varied (between 43% and 100%), but it was greater after one year of the intervention than in communities given other forms of DEC, such as low dose, semi-annual single dose, standard 12-day dose, or placebo (between 0% and 54%). In studies that measured the impact in the same community before and after administering DEC-medicated salt, the percentage reduction was also very high, between 86% and 100%.

In two studies, where the households for the control and the treatment group were randomly selected from the same community (Narasimham 1979; Krishna Rao 1991), the percentage reductions in mf prevalence in the control and treatment groups one year after intervention were 46% and 86% respectively. After eight years the percentage reduction was only 32% (Krishna Rao 1991). This indicates that the transmission continued to occur because of the presence of the infection reservoir (the control group) within the same community. This emphasizes the need for high coverage of the entire community.

Studies that measured vector infection and infectivity found large reductions, sometimes as high as 100%. These data should be cautiously interpreted as the number of vectors dissected was either not reported or were small. However, three studies found that even after eight to 19 years, vector infection and infectivity were significantly lower compared with the pre-trial values (Reddy 1986; Fan 1990a; Fan 1990b).

DEC-medicated salt seemed to have little immediate effect on disease rates (either acquisition of new disease or improvement in disease). Adverse events also appeared to be very minimal and were mentioned as manageable in communities administered with DEC-medicated salt. However, few studies described any procedure to record adverse events; hence these may be under reported.

Most studies had relatively short follow-up periods (one year or less), but seven with longer term follow up found that reductions in mf prevalence, density, and vector infectivity appeared to be sustained over time. Community coverage of DEC-medicated salt was high in these studies, and there also appeared to be a relationship between per capita DEC consumption and the percentage reduction in mf prevalence, but this was not statistically significant.

Most studies (14) were before and after in design, simply measuring infection and disease before and after administering DEC-medicated salt. The remaining studies had some form of control group (eg placebo or other means of distributing DEC). The lack of randomized comparisons means we cannot exclude the possibility that selection bias or confounding factors may have affected the results. The reductions in mf prevalence were sizeable and consistent in most studies (between 43% and 100%), and it unlikely that reductions of this magnitude could be entirely due to the influence of confounding factors. As with any 'community study' it is difficult to attribute any falls in infection solely to DEC-medicated salt. In several studies, other filariasis infection control measures were also implemented or had been carried out shortly before the administration of DEC-medicated salt. These included administration of other forms of DEC in the community or vector control measures (Fan 1990b). In some communities, these other measures may have added to the apparent success of distributing DEC-medicated salt.

The quality of the studies was assessed as part of the data extraction and was taken into consideration in the review by presenting results according to study type and meta-regression. The regression model, which explained over 90% of the variation in the data, showed that variables such as the duration of the trial and concentration of the DEC-medicated salt were associated with the observed reduction in mf prevalence one year after start of the intervention.

In addition to the lack of randomized comparisons, some outcomes were poorly reported, particularly mf densities (which ideally should be reported for whole communities), vector infection and infectivity rates, disease rates, and adverse events. Most studies reported changes in mf prevalence (or antigen prevalence), but this is a less sensitive measure of effectiveness than mf density (Das 2001). Most studies calculated the arithmetic mean for mf densities instead of giving geometric means, which is more appropriate for a variable that is so over dispersed in character. Some of the studies have reported mf densities only among those mf positive at baseline survey instead of the entire community. Outcomes for all people in the community, or a representative sample of them regardless of baseline mf status, would be preferable in assessing the community impact of a mass treatment strategy such as DEC-medicated salt. Vector infection and infectivity rates should be viewed cautiously because of the small number of mosquitoes sampled in these studies. As far as the disease rates are concerned, though there is no immediate effect of DEC-medicated salt, the method of clinical examination was not described in most studies. Also, a duration of one year is too short a period to have even a minimal effect on disease, and studies also did not have sufficient statistical power to assess changes in disease prevalence at three to five years. In most studies, adverse events were described as minimal and manageable, but it was not clear how these were monitored.

In spite of all the limitations that exist in measuring the impact of the DEC-medicated salt, large reductions of up to 100% in mf prevalence were observed in many studies (Reddy 1986; Fan 1990a; Fan 1990b). DEC-medicated salt even appears to have achieved elimination in parts of China (Gelband 1994). Where DEC-medicated salt was compared with other forms of DEC (low dose, semi-annual single dose, the 12-day standard dose, or placebo), the community that received DEC-medicated salt showed greater reductions in mf prevalence even four years after the trial (Meyrowitsch 1998). One study of Malayan filariasis showed that treated communities remained mf negative even 10 years after the intervention (Kaul 1992). Vector infection and infectivity rates suggest that DEC-medicated salt has been able to break transmission 19 years after the first administration of DEC-medicated salt (Reddy 1986). DEC-medicated salt has been effective for both Bancroftian filariasis (Reddy 1986; Fan 1990a; Fan 1990b) and Malayan filariasis (Kaul 1992), where the infection levels both in humans and vectors have fallen greatly. These imply that DEC-medicated salt provides a viable means of breaking transmission in areas having persistent foci. Particularly, DEC-medicated salt may be essential in those areas where adherence to mass annual DEC is not high. However, DEC-medicated salt has only been successful in breaking transmission where coverage has been high, implying that strong support from local communities and political commitment to ensure supplies are essential.

