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Single-dose diethylcarbamazine in the control of periodic brugian filariasis in Peninsular Malaysia

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Abstract

The study compared the effectiveness of a single dose of diethylcarbamazine (DEC) (6mg/kg) with the standard regimen of 6 doses (total 36mg/kg) in mass chemotherapy for the control of brugian filariasis. Mass chemotherapy with single-dose DEC was instituted in one area and standard dose in the other and treatment was repeated after one year. Parasitological surveys were conducted before, and 3, 7 and 12 months after treatment. Pretreatment characteristics were not significantly different between the 2 treatment areas. There was a significant reduction in microfilaraemia prevalence rate from 24.7% to 14.7% at 12 months and to 6.8% at 19 months in the single dose area and from 22.8% to 9.6% at 12 months and to 2.7% at 19 months with the standard dose. Maximum reduction was at 7 months after treatment with both regimens. There was also significant progressive reduction in mean microfilarial density from 4.39±20.37 to 0.89±4.16 per 60 μL in the single-dose area and from 4.43±17.31 to 0.75±4.95 per 60 μL in the standard dose area.

There was a greater reduction of both microfilarial prevalence and density using the standard regimen but it was not statistically significant. Thus, a single dose of DEC is as effective as the standard dose in controlling periodic brugian filariasis.

Keywords: filariasis, Brugia malayi, diethylcarbamazine, single dose therapy, Malaysia

Introduction

Filariasis in Malaysia is caused by Brugia malayi and Wuchereria bancrofti. However, more than 90% of the cases reported are brugian filariasis. Although the urban form of the disease has been eradicated, it has remained a public health problem in rural areas. The overall prevalence was rather low, with microfilaraemia prevalence of only 0.35% among 178,921 persons examined in 1994. There were, however, areas with high endemicity with more than 10% prevalence (CHANG et al., 1992).

Diethylcarbamazine (DEC) has been the drug of choice in filariasis control in Malaysia, as a yearly standard regimen of 6 mg/kg body weight given in 6 doses for brugian, and 12 doses for bancroftian, filariasis. Mass chemotherapy is employed in areas with microfilaria (mf) rates of more than 5% and selective treatment in other cases. Although the regimen has proved to be very effective in reducing mf prevalence and density rates and may lead to interruption of transmission (CHADEE et al., 1995) and subsequent eradication, particularly of the periodic forms, problems of compliance still arise because of the known side effects of DEC. In remote endemic areas of filariasis where communication is difficult, such as the aboriginal settlements in Peninsular Malaysia and the ethnic minorities in Sarawak and Sabah, effective supervision of this mass chemotherapy regimen may be difficult and costly.

The usefulness of annual single dose treatment in the control of bancroftian filariasis has been demonstrated (KIMURA et al., 1985; CARTEL et al., 1992). Mass single-dose DEC has been shown to be effective treatment in the control of brugian filariasis by PANICKER et al. (1991), who compared the effectiveness of single-dose DEC given annually and biannually. Since the current regimen used in Malaysia is the standard 36 mg/kg given in 6 doses for brugian filariasis, we studied the effectiveness of mass single-dose DEC treatment with the standard regimen among inhabitants of aboriginal settlements in Perak.

Materials and Methods

Study areas

The study was carried out in 2 aboriginal resettlements situated in Ulu Perak district, Perak, which borders Thailand about 400 km from Kuala Lumpur. The 2 localities, RPS Air Banun and Dala, are about 100 km apart and are endemic for filariasis. The villages in each area were similarly located close to Lake Temengor and Lake Kenering in Air Banun and Dala respectively. Preliminary population censuses and parasitological and entomological surveys were conducted in November 1992. There were 2 villages in Air Banun with a population of 245, and 4 villages in Dala with a population of 254, were selected for the study, based on their filariasis prevalence, proximity to each other, and accessibility for effective parasitological surveys and institution of mass chemotherapy.

