Efficacy of a Single-Dose Treatment with 300 mg Diethylcarbamazine and a Combination of 400 mg Albendazole in Reduction of *Wuchereria bancrofti* Antigenemia and Concomitant Geohelminths in Myanmar Migrants in Southern Thailand

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Background: *There seems to be a large magnitude of parasitic worm loads caused by nocturnally periodic Wuchereria bancrofti and geohelminths, in cross-border Myanmar migrant workers in Thailand. We are therefore considering an effective Mass Drug Administration (MDA) with Diethylcarbamazine (DEC) and Albendazole (ABZ). Due to short periods of their residency and current situation of W. bancrofti antigenemics and concomitant geohelminths, treatment effects on the containment of the infections need to be analyzed.*

Objectives: *Analyze short-term effects on reduction of W. bancrofti antigen (WbAg) and geohelminths' egg (GhE) loads. The efficacy of a single-dose combined treatment with 300 mg DEC (for filariasis) and 400 mg ABZ (for helminthiasis) was evaluated and compared with a single-dose treatment arm with 300 mg DEC alone.*

Material and Method: *A randomized clinical trial of two treatment choices in 28 Myanmar male workers (DEC/ABZ or group I = 15, DEC or group II = 13) was conducted in Phang Nga province, Southern Thailand. Because of the withdrawal of three subjects of the DEC group, all the 10 DEC subjects were follow-up monitored at post treatment 2, 4, 8 and 12 weeks. Their mean age was 26.4 years; worm loads (mean SD 10^3) of W. bancrofti, Ascaris and Trichuris was 103.9 44.1 antigen units (AU)/ml, 47.3 38.7 eggs per gram (EPG) and 16.6 22.2 EPG, respectively. The data on the 15 DEC/ABZ subjects showed a mean age of 25.7 years; corresponding worm loads = 96.1 54.6 AU/ml, 397.0 117.3 EPG and 54.5 42.8 EPG, respectively. The Antigen Reduction Rates (ARR) and Egg Reduction Rates (ERR) were presented.*

Results: *At the 12-week post treatment, WbAg loads (mean SD 10^3 AU/ml) were 61.5 58.4 for group I and 76.8 40.7 for group II. A significant WbAg reduction was noted for both groups at weeks 8 and 12 ($p < 0.05$). Also, the significant reduction of GhE loads was more pronounced for both groups after week 2 ($p < 0.05$). When comparing efficacy of the treatment choices by the treatment retention time, it was more likely to show both groups had similar adulticidal effects on either WbAg, denoted as the ARR ($F = 0.064$, $p = 0.806$) or GhE, denoted as the ERR ($F = 0.196$, $p = 0.669$).*

Conclusion: *The single-dose 300 mg DEC plus 400 mg ABZ, or 300 mg DEC alone, can be effectively used for treating infections with W. bancrofti and concomitant geohelminths commonly observed in the area. But treatment rounds are required to clear the infections. The reduction of the parasitic worm loads in the legal Myanmar migrants provide values in monitoring and evaluating an effective MDA program with the DEC/ABZ at the provincial level.*

Keywords: *Wuchereria bancrofti, Geohelminths, Diethylcarbamazine, Albendazole, Myanmar migrants*

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Due to a large number of cross-border foreign migrants to Thailand, one of the major public health problems has become a current magnitude and distribution of potentially infectious diseases[1]. Among foreign migrant workers, Myanmar migrants play an important role in disease transmission. Regarding critical health consequences, they have been considered a source of the emerging diseases[1-4], caused by Human Immunodeficiency Virus (HIV), Tuberculosis (TB), Sexually-Transmitted Diseases (STD), dengue fever/ dengue hemorrhagic fever, hepatitis viruses, leprosy, malaria and Lymphatic Filariasis (LF). The parasitic worm is caused by nocturnally periodic *Wuchereria bancrofti* and geohelminths, in at-risk Myanmar migrants[3-7]. Its burden remains to be established. Prevalence of infection and intensity need to be logistically assessed before a Mass Drug Administration (MDA) can be effectively used on a wide scale.

The MDA with 300 mg (or 6 mg/kg) single-dose Diethylcarbamazine (DEC), for filariasis, and 400 mg Albendazole (ABZ), for helminthiasis, applied to foreign migrant workers is followed by Guidelines on Migrant Health Services[2]. It has been applied to containment of the infections in those with work permits in permitted provinces. It is, however, not guaranteed that all of them are given the drugs once every year due either to their movement from one area to another, or their avoidance in renewing their work permits. Moreover, no reports establish added-in benefits of a single-dose combination of the drugs that have an effect on parasitic worm loads in those Myanmar migrants infected with *W. bancrofti* and concomitant geohelminths.

It has been suggested that a single-dose combination (DEC + ABZ) has short- and long-term effects on *W. bancrofti* microfilaremics in the endemic populations[8-11]. Compared to those receiving DEC alone, an additional benefit of the combined drugs results in decline in annual cyclic infection prevalence due to progressive reduction in the density of *W. bancrofti* Microfilaremia (WbMf). Also, its macrofilaricidal effect on clearance of *W. bancrofti* Antigenemia (WbAg) has been reported[10,12]. A 400 mg single oral-dose ABZ regimen is broad-spectrum effective against helminthiases[9,13-17] and, as co-administered orally with DEC, a synergistic and long-term effect on geohelminths has been proven useful for 'beyond-lymphatic filariasis' elimination program[9,15,16,18-22].