AUTHORS' CONCLUSIONS

Implications for practice

The evidence reviewed supports the conclusion that DEC-medicated salt is safe, feasible, and stable in field conditions and mainly accepted by the community. The range of DEC concentration in the salt was 0.1% to 1% in the studies. Concentrations between 0.1% and 0.5% w/w were effective in reducing mf prevalence and intensity in communities, and increasing the DEC concentration more than 0.5% w/w did not show more pronounced reduction in mf prevalence or intensity. Only minimal or manageable adverse

events were observed in the studies suggesting DEC-medicated salt is safe to use as mass treatment in communities. In the limited number of available studies, DEC-medicated salt performed better than other forms of DEC (low dose, semi-annual single dose, 12-day standard dose) in its ability to reduce infection levels, with limited adverse events.

As with all filariasis control strategies, transmission can be stopped only when DEC-medicated salt is used by entire communities. Political and administrative commitment and community motivation is a necessity for community programs to be successful.

Implications for research

The review suggests that DEC may be more effective when given in a very low dose continuously over a long duration (such as six months), than in higher doses at one point of time. The effect of continuous low doses of DEC on killing or sterilizing adult worms could be explored.

Studies mostly measured the presence of mf and not that of antigenaemia, which is a more sensitive measure of infection in humans. It would be interesting to see the effect of DEC-medicated salt on antigenaemia levels in humans. This review has given some insight regarding the effect of the DEC-medicated salt on the filarial infection. Clinical outcomes are also important due to the high morbidity associated with disease. However, this review shows that there are insufficient data concerning the effect of DEC-medicated salt on these clinical manifestations, and this aspect could be further explored by carrying out longitudinal studies on populations administered DEC-medicated salt.

Another important factor is the possibility that widespread use of DEC-medicated salt over a prolonged period could encourage the development of drug resistance. In theory, drug resistance is more likely to arise when a drug is given in low doses for a longer period of time, but there have been few studies assessing resistance to DEC. New or ongoing studies of DEC-medicated salt should carefully document any changes in drug resistance.

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Ongoing. No details available.

Krishnamoorthy 2004 *{unpublished data only}*
Ongoing. No details available.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Davis 1969

Methods	Design: before-and-after study of individuals Follow up: 6 months (47 could be followed up at 3 months and 22 at 6 months)
Participants	Bancroftian filariasis 64 microfilaraemic prison inmates
Interventions	DEC-medicated salt (0.1%) mixed in food for 6 months
Outcomes	Mf density
Notes	Location: Tanga, Tanzania

Fan 1990a

Methods	Design: before-and-after study of communities Follow up: 8 yr
Participants	Bancroftian filariasis One community with a population of 7125 individuals
Interventions	0.33% DEC-medicated salt for 6 months For 3 yr before study began, a programme using a combined strategy with selective chemotherapy (5000 mg of DEC annually for 3 yr) and larviciding had been in place
Outcomes	1. Mf density 2. Mf prevalence 3. Vector infection and infectivity
Notes	Location: Kinmen Proper, China

Fan 1990b

Methods	Design: before-and-after study of communities Follow up: 6 yr
Participants	Bancroftian filariasis 1 community with a population of 54,016 individuals
Interventions	0.33% DEC-medicated salt for 6 months
Outcomes	1. Mf density 2. Mf prevalence 3. Vector infection and infectivity rates

Fan 1990b (*Continued*)

	4. Changes in disease rates at 1 year 5. Adverse events
Notes	Location: Little Kinmen Islands, China

Freeman 2001

Methods	Design: before-and-after study of communities Follow up: 1 yr
Participants	Bancroftian filariasis 1 community with 1932 individuals
Interventions	DEC-medicated salt (0.25%) for 1 yr
Outcomes	1. Mf prevalence/density 2. Antigenaemia density 3. Prevalence of adult worms based on ultrasound examination (mf viability) 4. Vector infection and infectivity rates
Notes	Location: Haiti

FRG 1979

Methods	Design: before-and-after study of communities Follow up: 5 yr
Participants	Bancroftian filariasis 2 villages with a population of 1100 individuals
Interventions	DEC-medicated salt (0.24%) for 6 months
Outcomes	1. Mf density only among those who were mf positive at baseline 2. Mf prevalence 3. Vector infection and infectivity rates
Notes	Location: China