Parasitological surveys

Finger-prick blood samples (60 μL) were collected with the aid of a micropipette from all persons aged 6 months and above and blood smears were made, stained with 3% Giemsa’s stain for 1 h and examined entirely. The survey started at 18:00 and was carried out before mass treatment and 3, 7 and 12 months after treatment.

Microfilaraemia periodicity study

To determine the periodicity of the filaria strain in the study areas, 4 microfilaraemic volunteers with high counts in each locality were studied. Finger-prick blood samples (60μL) were collected every 2 h for 24 h and stained with Giemsa before examination as described above. The periodicity index was then calculated based on the method described by SASA & TANAKA (1972). Blood samples were also collected from domestic cats in the study areas, stained and examined similarly.

Mass chemotherapy

Diethylcarbamazine citrate (Hetrazan®, Iederic Laboratories, England), 50mg per tablet, was used. A single dose of 6 mg/kg was given to all participants in Air Banun over 6 months of age. Pregnant women, infants aged less than 6 months, and those with other severe illnesses were excluded. In Dala, participants received the standard 36 mg/kg of DEC divided into 6 doses.

The doses were calculated to the nearest one tablet based on the body weight measured on a portable weighing machine. The drugs were given under supervision in Air Banun. In Dala, the first dose was given under supervision and the subsequent doses were supplied as pre-packed daily treatments. Medical orderlies and malaria control staff in each locality were instructed to supervise the subsequent treatment.

Mass chemotherapy following the same schedule for each area was repeated a year after the first treatment. Parasitological surveys were carried out as described.
above after the second mass treatment also.
This study protocol was approved by the Human Use Ethical Committee, Ministry of Health, Malaysia.

Statistical analysis
Data were analysed using the SPSS® program. Differences in proportions were examined using the $\chi^2$ test. Differences in means were analysed using Mann–Whitney and Kruskal–Wallis one way analysis of variance where appropriate.

Results
Pre-treatment characteristics of study areas
There was no significant difference in the pre-treatment mf prevalence rates (24.8% and 22.7%) or mean mf density per 60 µL of blood (4.39±20.37 [range 0–200] and 4.43±17.31 [range 0–112] in Air Banun and Dala respectively). The distribution of microfilaraemic cases by age groups showed a similar bimodal distribution in both areas, with peaks in the 10–19 and over 40 years age groups. There was no significant difference in mf prevalence between males and females (24.6% and 25.0% respectively in Air Banun and 22.8% and 22.4% respectively in Dala). The youngest microfilaraemic subject was an 8 months old infant in Air Banun.

The average percentage coverage during parasitological surveys was 53.6% (range 35.9%–73.9%) and 62.3% (range 57.7%–67.7%) in Air Banun and Dala, respectively.

Four species of potential vectors were collected in Air Banun (Anopheles donaldi, A. nigerrimus, Mansonia uniformis and M. dives); in Dala only the first 3 species were collected. The mosquito implicated as vector was A. donaldi, with filarial infection and infectivity rates of 3.9% and 0.8% respectively in Air Banun and 6.5% and 2.2% respectively in Dala.

Periodicity of microfilaraemia
The mf periodicity index in both Air Banun (85.6) and Dala (78.8) indicated nocturnal periodicity. Ten domestic cats in Air Banun and 7 in Dala were examined and none was microfilaraemic, providing supporting evidence for the nocturnal periodicity of the filaria strains in both areas.

Effect of treatment on microfilarial prevalence rates
There was a significant reduction in mf prevalence rate to 59.1% of the pre-treatment level ($P=0.05$) at 12 months after single-dose treatment, with the maximum reduction 7 months after treatment (Fig. 1). Similarly, the prevalence rate was reduced to 42.1% of the pre-treatment level at 12 months in the standard dose area ($P=0.001$). The prevalence rate 19 months after initial treatment did not differ significantly between the 2 treatment areas ($P=0.103$).