It is postulated that, if there are synergistic effects of combined drugs on WbMf or WbAg in those Myanmar workers with a renewal of work permits or a long-term migration, such a single-dose combination can result, from no repeated infection, in a decline in annual cyclic infection prevalence and intensity of *W. bancrofti* and concomitant geohelminths. There have been doubts because they may not renew their work permits and become a 'would-be' short period of stay. In the present study, the authors demonstrate adulticidal effects of a single-dose 300 mg DEC + 400 mg ABZ, compared with a 300 mg DEC alone, on WbAg and concomitant geohelminths after a quarter course of treatment in Myanmar migrant workers, in Phang Nga province, Southern Thailand.

Material and Method

Study subjects and imported bancroftian filariasis epidemiology

In the *en-route* province, Myanmar male migrant workers outnumber female workers. More than 10,000 Myanmar migrants (up to twenty thousand) eligible for treatment with DEC/ABZ regimen have been reported annually[1,23]. Determination of the infection prevalence and intensity was made by the *W. bancrofti* Circulating Filarial Antigen (CFA) detection, rather than by microfilariae detection methods. This has been shown to permit estimates in the area[23,24]. The antigenemics and/or microfilaremics commonly observed in Myanmar males, rather than in females, have been reported and persons with 20 years (yr) of age are at risk of *W. bancrofti* infection[5,23-25]. Looking at the possibility of an effective mass annual single dose treatment for Myanmar migrants, we must understand that *W. bancrofti* antigenemics outnumbered microfilaremics 20:1[24]. A current status of WbMf infection prevalence in Myanmar migrant workers in the area has been expected to fall to a zero-ground prevalence since the fiscal year 2002. Therefore, the Myanmar male subjects were used to present the *W. bancrofti* worm burden concomitant with the geohelminths in the study area.

Study design

Subject recruitment and consent

Inclusion criteria for subject recruitment were antigenemic Myanmar male migrants 20 to 45 years of age residing in the area for no more than one year. They must have no history of DEC or anthelminthic treatment, no subside manifestations of infectious or chronic conditions involving HIV, TB, STD, malaria and drug abuse (amphetamines). They have normal limits of hematologic parameters and vital signs. In the authors' experience, those who had long-term migration (≥ 1 yr of residency) may have received oral doses

of biannual DEC mass treatment in the province thus they were all excluded. During a hospital-based health survey of infectious diseases and drug abuse in Thakua Thung district, in August 2004, all the 1,000 registered Myanmar male migrants were examined for WbMf present in day blood samples[24]. None was microfilaremic. Then the 250 (4:1) was randomly selected with enumeration list for WbAg examination. They were informed about the purpose of the present study in assistance with well-trained Myanmar translators. The oral and/or informed consents with permission of the employers were obtained.

W. bancrofti CFA examination

The Ethylene Diamine Tetra-acetic Acid (EDTA) intravenously day blood samples in individuals were collected for plasma preparation and for complete blood counts. After the blood was centrifuged at 5000*g* for 5 minutes, freshly prepared plasma samples (100 µl each) were examined for the *W. bancrofti* CFA using the qualitative format (NOW® ICT Filariasis, Binax, Portland, Maine, USA). The same amount of plasma sample (100 µl each) was also examined, using the principally same sandwiched immunoassay specific for the *W. bancrofti* CFA by the qualitative and quantitative format (Og4C3 ELISA, Tropical Biotechnology, Townsville, Queenland, Australia). The WbAg load was presented as the Antigen Units (AU)/ml blood. Both *W. bancrofti* CFA assays' procedures and interpretation of reading test results were described elsewhere[7,23,24]. In addition, all the fresh samples, prior to or post treatment, were tested at the time of blood collection using the ICT card test. But with post treatment sample collection, the antigenemic plasma samples in individuals frozen at -20 C were tested with the Og4C3 ELISA.

Geohelminths' egg examination

Prior to and post treatment, all the single stool samples were collected from their residence location, transferred to the laboratory and refrigerated at 4 C until use. They were afterward examined, by Kato-Katz method[26,27], for Geohelminths' Egg (GhE) loads to determine worm burden. Infection intensity, ie Eggs Per Gram (EPG) of feces, was estimated by multiplying the ova of parasites counted; EPG = 1000 X / Y, where X is the number of eggs per thick smear and Y is weight of fecal sample in milligram (average = 43.7). The worm burden[28] was defined by EPG per thick smear × 23: *Ascaris*: light < 7,000 EPG; medium 7,000 to ≤ 35,000 EPG; heavy > 35,000 EPG; hookworm: light < 2,000 EPG; medium 2,000 to ≤ 7,000 EPG; heavy > 7,000 EPG; *Trichuris*: light < 1,000 EPG; medium 1,000 to ≤ 10,000 EPG; heavy > 10,000 EPG.

Treatment efficacy and safety

Prior to treatment, a total of 34 antigenemics (ICT-positive) was obtained after being surveyed in August 2004. They were informed about a course of treatment and monitoring, between September and November 2004. Six persons refused to participate in the study afterwards. Therefore, the 28 antigenemics that gave consents and were subject to the treatment arms were randomly assigned with block stratification for age and *W. bancrofti* Ag load (Table 1), assuming that WbAg and/or GhE loads in untreated male subjects were stable. The treatment arms included group I (n = 15), 300 mg DEC plus 400 mg ABZ and group II (n = 13), 300 mg DEC alone. The drugs were DEC as a 300 mg FILADEC (Pond's Chemical Thailand ROP, Bangkok, Thailand) and ABZ as a 200 mg FALBEN® (The Government Pharmaceutical Organization, Bangkok, Thailand). They were supplied by the Phang Nga Provincial Health Office (PPHO), Ministry of Public Health (MoPH). Of the 13 who received DEC, three subjects were lost to follow-up in the first week of treatment, due to subject migration. All the other participants were followed-up with repeated measurement of WbAg and GhE loads. The group 1 mean age was 25.7 yr and the group 2 mean age was 26.4 yr. Any subject of the treatment groups who requested to visit the hospital, if any health outcomes developed after oral administration, were reported. In each treatment group, they were followed-up examined for WbAg, using both the ICT card test and Og4C3 ELISA, at post-treatment, 2, 4, 8, and 12 weeks. In similar fashion, the stool samples were examined for GhE at the same time-points of the blood collection.