Hawking 1967

Methods	Design: before-and-after study of individuals Follow up: 45 wk
Participants	Bancroftian filariasis Hospital mf-positive inpatients: 15 in Hospital 1; 7 in Hospital 2
Interventions	DEC-medicated salt mixed with food (0.2%) in Hospital 1 and (0.3%) in Hospital 2

Hawking 1967 (*Continued*)

Outcomes	Mf density
Notes	Location: Recife, Brazil

Katiyar 1977

Methods	Design: before-and-after study of communities Follow up: 1 yr
Participants	3 villages; 1 village with a population of 340 individuals treated with DEC-medicated salt and the other 2 did not receive salt
Interventions	DEC-medicated salt (0.26%) for 2.7 months
Outcomes	Mf density (only among those who were mf positive at baseline)
Notes	Location: India

Kaul 1992

Methods	Design: DEC-medicated salt versus control study of communities Follow up: 10 yr
Participants	Malayan filariasis 4 communities (3 receiving DEC-medicated salt and one receiving no salt) each with an average population of 430 individuals
Interventions	1. DEC-medicated salt (0.23%) for 1 yr: 3 communities 2. No intervention: 1 community
Outcomes	1. Pretreatment and post-treatment mf prevalence for the communities 2. Mf density 3. Disease rates (measure not specified) 4. Vector infection and infectivity rates in the DEC-medicated salt villages only
Notes	Location: remote hill settlements in Karala, India

Krishna Rao 1976

Methods	Design: DEC-medicated salt versus control study of communities Follow up: 2 to 5 yr
Participants	Bancroftian filariasis 3 communities with population of 24,094, 2489, and 4557 individuals

Krishna Rao 1976 (*Continued*)

Interventions	1. DEC-medicated salt (0.1%) for 45 wk (1 community) 2. DEC-medicated salt (0.1%) for 12 wk (1 community) 3. No salt (1 community)
Outcomes	1. Community mf prevalence before and after treatment 2. Mf density 3. Disease prevalence 2. Vector infection and infectivity 3. Adverse events
Notes	Location: Andhra Pradesh, India

Krishna Rao 1991

Methods	Design: DEC-medicated salt versus control study of communities Follow up: 8 yr
Participants	Bancroftian filariasis Participation was limited to 611 individuals in 84 households with at least one mf-positive person
Interventions	1. DEC-medicated salt (2%) for 6 months 2. Untreated common salt for 6 months
Outcomes	1. Mf prevalence for the whole group 2. Mf density 3. Vector infection and infectivity 4. Adverse events
Notes	Location: India

Liu 1992

Methods	Design: before-and-after study of communities Follow up: 1 yr
Participants	Bancroftian and Malayan filariasis 20 endemic counties and cities with population of 5,189,126 individuals for Bancroftian filariasis Endemic region with a population of 67,778 individuals for Malayan filariasis
Interventions	DEC-medicated salt (0.5% to 1%) for 4 months
Outcomes	1. Mf density only among those who were mf positive at baseline 2. Vector infection and infectivity rates 3. Adverse events
Notes	Location: China

Meyrowitsch 1998

Methods	Design: DEC-medicated salt versus other forms of DEC in communities Annual follow up: 4 yr
Participants	Bancroftian filariasis 4 communities with varying levels of mf prevalence
Interventions	1. DEC-medicated salt for 1 year (0.33%) 2. Monthly single low dose for 1 yr (50 mg DEC for children < 15 yr; and 100 mg DEC for adults > 15 yr) 3. DEC standard dose (6 mg/kg/day for 12 days) 4. Semi-annual single dose (standard dose twice a yr)
Outcomes	1. Mf prevalence before and after treatment for all 4 communities 2. Mf densities measured only for those who were both mf positive at baseline and completed the DEC regimens in different groups 3. Disease prevalence (hydrocoele, elephantiasis)
Notes	Location: Tanzania

Narasimham 1979

Methods	Design: DEC-medicated salt versus control study of communities Follow up: 1 yr
Participants	Bancroftian filariasis Participation was limited to 769 individuals in 63 households with at least 1 mf-positive person
Interventions	1. DEC-medicated (0.1 %) salt for 6 months 2. Untreated common salt for 6 months
Outcomes	1. Mf prevalence for the whole group 7 and 11 months after start of intervention 2. Mf density
Notes	Location: India

Panicker 1997

Methods	Design: DEC-medicated salt versus control study of individuals Follow up: 1 yr
Participants	Malayan filariasis 18 patients positive for Brugia malayi microfilaraemia
Interventions	1. DEC-medicated iodized salt (0.22%) for 7.5 months (30 weeks): 14 participants 2. Placebo (iodized salt) for 7.5 months: 4 participants
Outcomes	Mf density