There was a significant reduction in mf prevalence rate in all age groups in both treatment areas (Fig. 2). Before treatment, there was a higher proportion of mf carriers in those aged 10–19 years and those above 40 years old in the single dose area ($P=0.036$) and the standard dose area ($P=0.024$). There was no linear association between age group and microfilaraemia rates in either treatment area (Mantel–Haenszel test, $P=0.237$ and $P=0.256$ respectively). After 19 months of initial mass therapy, there was no significant difference in the proportion of mf carriers in the different age groups in either the single dose ($P=0.476$) or the standard dose areas ($P=0.842$).

Effect on microfilarial density
There was a progressive reduction in mean mf density per 60 µL from 4.39±20.37 to 0.89±4.16 (range 0–28)
and from $4.43 \pm 1.71$ to $0.75 \pm 4.95$ (range 0-20) in the single dose ($P < 0.001$) and standard dose ($P < 0.001$) areas respectively 19 months after the initial treatment (Fig. 3); the reduction was greater in the standard dose area but the difference was not statistically significant ($P = 0.178$).

The mf density and prevalence rate 7 months after treatment in the single dose area were both much lower than in the standard dose area, but this reduction appeared to be an artefact. At 7 months after treatment, there was a significant reduction in the proportion of the population surveyed from 62.8% (before treatment) to 35.9% ($P = 0.042$) in the single dose area, compared to 43.9% ($P = 0.047$) in the single dose area, compared to 67.7% and 64.5% coverage in the standard dose area, due to inaccessibility of one of the villages in Air Banun as a result of heavy rain.

Discussion

Both the standard 6 doses regimen and a single dose of DEC were equally effective in controlling periodic brugian filariasis when given annually for 2 years. In a country where financial resources are limited, and there is a need to allocate limited resources to the more important prevailing health problems such as malaria and other mortality-associated illnesses, a single dose mass treatment strategy for controlling brugian filariasis appears to be more acceptable and cost-effective. It is also operationally more feasible as filariasis endemic areas in Malaysia are in remote and less accessible places. A single dose regimen would also improve compliance, as taking the drug could be individually supervised. It would also prevent wastage arising from the tendency not to complete the treatment as a result of side effects from the initial dose.

The overall reduction of 72.5% in the mf prevalence rate in the single dose treatment area in our study was slightly lower than the 78% reported by PANICKER et al. (1991). These authors achieved 90% reduction with a biannual single dose regimen compared with our 88% with the standard 36 mg/kg regimen after about 2 years. The higher reduction was probably due to their lower initial mf prevalence rates (4.9%-6.27%), compared to ours, and the timely intervention of the second mass therapy of the biannual single dose regimen. As shown in our study, the mf prevalence rate tends to increase slightly 7 months after the initial treatment and thus repeated treatment after 6 months would further reduce the prevalence rate.

We did not examine the rate of side reactions between the 2 regimens. As side reactions normally occur soon after the first dose and since the first dose in both of our regimens was the same (6 mg/kg), we did not expect any difference in rate.

The prospect of complete eradication of periodic brugian filariasis in this locality appears to be bright. The concept of a threshold level stipulates that, with anopheline transmitted filariasis, the disease disappears spontaneously if the mf density is brought below a certain level (SHAOLING et al., 1991). This could be achieved by the practical single dose regimen. Furthermore, eradication can be achieved earlier if vector control measures such as residual insecticide spraying are concurrently implemented. In fact, many areas with periodic brugian filariasis in Peninsular Malaysia were effectively controlled as a result of the aggressive anti-malaria campaigns (MAK et al., 1977).

DEC medicated salt has recently generated much interest. Apart from its use having resulted in the eradication of filariasis (FAN, 1990), low dosage used minimizes or prevents the undesirable side effects. However, for it to be effective, it is necessary that only the medicated salt is available to the community. In a free market, it would entail considerable administrative and legislative commitment to ensure this.

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