Data analysis and statistical methods

In order to test adulticidal effects of the treatment arms on WbAg detection, the determination of antigenemia rate (%) at each period follow-up of treatment by means of the performance efficiency (*eg* concordance, discordance and discrepancy) of the *W. bancrofti* CFA assays was computed, using 2×2 contingency table. Concordance was computed as: $a / (a + b + c + d) \times 100$; where a is no. subjects positive with the ICT/Og4C3 ELISA and $a + b + c + d$ is a total of subjects in the group. Discordance was computed as: $c / (a + b + c + d) \times 100$; where c is no. subjects negative with the ICT but positive with the Og4C3 ELISA. Discrepancy is computed as $(a + c) – (a + b) / (a + b + c + d) \times 100$; where $a + c$ is no. subjects positive with the

Og4C3 ELISA and *a* + *b* is no. subjects positive with the ICT. The χ^2 test, or Fisher's exact test as appropriate, for two independent samples was used to describe significant differences in concordance or discordance by the CFA assays between the treatment arms.

The resulting WbAg or GhE loads were presented as mean ± SD or median as appropriate. Normal distribution of the data was tested using Shapiro-Wilk test ($p > 0.05$). For unpaired data analyses, to test adulticidal effects of the treatment arms on the worm loads at each period of follow-up of treatment, the unpaired Student's *t*-test, or Mann-Whitney *U* test as appropriate, was used. If they had similar effects, WbAg at similar pre-treatment levels (not for the GhE) was likely, equally, changed, by the treatment retention time, within the groups. For paired data analyses, the paired Student's *t*-test, or Wilcoxon signed rank test as appropriate, was used to describe significant differences in WbAg or GhE loads by the treatment retention time between pre- and post-treatment, 2, 4, 8 and 12 weeks.

On the other hand, the treatment efficacy (*ie* reduction in infection intensity of *W. bancrofti* or geohelminths) was analyzed by means of the Antigenemia Reduction Rate (ARR) and Egg Reduction Rate (ERR). The ARR (%) in each drug group was computed as follows: $(A_0 - A_T) / A_0 \times 100$; as A_0 is an infection intensity [Geometric Mean (GM) of WbAg load] at initial treatment and A_T is an infection intensity at post-treatment (weeks). Since there were few numbers of having concomitant geohelminths in both drug groups, the ERR (%) in each drug group was, therefore, computed as follows: $(E_0 - E_T) / E_0 \times 100$; as E_0 is an infection intensity (mean GhE load) at initial treatment and E_T is an infection intensity at response treatment (weeks). The one-way analysis of variance (ANOVA) for 2-sided analysis was used to describe significant difference in the ARR or ERR values obtained for all the 5 time-points between the treatment arms. Statistical significance was set at $p < 0.05$.

Results

Performance efficiency of W. bancrofti CFA assays

In the initial treatment, group II (DEC alone) had *W. bancrofti* infection intensity (GM = 92,007 AU/ml) (Table 1). In post-treatment, the antigenemia rates were the same, 100%, over the points in time (Table 2). Group I (DEC/ABZ) had infection intensity (GM = 64,749 AU/ml) ($p = 0.729$) (Table 1) at pre-treatment level. But they were more likely to have a dramatic decline in the *W. bancrofti* antigenemia. At 12 weeks, overall antigenemia rate (75%) was found. In both drug groups, there were no significant differences in the concor-

Table 1. Baseline characteristics between the drug groups at pre-treatment level

Characteristic	DEC/ABZ (n = 15)	DEC (n = 10)	p-value
Age (yr)	25.7±5.5	26.4±3.7	0.742
Hematologic parameters :			
White blood cell (4.6-10.2 × 10^3 cells/μl)	7.8±1.2	7.7±2.4	0.893
Neutrophil (37.0-80.0 %)	50.6±7.9	34.1±14.4	0.006†
Lymphocyte (10.0-50.0 %)	32.1±5.0	45.7±11.2	0.004†
Monocyte (0.0-12.0 %)	6.1±1.5	6.2±2.2	0.947
Eosinophil (0.0-7.0 %)	9.9±6.6	10.8±4.0	0.683
Basophil (0.0-2.5 %)	1.3±0.4	3.4±1.6	0.002†
Blood pressure (mm Hg) :			
Systolic	130.0±10.7	125.0±9.7	0.247
Diastolic	75.3±9.2	74.0±8.4	0.716
Body temperature (C)	36.9±0.4	37.0±0.3	0.371
Pulse rate (times/min)	82.3±9.2	74.3±11.5	0.067
Respiratory rate (times/min)	21.2±1.5	20.6±1.4	0.228
W. bancrofti infection intensity :	64.8±54.7	92.0±44.1	0.709
Geohelminth infection intensity*:			
Ascaris lumbricoides	384.0±117.3	26.3±38.7	0.02 ‡
Trichuris trichiura	39.8±42.8	8.8±22.2	<0.001 ‡

The data were expressed as mean ± SD , GM ± SD (× 10^3 AU/ml) and GM ± SD (× 10^3 EPG)*. Hemotologic parameters with normal ranges are shown in parentheses

Significant ($p < 0.05$) with either the † Unpaired student's *t*-test or ‡ Mann-Whitney *U* test for two independent samples

dance and discordance in qualitative WbAg detection ($p > 0.05$) (Table 2). Discordance was seen for at least week 4 (up to 12 weeks post treatment). Using the Og4C3 ELISA as reference, group II had discordance (with the ICT card test) of varying from 50% to 71%. Discordances for group I were 33%, 60% and 25%, respectively. On the other hand, by the treatment retention after week 4, both *W. bancrofti* CFA assays had discrepancies (up to 60%).