Panicker 1997 (*Continued*)

Notes	Location: Kerala, India

PIPD 1976

Methods	Design: before-and-after study of communities Follow up: 1 yr
Participants	Bancroftian filariasis 6 villages in a county with an average population of 990 individuals participated
Interventions	DEC-medicated salt (0.3%) for 6 months
Outcomes	1. Mf density only among those who were mf positive at baseline 2. Vector infection only after the intervention (excluded from the table and text) 3. Adverse events
Notes	Location: China

Raghavan 1968

Methods	Design: before-and-after study of communities Follow up: 3 months
Participants	Bancroftian filariasis 1 community with a population of 204 individuals
Interventions	0.1% DEC for 2 months
Outcomes	1. Mf density only among those who were mf positive at baseline 2. Vector infection and infectivity rates 3. Adverse events
Notes	Location: India

Rao 1981

Methods	Design: before-and-after study of communities Follow up: 1 yr
Participants	Bancroftian filariasis 9 endemic islands with 26,000 population
Interventions	DEC-medicated salt (0.1% to 0.15%) for 6 to 20 months
Outcomes	1. Mf prevalence 2. Mf density 3. Vector infection and infectivity rates

Rao 1981 (*Continued*)

Notes	Location: India

Reddy 1986

Methods	Design: before-and-after study of communities Follow up: 20 yr/19 yr
Participants	Bancroftian filariasis One community with a population of 119,978 individuals
Interventions	DEC-medicated salt (0.1% to 0.2%) for 48 months
Outcomes	1. Mf prevalence 2. Mf density 3. Vector infection and infectivity rates 4. Changes in disease rates
Notes	Location: India

Ru 1984

Methods	Design: before-and-after study of communities Follow up: 3 yr
Participants	Bancroftian filariasis 8 farm brigades in a county were selected for participation
Interventions	DEC-medicated salt (0.38% to 0.57%) for 5 months
Outcomes	1. Mf prevalence 2. Vector infection only after the intervention (excluded from the table and text)
Notes	Location: China

Sapak 2000

Methods	Design: DEC-medicated salt versus other forms of DEC in communities Follow up: 6 months; only those who agreed to give blood, receive treatment, and remain in the study area were followed up
Participants	Bancroftian filariasis 6 villages (DEC-medicated salt) 5 villages (DEC tablets) Individuals with age 5 or greater

Sapak 2000 (*Continued*)

Interventions	1. DEC-medicated salt (0.2%) for 1 yr: 6 villages 2. Single annual dose DEC: 5 villages
Outcomes	Mf and antigen prevalence
Notes	Location: Papua New Guinea Neither per capita consumption of DEC-medicated salt nor the percentage coverage of the population were reported

Shenoy 1998

Methods	Design: before-and-after study of individuals Hospital-based study Follow up: 1 yr
Participants	Malayan filariasis 20 microfilaraemic individuals
Interventions	DEC-medicated salt (0.22%) for 1 yr
Outcomes	Mf density as a geometric mean
Notes	Location: India

DEC: diethylcarbamazine; mf: microfilariae

Characteristics of excluded studies *[ordered by study ID]*

Li 1990	Report of strategies used in a country-wide filariasis control programme over one decade used to reduce mf prevalence to < 1%; no report specific to DEC-medicated salt with relevant outcomes
Pan 1993	Report of DEC-medicated salt and mass chemotherapy with DEC given simultaneously; data on effects of each component not available
Sethumadhavan 1982	A comparison of 2 strategies for DEC-medicated salt with DEC tablets given in a 5-day schedule. These 2 trials were conducted in 2 different periods (DEC tablets in 1965 and DEC-medicated salt in 1976 in the same community). These sorts of comparisons are not valid for this review
Sharma 1982	DEC-medicated salt was given to the community, but the observations made are related to the follow up of a different DEC dosage regimen following the salt trial to look at development of resistance to DEC after community use of DEC-medicated salt

DEC: diethylcarbamazine

Characteristics of ongoing studies *[ordered by study ID]*

Addis 2005

Trial name or title	Not available
Methods	Not available
Participants	Not available
Interventions	DEC-medicated salt
Outcomes	Not available
Starting date	Not available
Contact information	Dr David Addiss (dga1@cdc.gov)
Notes	Guyana

Krishnamoorthy 2004

Trial name or title	Not available
Methods	Not available
Participants	Communities endemic for lymphatic filariasis
Interventions	DEC-medicated salt and mass DEC
Outcomes	Mf prevalence and density
Starting date	2004
Contact information	Dr K Krishnamoorthy (kkrish˙3@yahoo.com)
Notes	India

DEC: diethylcarbamazine; mf: microfilariae

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Search methods: detailed search strategies

Search set	CIDG SR[a]	CENTRAL	MEDLINE[b]	EMBASE[b]	LILACS[b]
1	diethylcarbamazine	diethylcarbamazine	diethylcarbamazine	diethylcarbamazine	diethylcarbamazine
2	DEC	DEC	DEC	DEC	DEC
3	salt	salt	salt	salt	salt
4	sodium chloride	sodium chloride	sodium chloride	sodium chloride	sodium chloride
5	1 or 2 or 3 or 4	1 or 2 or 3 or 4	1 or 2 or 3 or 4	1 or 2 or 3 or 4	1 or 2 or 3 or 4
6	elephantiasis	elephantiasis	elephantiasis	elephantiasis	elephantiasis
7	Wucher[b] bancrofti	Wucher[b] bancrofti	Wucher[b] bancrofti	Wucher$[b]bancrofti	Wucher[b] bancrofti
8	filaria bancrofti	filaria bancrofti	filaria bancrofti	filaria bancrofti	filaria bancrofti
9	Brugia malayi	Brugia malayi	Brugia malayi	Brugia malayi	Brugia malayi
10	Brugia timori	Brugia timori	Brugia timori	Brugia timori	Brugia timori
11	Brugia pahangi	Brugia pahangi	Brugia pahangi	Brugia pahangi	Brugia pahangi
12	filariasis	filariasis	filariasis	filariasis	filariasis
13	6-12/OR	6-12/OR	6-12/OR	6-12/OR	6-12/OR
14	5 and 13	5 and 13	5 and 13	5 and 13	5 and 13
15	-	-	limit 14 to human	limit 14 to human	limit 14 to human

[a] Cochrane Infectious Diseases Group Specialized Register.

[b] Search terms used in combination with the search strategy for retrieving trials developed by The Cochrane Collaboration (Higgins 2005); upper case: MESH or EMTREE heading; lower case: free text term.

Appendix 2. Studies of individuals: overview

Study	Country	DEC concentration	Intervention period	Follow up
DEC-medicated salt vs control group	-	-	-	-
Panicker 1997	India	0.2%	7.5 months	1 yr
Before and after	-	-	-	-
Hawking 1967	Brazil	0.3%	1 yr	-
Davis 1969	Tanzania	0.1%	6 months	6 months
Shenoy 1998	India	0.22%	1 yr	1 yr

DEC: diethylcarbamazine.

Appendix 3. Studies of communities: overview

Study	Country	Population coverage	DEC concentration	Intervention period	Follow up
DEC-medicated salt vs other forms of DEC	-	-	-	-	-
Meyrowitsch 1998	Tanzania	100%	0.33%	1 yr	2 to 5 yr
Sapak 2000	Papua New Guinea	100%	0.2%	1 yr	6 months
DEC-medicated salt vs control group	-	-	-	-	-
Krishna Rao 1976	India	100%	0.1%	3 to 11 months	2 to 5 yr
Narasimham 1979	India	7.7%	0.1%	6 months	1 yr
Krishna Rao 1991	India	25%	0.2%	6 months	8 yr
Kaul 1992	India	100%	0.23%	1 yr	10 yr

(*Continued*)

Before and after	-	-	-	-	-
PIPD 1976	China	100%	0.3%	6 months	1 yr
Katiyar 1977	India	100%	0.26%	2.7 months	1 yr
FRG 1979	China	100%	0.24%	6 months	5 yr
Rao 1981	India	100%	0.1% to 0.15%	6 to 24 months	1 yr
Raghavan 1968	India	100%	0.1%	2 months	3 months
Ru 1984	China	Not available	0.38% to 0.56%	5 months	3 yr
Reddy 1986	India	100%	0.1% to 0.2%	48 months	19 yr
Fan 1990a	China	100%	0.33%	6 months	5 yr
Fan 1990b	China	100%	0.33%	6 months	6 yr
Liu 1992	China	98%	0.5% to 1%	2 to 4 months	1 yr
Freeman 2001	Haiti	100%	0.25%	1 yr	1 yr

DEC: diethylcarbamazine.

Appendix 4. Microfilariae density: individuals

Study	Intervention	No. participants	Follow up	Pre-DEC	Post-DEC	% reduction
Before and after	-	-	-	-	-	-
Hawking 1967	0.1% DEC for 1.2 weeks	15 in Hospital 1	45 wk	24.0 mean no. mf/30 mm3	0.3	99
	-	7 in Hospital 2	45 wk	50	13.6	73
Davis 1969	0.1% DEC for 6 months	47 (of 64 available)	3 months	44.3 mean no. mf/40 mm3	20.89	Cannot be calculated
	-	22 (of 64 available)	6 months	No data	5.96	Cannot be calculated

(*Continued*)

Shenoy 1998	0.22% DEC for 1 yr	20	1 yr	912.3 mean no. mf/mL	202.3	77.8
DEC-medicated salt vs placebo	-	-	-	-	-	-
Panicker 1997	0.22% DEC for 30 wk	14	30 wk	20.6 mean no. mf/20 mm3	0.0	100
	Placebo	4	30 wk	No data	No data	No data

DEC: diethylcarbamazine; mf: microfilariae.