W. bancrofti antigen reduction

Table 3 shows that there was no significant difference in pre-treatment levels of WbAg loads (mean $\pm$ SD $\times 10^3$ AU/ml) between the drug groups: 103.9 $\pm$ 44.1 (95%CI = 72.4-135.4) for group II and 96.1 $\pm$ 54.6 (95%CI = 61.5-126.4) for group I ($p > 0.05$). Overall, when comparing post-treatment, WbAg levels by the adulticidal effects at each follow-up period of treatment showed no significant differences in WbAg loads between the treatment arms ($p > 0.05$). But each treatment arm had a dramatic decline in WbAg load. The WbAg load (mean $\pm$ SD $\times 10^3$ AU/ml) of group I was 61.5 $\pm$ 58.4 (95%CI = 24.4-98.6) at week 12. For paired data analyses, there were significant differences in WbAg loads of group I between pre- and post treatment levels at weeks: 4 ($t = 2.172$, $p = 0.047$), 8 ($t = 2.407$, $p = 0.03$) and 12 ($t = 2.736$, $p = 0.019$). The lowest level of WbAg load of group II was 65.8 $\pm$ 32.3 (95%CI = 35.8-95.7) at week 8, but at week 12 was slightly increased 76.8 $\pm$ 40.7 (95%CI = 39.1-114.5). Similar to that of group

Table 2. Adulticidal effects on *Wuchereria bancrofti* antigen detection by two CFA assays between the drug groups

Group	Determination of antigenemia rate (%) at post-treatment (weeks)				
	0	2	4	8	12
DEC/ABZ					
No. subjects †	15	15	15	15	12
Overall	100	80.0	73.3	86.7	75.0
Concordance	100	80.0[a]	40.0[b]	26.7[c]	50.0[d]
Discordance	0	0	33.3[e]	60.0[f]	25.0[g]
DEC					
No. subjects ‡	10	8	8	7	7
Overall	100	100	100	100	100
Concordance	100	100[a]	50.0[b]	42.9[c]	28.6[d]
Discordance	0	0	50.0[e]	57.1[f]	71.4[g]
Discrepancy	0	0	39.1	59.1	42.1

Subjects with loss to follow-up: † 3 harboring levels of WbAg loads (15,256 to 121,407 AU/ml), who dropped out of the study before week 12; ‡2 harboring 133,226 to 156,218 AU/ml before week 2, and another one harboring 58,018 AU/ml before week 8

Not significant with the Fisher's Exact Test: [a]$p = 0.526$; [b]$p = 0.685$; [c]$p = 0.630$; [d]$p = 0.633$; [e]$p = 0.657$; [f]$p = 1.000$; [g]$p = 0.074$, for two independent samples

Table 3. Adulticidal effects on *Wuchereria bancrofti* antigenemia (WbAg) between the drug groups

Group	WbAg load† at post-treatment (weeks)				
	0	2	4	8	12
DEC/ABZ	96.1$\pm$54.6	77.9$\pm$52.2	66.7$\pm$55.1 ‡	61.6$\pm$56.1 ‡	61.5$\pm$58.4 ‡
DEC	103.9$\pm$44.1	86.9$\pm$43.7	84.1$\pm$45.0	65.8$\pm$32.3 ‡	76.8$\pm$40.7 ‡

† The data, which were derived using subjects examined at each period follow-up of the treatment arms in Table 2, were ‡ presented as mean SD ($\times 10^3$ AU/ml).

Significant with the paired student's *t*-test ($p < 0.05$) for two dependent samples within the groups.

Not significant with the unpaired student's *t*-test ($p > 0.05$) for two independent samples between the groups

Table 4. *Wuchereria bancrofti*-infected subjects concomitant with geohelminths in the drug groups at pre-treatment level

Level	DEC/ABZ (n = 15)†		DEC (n = 10)‡	
	Ascaris	*Trichuris*	*Ascaris*	*Trichuris*
Light	0	0	2 (4.8±2.9)	0
Medium	0	0	1 (14.8)*	4 (4.5±2.3)
Heavy	3 (397.0±117.3)††	12 (54.5±42.8)	4 (76.7±16.9)‡‡	3 (32.8±28.0)

Intensity of concomitant geohelminths (mean±SD $\times 10^3$ eggs per gram) is shown in parentheses

† Including 3 GhE-negative and 12 heavy infections (9 single *Trichuris* + 3 mixed ††)

‡ Including one GhE-negative and 9 infections: 2 single Trichuris (1 medium + 1 heavy); 2 single heavy *Ascaris*‡‡; 5 mixed (1 heavy ‡‡ + 1 heavy *Ascaris* ‡‡plus medium *Trichuris* + 1 medium* + 1 light *Ascaris* plus heavy *Trichuris* + 1 light *Ascaris* plus medium *Trichuris*)

I, significant differences in WbAg loads of group II between pre- and post-treatment levels were noted at weeks: 8 (t = 4.632, p = 0.004) and 12 (t = 3.967, p = 0.007). Also, week 8 had WbAg load significantly different from weeks: 2 (t = 2.871, p = 0.028) and 4 (t = 3.492, p = 0.013) (data not shown). On the other hand, the ARR (%) for group II reached the similar rates between 32% at week 8 and 30% at week 12 (Fig. 1). But group I reached the maximum ARR of 32% for week 8 post-treatment and, at week 12, it fell to 20%. However, by using one-way ANOVA, there was no significant difference in the ARR between the groups (F = 0.064, p = 0.806).

Geohelminths' egg reduction

Both drug groups had concomitant infections with *Ascaris* and *Trichuris* and none was positive with hookworm (Table 4). Group I had heavy infections with *Ascaris* or *Trichuris* while group II had varied degrees of worm burdens. There was evidence that, at pre-treatment level, significant differences in infection intensities (both *Ascaris* and *Trichuris*) between the drug groups ($p < 0.05$) were noted (Table 1). This had been shown for GhE load-dependent treatment effects of the treatment arms. The GhE load reduction by the treatment retention time within the group was consi-

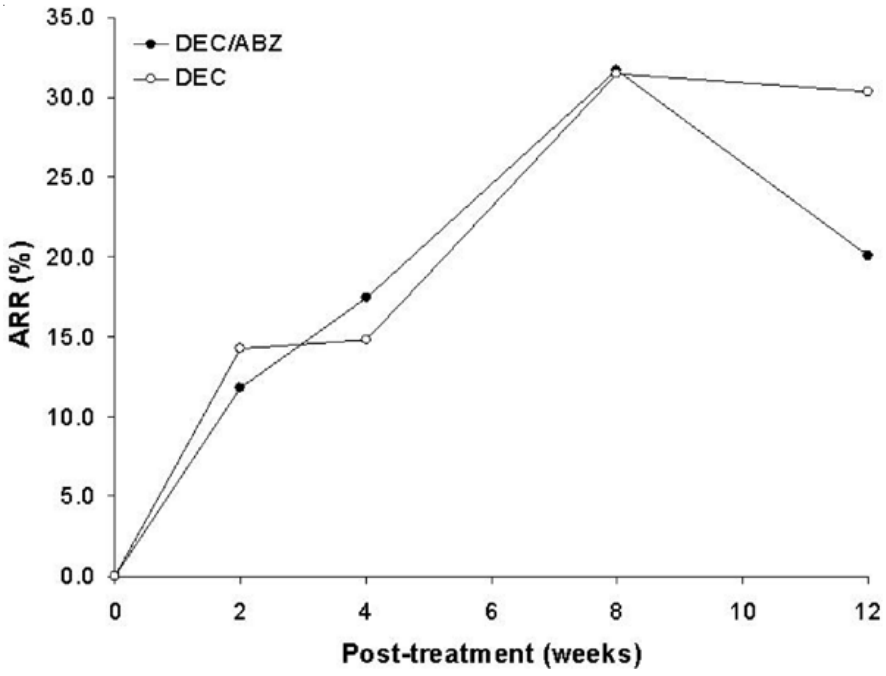

Fig. 1 The antigen reduction rate (ARR) (%) at a complete measurement within the groups: DEC/ABZ (n = 8); DEC (n = 7)

Table 5. Adulticidal effects on geohelminths' egg (GhE) load between the drug groups

Group	GhE load at post-treatment (weeks)				
	0	2	4	8	12
Ascaris					
DEC/ABZ †	443.8	383.5	111.1	0	2.9
(n = 3)	(265.7-491.4)	(48.7-412.1)	(0-387.2)	(0-162.7)	(0-5.8)
DEC ‡	60.8	15.9*	2.1*	0.8*	1.6*
(n = 7)	(2.6-93.1)	(0-23.3)	(0-11.1)	(0-2.6)	(0-4.8)
Trichuris					
DEC/ABZ †	57.4	6.9*	2.4*	0*	0.5*
(n = 12)	(1.1-158.7)	(1.6-60.8)	(0-12.7)	(0-1.1)	(0-24.3)
DEC ‡	6.9	2.4*	1.3*	0.5*	1.1*
(n = 7)	(1.6-65.1)	(0.5-4.2)	(0-5.8)	(0-0.5)	(0-3.7)

A sum of subjects of the treatment arms either with *Ascaris* or with *Trichuris* in Table 4 was used by following GhE examination regardless of mixed infections and worm burdens.
Subjects with loss to follow-up: † 3 DEC/ABZ-treated including 2 harboring the same single *Trichuris* (0 EPG) and one harboring mixed *Ascaris* and *Trichuris* (0 EPG each), who dropped out of the study before week 12; ‡ 2 DEC-treated including one harboring single *Trichuris* (17,986 EPG) before week 2 and another one harboring mixed *Ascaris* (1,587 EPG) and *Trichuris* (2,645 EPG) before week 8.
The data were presented as median ($\times 10^3$ eggs per gram) and range in the parentheses.
Significant with the *Wilcoxon signed rank test ($p < 0.05$) for two dependent samples within the groups

dered. There is evidence that, regardless of the initial GhE loads for *Ascaris* or *Trichuris*, geohelminths' egg reduction (median GhE loads) has improved remarkably for both drug groups as shown in Table 5. For *Ascaris*, although mean differences in GhE loads of group I could not be tested with statistical significance, it was more likely to show GhE load reduction by the treatment retention time. Group II had significant GhE load reduction shown for at least week 2 ($p < 0.05$). For *Trichuris*, both groups had significantly dramatic decline in GhE loads after week 2 ($p < 0.05$).