Appendix 5. Microfilariae prevalence: communities

Study	Intervention	Follow up	Measure	Pre-DEC	Post-DEC	% reduction
DEC-medicated salt vs other forms of DEC						
Meyrowitsch 1998	0.33% DEC-medicated salt	4 yr	Mf	31.05	12.46	60
	Monthly single low DEC dose (50 mg or 100 mg)	1 yr	Mf	34.67	15.87	54
		4 yr			14.01	60
	Standard DEC dose (6 mg/kg/day for 12 days)	1 yr	Mf	24.48	15.18	33
		4 yr			19.83	30
	Semi-annual single DEC dose	1 yr	Mf	17.74	11.67	34
		4 yr			11.38	36
Sapak 2000	0.2% DEC-medicated salt for 1 yr	1 yr	Ag	55	36.30	34
	DEC tablets - single annual dose of 6 mg/kg body weight	1 yr		71	66.03	7
DEC-medicated salt vs control						

(*Continued*)

Krishna Rao 1976	0.1% DEC for 45 wk	1 yr	Mf	26.32	3.72	86
		5 yr			10.06	62
	0.1% DEC for 12 wk	1 yr	Mf	17.58	10.16	42
		2 yr			10.59	40
	No salt	1 yr	Mf	16.60	20.07	21 increase
		5 yr			20.48	23 increase
Narasimham 1979	0.1 % DEC for 6 months	7 months	Mf	25.81	10.48	59
		11 months			14.05	46
	Untreated salt	7 months	Mf	18.05	19.85	22 increase
		11 months			23.47	30 increase
Krishna Rao 1991	0.2 % DEC for 6 months	6 months	Mf	33.11	3.8	88.5
		8 yr			22.6	31.7
	Untreated salt	1 yr	Mf	33.20	27.8	5.4
		8 yr			25.2	24.1
Kaul 1992	0.23% DEC for 1 yr: village 1	1 yr	Mf	8.1	0.0	100
		10 yr			0.0	100
	0.23% DEC for 1 yr: village 2	1 yr	Mf	2.7	0.0	100
		10 yr			0.0	100
	0.23% DEC for 1 yr: village 3	1 yr	Mf	6.2	0.0	100
		10 yr			0.0	100
	No intervention	1 yr	Mf	5.5	3.5	36
		10 yr			5.7	4 increase
Before and after						
Freeman 2001	0.25% DEC for 1 yr	1 yr	Mf	20.05 (95% CI 16.17 to 23.93)	0.98 (95% CI 0.02 to 1.93)	95

(*Continued*)

		1 yr	Ag	40.2	2.01	95
PIPD 1976	0.3% DEC for 6 months	6 months	-	8.05	0.88	89
		1 yr	-		0.36	96
FRG 1979	0.24% DEC for 6 months	6 months	Mf	8.75	0.72	92
		1 yr			0.43	95
		5 yr			0.17	98
Rao 1981	0.1% to 0.15% DEC for 6 to 20 months	3 yr	Mf	4.4	0.9	80
		4 yr	-	-	1.2	73
Ru 1984	0.38% to 0.56% % DEC for 5 months	6 months	Mf	9.3	0.07	99
		1 yr			0.6	94
		6 months	Mf	7.9	0.13	98
		1 yr			0.27	97
		6 months	Mf	1.0	0	100
		1 yr			0	100
Reddy 1986	0.1% to 0.2% DEC for 48 months	1 yr	Mf	4.49	0.32	93
		7 yr			0.40	91
		19 yr			0.09	98
Fan 1990a	0.33% DEC-medicated salt for 6 months	1 yr	Mf	0.7	0.0	100
		3 yr			0.2	100
		6 yr			0.0	100
Fan 1990b	0.33% DEC-medicated salt for 6 months	1 yr	Mf	9.6	0.0	100
		5 yr			0.0	100
		8 yr			0.0	100
Liu 1992	0.5% to 1% DEC for 4 months	6 to 9 months	Mf	3.09	0.11	96

(*Continued*)

	(*Wuchereria bancrofti*)					
	0.5% DEC for 2 months (Brugia malayi)	6 to 9 months	Mf	4.08	0.26	94

Ag: antigenaemia; DEC: diethylcarbamazine; mf: microfilariae.