On the other hand, the ERR (%) for group I with the concomitant *Ascaris* reached 99% at week 12, but in group II more than 90% ERR was noted between week 4 and week 12 (Fig. 2). By using one-way ANOVA, there was no significant difference in the ERR between the groups with the concomitant *Ascaris* ($F = 0.196$, $p = 0.669$). Group I with the concomitant *Trichuris* reached over 80% ERR as early as week 2, or up to 100% at week 12, but in group II it was shown for at least week 4 (Fig. 2). Similar to that of group I, no significant difference in the ERR was noted ($F = 0.709$, $p = 0.424$).

Discussion

LF in endemic in parts of Thailand has been addressed as a potentially eradicable disease[29]. The mainstay of LF elimination strategy, the DEC/ABZ combination, can be effectively used at the field-implementation level to reduce annual cyclic infection prevalence and intensity. It can lower the transmission to fall to a zero-ground infection prevalence[9,21,22]. This has been designed to interrupt LF transmission and eliminate the infection in the at-risk population. This can be used to meet the National Program to Eliminate Lymphatic Filariasis (PELF) by fiscal years 2002-2006[29]. The on-going PELF is run at the administrative levels in the *W. bancrofti* and *B. malayi* transmission areas[29], and in areas prone to the *W. bancrofti* imported by the at-risk Myanmar migrants[23,25,30]. One line of approach to prevent introduced *W. bancrofti* infection in the at-risk Thai population in transmission-prone areas focuses on multiple-dose DEC treatment[31]. This primarily reduces microfilaremics in the at-risk Myanmar migrants. At the provincial level, the LF and parasitic disease management done by the PPHO relies on the 'deworming' DEC/ABZ mass treatment program of legal Myanmar migrants. The key elements of the program implementation approach involve foreign labor force policy and regulation, hospital-based surveillance, reporting systems (*e.g.* evaluation of MDA coverage, monitoring of adverse drug reactions, and gathering of health records), delivery systems (*e.g.* drug supplies and logistics and administration of DEC/ABZ), and supervision of health personnel. The

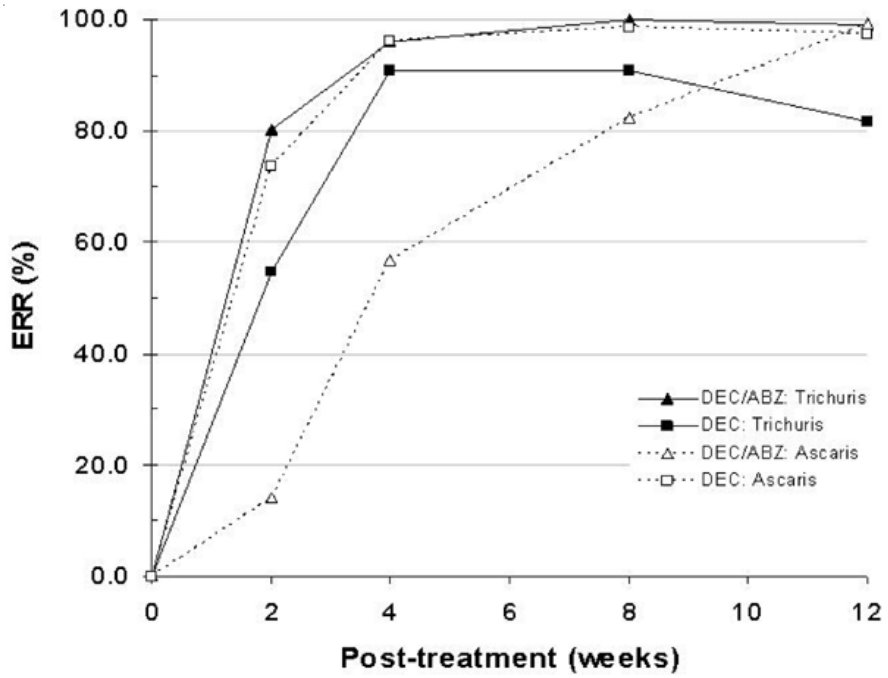

Fig. 2 The egg reduction rate (ERR) (%) at a complete measurement within the groups: DEC/ABZ plus *Trichuris* (n = 9) and *Ascaris* (n = 2); DEC plus *Trichuris* (n = 5) and *Ascaris* (n = 6)

program effectiveness covers those who come for a long-term migration. They are known as an influencing factor that favors coverage and compliance of the MDA[30,31]. However, there is little evidence that such a combined DEC/ABZ can be effectively used for treating those with short periods of residency (usually 3 to 6 months), regardless of treatment rounds. There must be necessary information on within-subject variation of susceptibility in the group. In the present study, short-term effects of the 'de-worming' DEC/ABZ on WbAg and concomitant geohelminths[9,10,19-22] need to be evaluated so as to know whether treatment rounds or effective dosages are required to clear the parasitic worm loads on a wide scale in Phang Nga.