Appendix 6. Microfilariae density: communities

Study	Intervention	Follow up	Pre-DEC[a]	Post-DEC	% reduction
DEC vs other forms of DEC					
Meyrowitsch 1998	0.33% DEC-medi-		1023 (1288)[b]		
		4 yr		9	99.3
	Monthly single low DEC dose (50 mg or 100 mg)	1 yr	1122 (1202)[b]	7 (9)	99.3
		4 yr		6	99.5
	Standard DEC dose (6 mg/kg/day for 12 days)	1 yr	645 (631)[b]	9 (10)	98.4
		4 yr		43	93.2
	Semi-annual single DEC dose	1 yr	257 (240)[b]	20 (21)	91.2
		4 yr		8	96.7
DEC-medicated salt vs control groups					
Krishna Rao 1976	DEC-medicated salt for 45 wk	2 yr	47.5	2.6	95
		4 yr		5.8	88
	DEC-medicated salt for 12 wk	1 yr	16.6	6.8	59
		2 yr		8.1	51
	No salt	1 yr	14.0	32.5	132 increase
		2 yr		13.3	5

(*Continued*)

Narasimham 1979	0.1% DEC-medicated salt for 6 months	7 months	23.8	7.2	70
		11 months		8.6	64
	Untreated salt	6 months	14.6	23.2	22 increase
		11 months		21.0	44 increase
Krishna Rao 1991	0.1 % DEC-medicated salt for 6 months	6 months	22.7	5.2	77.1
		8 yr		18.1	20.3
	No salt	6 months	10.2	21.3	108.8% increase
		8 yr		31.3	206.9% increase
Kaul 1992	0.23% DEC-medicated salt for 1 yr: village 1	1 yr	7.3	0.0	100
		8 yr		0.0	100
	0.23% DEC for 1 yr: village 2	1 yr	24.0	0.0	100
		8 yr		0.0	100
	0.23% DEC-medicated salt for 1 yr: village 3	1 yr	9.6	0.0	100
		8 yr		0.0	100
	No intervention	1 yr	7.7	11.1	43 increase
		10 yr		5.7	31
Before and after					
Raghavan 1968	0.1% DEC-medicated salt for 2 months	2 months (18/18 available)	25.3	1.5	94
Katiyar 1977	0.26% DEC-medicated salt for 2.7 months	4 months (28/28 available)	48.0	8.25	83
PIPD 1976	0.3% DEC-medicated salt for 6 months	6 months (39/281 available)	51.0	4.7	89
		1 yr (39/281 available)		2.7	96

(*Continued*)

FRG 1979	0.24% DEC-medicated salt for 6 months	6 months (8/96 available)	53.9	1.4	97.4
		1 yr (5/96 available)		7.0	87
		5 yr (2/96 available)		37.5	48
Rao 1981[d]	0.1% to 0.15% DEC-medicated salt for 6 to 20 months	3 yr	14.1[d]	7.4	48
		4 yr		6.2	56
Reddy 1986[d]	0.1% to 0.2% DEC-medicated salt for 48 months	1 yr	4.49	0.32	93
		7 yr		0.40	91
		19 yr		0.09	98
Fan 1990a[d]	0.33% DEC-medicated salt for 6 months	1 yr	5.3	0	100
		3 yr		0.2	100
		6 yr		0	100
Fan 1990b[d]	0.33% DEC-medicated salt for 6 months	1 yr	14.1	0	100
		3 yr		0	100
		6 yr		0	100
Liu 1992	0.5% to 1.0% DEC-medicated salt for 4 months	2 months (64/223 available)	17.0	5.1	69.6
		4 months (7/223 available)		1.3	94
Freeman 2001[c]	0.25% DEC-medicated salt for 1 yr	1 yr	8[c]	0.04	98.8

DEC: diethylcarbamazine

[a] Estimates of mf density reported only for those mf positive at baseline; mean number per cubic cm or geometric mean.

[b] Discrepancies between values reported in 1996 publication (first values) and 1998 publication (values in brackets).

[c] Approximate value, read off graph.

[d] Unclear whether estimate for whole community or only those mf positive at baseline.

Appendix 7. Disease prevalence: communities

Study	Intervention	Follow up	Disease symptom	Pre-DEC (%)	Post-DEC (%)	% reduction
DEC-medicated salt vs other forms of DEC						
Meyrowitsch 1998	0.33% DEC-medicated salt	4 yr	Hydrocoele	32.1	28.1	12.6
		1 yr	Elephantiasis	6.0	7.6	26.7 increase
		4 yr			6.1	1.7 increase
	Monthly single low DEC dose (50 mg or 100 mg)	1 yr	Hydrocoele	40.0	20.2	49.5
		4 yr			21.8	45.3
		1 yr	Elephantiasis	3.8	3.1	18.4
		4 yr			7.3	92.1 increase
	Standard DEC dose (6 mg/kg/day for 12 days)	1 yr	Hydrocoele	37.9	27.0	28.8
		4 yr			13.9	63.3
		1 yr	Elephantiasis	6.8	3.6	47.1
		4 yr			3.7	45.6
	Semi-annual single DEC dose	1 yr	Hydrocoele	30.2	22.5	25.5
		4 yr			20.7	31.5
		1 yr	Elephantiasis	4.3	2.2	48.8
		4 yr			0.9	79.1
DEC-medicated salt vs control groups						
Narasimham 1979	0.1% DEC for 6 months	6 months	Not specified	6.5	6.0	8
	Untreated salt	11 months		11.6	11.9	3 increase
Krishna Rao 1976	0.1% DEC for 45 wk	1 yr	Not specified	10.2	7.7	25
		5 yr			4.8	53