The treatment was more likely to show the short-term macrofilaricidal effects of DEC/ABZ, or DEC alone, on the infection prevalence and intensity of *W. bancrofti* in the studied subjects. A significant reduction of WbAg loads in DEC group was shown for at least 8-week post-treatment. In the DEC/ABZ group, a significantly progressive reduction was more pronounced by the treatment retention time. But it was clear that the two treatment arms had similar macrofilaricidal effects on changes in the *W. bancrofti* intensities (mean WbAg loads) (Table 3). Such DEC/ABZ combination appears to have no greater effects on WbAg loads. In other words, the maximum ARR, > 30%, was at week 8 after treatment in both groups. In the present study, the macrofilaricidal effects of the DEC were not significantly increased when co-administered with the ABZ. Both treatment arms can reduce large amounts of WbAg loads after short periods of drug intake in the groups. Most studies demonstrated that the DEC alone or co-administered with the ABZ did not clear rapidly the antigenemia[7,10,12,23-25,32,33]. The adult worm loads that are age-dependent[12,34] are susceptible to treatment with the DEC/ABZ or DEC alone[12,35]. The groups had similar age thus the serological response to treatment arms implied no or less variation of the susceptibility. Nonetheless, it was possible that recurrent WbAg loads in both groups were seen at week 12 or longer after treatment. The MDA with the DEC alone will likely increase the antigenemia prevalence of *W. bancrofti* unless there is yearly-round MDA in the population[12]. The authors could not rule out the possibility that a recrudescence of *W. bancrofti* antigenemia is likely due to the infections with *W. bancrofti* subpopulations in the Myanmar individuals. The benzimidazole (ABZ) involves genetically-induced resistance in the nematode worms[36,37]. Although the combined DEC/ABZ that have different molecular targets may reduce resistant mechanism of the adult

worms, it is unwise to suggest the antigenemic infections harbor the subpopulation resistant to the ABZ or even the DEC. Therefore, a rationale approach to clearing adult *W. bancrofti* infection in them needs repeat treatment and time required to clear antigenemia[7,23-25].

A mass drug co-administration with single-dose DEC/ABZ has been proven useful to have synergistic effects against all geohelminths (*Ascaris*, *Trichuris* and hookworms)[19,20]. It has added-in benefits of reduction of prevalence and intensity of the geohelminthiases in the population under 15 years of age. The MDA with single-dose DEC has been relatively less effective against the adult *W. bancrofti* and *Trichuris* infections[12,19,20]. In the present study, it was clear that a progressive reduction of parasitic worm loads in both groups was truly affected by the anthelminthic activity. A significant reduction of initial GhE loads for *Trichuris* in both groups was pronounced by the treatment retention time. In the DEC group, it appeared to have the same effects for *Ascaris*. In the DEC/ABZ group, it reached the ERR (> 80%) for the concomitant *Ascaris* and *Trichuris* infections between weeks 4 and 12 and, the same ERR for the concomitant *Trichuris* infection was noted. The ERR for the concomitant *Ascaris* infection in the DEC group dramatically increased to almost 100% at week 12. Both groups had parasitological response and tolerated well and thereby showing no or less variation of susceptibility to the drugs. The findings suggested that the DEC/ABZ or DEC alone acted rapidly as the anthelminthic drugs against both *Ascaris* and *Trichuris* infections, regardless of the initial loads. A significant reduction of their infection intensity was time-dependent on clearing the GhE loads. However, the two treatment arms did not clear the daily parasites' egg products by the treatment retention time. In the present study, the authors could not rule out the possibility that low infection intensities of *Ascaris* and/or *Trichuris* in the Myanmar individuals might be caused by the repeat infection. Moreover, the authors had no additional data that the concomitant *Ascaris* and/ or *Trichuris* infections confer resistance to the drugs. This was confirmed by detecting or identifying resistant genes as molecular target[36,37]. Taken together, these findings come with the fact that the two treatment arms have the same anthelminthic activity against the concomitant *Ascaris* and *Trichuris* infections. The difference is in the initial loads and time required to clear the infection.

In conclusion, the single-dose 300 mg DEC plus 400 mg ABZ, or 300 mg DEC alone, can be effectively used for treating the infections of *W. bancrofti* and concomitant geohelminths commonly observed in the Myanmar subjects. The regimes have effects on reduction of the parasitic worm loads either WbAg or GhE loads. This confirms their value in a large-scale MDA program with the DEC/ABZ available at the provincial level in the legal Myanmar migrants. But the treatment rounds are required for those residing in areas where there is a long-term migration to clear the infections. Without repeat treatment or being continuously exposed to the drugs, recrudescence of the *W. bancrofti* antigenemia or even the parasites' egg loads may occur. This is especially true for those having short-term residency or no renewal of work permits. In particular, a reduction of the *W. bancrofti* antigenemia can be a proxy measure when monitoring and evaluating the effectiveness of single-dose treatment with DEC/ABZ, or DEC alone. This may be done by the antigen detection methods (*i.e.* ICT Filariasis and Og4C3 ELISA). The treatment effects of the regimes on the *W. bancrofti* antigen detection have the same test results in both concordance and discordance. Compared with the Og4C3 ELISA, the ICT card test will likely provide discordant antigen testing in the Myanmar subjects when significant reduction of the *W. bancrofti* antigen is pronounced.