(*Continued*)

	0.1% DEC for	1 yr	-	3.03	1.3	57
		2 yr	-	-	3.2	6 increase
	No salt	1 yr	-	7.9	9.2	17 increase
		5 yr	-		3.1	60
Kaul 1992	0.23 DEC for 1 yr (average of 3 villages)	1 yr	Not specified	5.4	0.5	90
	No intervention	1 yr	-	10.9	3.2	71
Before and after						
Reddy 1986	0.1% to 0.2 % DEC for 48 months	1 yr	Not specified	0.39	0.18	54
		7 yr		-	0.14	64
		19 yr		-	0.05	87
Fan 1990b	0.33% DEC-medicated salt for 6 months	1 yr	Includes elephantiasis, lymphangitis, orchitis, epididymitis, funiculitis, hydrocoele, chyluria, lymph node enlargement	26.2	18.3	47

DEC: diethylcarbamazine.

Appendix 8. Vector infection and infectivity rates: communities

Study	Intervention	Follow up	Vector measure	Pre-DEC	Post-DEC	% reduction
DEC-medicated salt vs control						
Krishna Rao 1976	0.1% DEC-medicated salt for 45 wk	1 yr	Infection	16.7	2.3	86.2
-	-	5 yr	-	-	7.3	56.2
-	-	1 yr	Infectivity	4.2	0.7	83.3

(*Continued*)

-	-	5 yr	-	-	0.9	78.5
-	0.1% DEC-medicated salt for 12 wk	1 yr	Infection	11.7	9.5	18.8
-	-	2 yr	-	-	10.7	8.5
-	-	1 yr	Infectivity	1.4	1.6	14.2 increase
-	-	2 yr	-	-	0.9	35.7
-	No DEC-medicated salt	1 yr	Infection	25.5	17.7	30.6
-	-	5 yr	-	-	10.8	57.6
-	-	1 yr	Infectivity	6.4	0.9	85.9
-	-	5 yr	-	-	2.4	62.5
Before and after						
Raghavan 1968	0.1% DEC-medicated salt for 2 months	2.2 months	Infection	9.5	7.4	22.1
FRG 1979	0.24% DEC-medicated salt for 6 months	1 yr	Infection	3.4	0.5	85.3
		3 yr	-	-	0.5	85.3
		5 yr	-	-	0.1	97.1
Rao 1981	0.1% to 0.15% DEC-medicated salt for 6 to 20 months	3 yr	Infection	0.7	0.07	90.0
		3 yr	Infectivity	0.1	0.04	60.0
Reddy 1986	0.1% to 0.2 % DEC-medicated salt for 48 months	1 yr	Infection	0.6	0.0	100.0
		7 yr	-	-	0.1	83.3
		19 yr	-	-	0.1	83.3
		1 yr	Infectivity	0.3	0.0	100.0
		7 yr	-	-	0.0	100.0

(*Continued*)

		19 yr	-	-	0.0	100.0
Liu 1992	0.5% to 1.0% DEC-medicated salt for 4 months	1 yr	Infection	1.1	0.04	76.3
		-	-	-	-	76.3

DEC: diethylcarbamazine.

WHAT'S NEW

Last assessed as up-to-date: 7 November 2006.

10 September 2008	Amended	Converted to new review format with minor editing.

HISTORY

Protocol first published: Issue 3, 2002

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CONTRIBUTIONS OF AUTHORS

AS assessed studies for inclusion, extracted data, performed analyses, and prepared the review. JC assessed studies for inclusion, extracted data, and edited the review. HG prepared the protocol, performed initial searches for studies, and edited the review. PKD edited the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Lymphatic Filariasis Support Centre, Liverpool School of Tropical Medicine, UK.
- Vector Control Research Centre, India.

External sources

- Department for International Development, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

S Adinarayanan, J Critchley, and PK Das joined the review team, and we revised the outcome measures to include vector infection and infectivity rates.

INDEX TERMS

Medical Subject Headings (MeSH)

Diethylcarbamazine [*therapeutic use]; Elephantiasis, Filarial [*drug therapy]; Filaricides [*therapeutic use]; Sodium Chloride [*administration & dosage]

MeSH check words

Humans