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ประสิทธิภาพของการรักษาแบบรับประทานครั้งเดียวด้วยยาไดเอทธิลคาร์บามาซีนขนาด 300 มิลลิกรัม และร่วมกับยาอัลเบนดาโซลขนาด 400 มิลลิกรัมในการลดแอนติเจนของเชื้อหนอนพยาธิเท้าช้างชนิดวูเชอริเรีย แบนครอฟไต และเชื้อหนอนพยาธิติดต่อทางดินในผู้อพยพชาวพม่าในภาคใต้ของประเทศไทย

พิสิฐ ยงยุทธ, สุรชาติ โกยดุลย์, นงนุช จตุราบัณฑิต, อนุชา เสมพืช, อดิศักดิ์ ภูมิรัตน์

ที่มา: *ประสิทธิผลของการรักษากลุ่มหนอนพยาธิด้วยยาไดเอทธิลคาร์บามาซีน (DEC) และยาอัลเบนดาโซล (ABZ) มีผลต่อการลดระดับความชุกของการติดเชื้อหนอนพยาธิเท้าช้างชนิด Wuchereria bancrofti และเชื้อหนอนพยาธิติดต่อทางดินในกลุ่มแรงงานชาวพม่าอพยพในประเทศไทย ผลการออกฤทธิ์ของยาต่อการควบคุมปริมาณเชื้อหนอนพยาธิ จำเป็นต้องได้รับการศึกษาเนื่องจากแรงงานเหล่านี้พำนักอาศัยในพื้นที่ต่าง ๆ เป็นระยะเวลาสั้น ๆ และสถานการณ์ การติดเชื้อหนอนพยาธิในปัจจุบันนั้นเป็นการติดเชื้อ W. bancrofti ระยะปรากฏแอนติเจน และการติดเชื้อร่วมของเชื้อหนอนพยาธิ ติดต่อทางดิน*

วัตถุประสงค์: *ประเมินประสิทธิภาพของการรักษาแบบรับประทานครั้งเดียวด้วยยา DEC ขนาด 300 มิลลิกรัม (มก.) (สำหรับเชื้อก่อโรคเท้าช้าง) ร่วมกับยา ABZ ขนาด 400 มก. (สำหรับเชื้อก่อโรคหนอนพยาธิ) โดยเปรียบเทียบกับยา DEC ขนาด 300 มก. เพียงชนิดเดียว เพื่อวิเคราะห์การออกฤทธิ์ของยาในระยะสั้นต่อการลดปริมาณแอนติเจนของเชื้อหนอนพยาธิเท้าช้าง (WbAg) และการลดปริมาณไข่ของเชื้อหนอนพยาธิติดต่อทางดิน (GhE)*

วัสดุและวิธีการ: *การทดลองควบคุมแบบสุ่มของการเปรียบเทียบประสิทธิภาพการรักษาในแรงงานชาวพม่า เพศชาย จำนวน 28 ราย (DEC/ABZ หรือกลุ่มที่หนึ่ง เท่ากับ 15 ราย และ DEC หรือกลุ่มที่สอง เท่ากับ 13 ราย) ในจังหวัดพังงา ภาคใต้ของประเทศไทย การติดตามประเมินผลในสัปดาห์ที่ 2, 4, 8 และ 12 ได้ดำเนินการในกลุ่มที่หนึ่ง จำนวน 15 ราย มีอายุเฉลี่ยเท่ากับ 25.7 ปี และปริมาณเชื้อหนอนพยาธิ (ค่าเฉลี่ย $\pm$ ค่าเบี่ยงเบนมาตรฐาน x 10^3) ของเชื้อ W. bancrofti, Ascaris และ Trichuris เท่ากับ 96.1 $\pm$ 54.6 antigen units (AU)/มล., 397.0 $\pm$ 117.3 eggs per gram (EPG) และ 54.5 $\pm$ 42.8 EPG ตามลำดับ ในกลุ่มที่สอง จำนวน 10 ราย (ถอนตัวจากการศึกษา 3 ราย) มีอายุเฉลี่ยเท่ากับ 26.4 ปี ปริมาณเชื้อหนอนพยาธิ เท่ากับ 103.9 $\pm$ 44.1 AU/มล., 47.3 $\pm$ 38.7 EPG และ 16.6 $\pm$ 22.2 EPG ตามลำดับ และใช้ข้อมูลอัตราการลดลงของปริมาณแอนติเจนหรือค่า ARR และอัตราการลดลง ของปริมาณไข่หรือค่า ERR ในการนำเสนอ*

ผลการศึกษา: *หลังการรักษาในสัปดาห์ที่ 12 กลุ่มที่หนึ่งมีปริมาณ WbAg (ค่าเฉลี่ย $\pm$ ค่าเบี่ยงเบนมาตรฐาน x 10^3 AU)/มล.) เท่ากับ 61.5 $\pm$ 58.4 และเท่ากับ 76.8 $\pm$ 40.7 ในกลุ่มที่สอง ในสัปดาห์ที่ 8 และ 12 ทั้งสองกลุ่มมีการลดปริมาณ WbAg อย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) ในทำนองเดียวกัน หลังจากสัปดาห์ที่ 2 มีการลดลงของปริมาณ GhE ของทั้งสองกลุ่มอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) และเมื่อเปรียบเทียบประสิทธิภาพของการรักษาทั้งสองขนานในช่วงเวลาที่มีติดตามการรักษา พบว่า ทั้งสองกลุ่มมีการออกฤทธิ์ฆ่าเชื้อหนอนพยาธิตัวแก่ไม่ว่าต่อการลดปริมาณ WbAg หรือแสดงโดยค่า ARR ($F = 0.064$, $p = 0.806$) หรือต่อการลดปริมาณ GhE หรือแสดงโดยค่า ERR ($F = 0.196$, $p = 0.669$)*

สรุป: *การรักษาแบบรับประทานครั้งเดียวด้วยยา DEC ขนาด 300 มก. ร่วมกับยา ABZ ขนาด 400 มก. หรือยา DEC ขนาด 300 มก. เพียงชนิดเดียว มีประสิทธิผลในการรักษาการติดเชื้อ W. bancrofti และเชื้อหนอนพยาธิติดต่อทางดิน ซึ่งพบได้บ่อยในกลุ่มตัวอย่างในพื้นที่ศึกษา แต่การกำจัดการติดเชื้อยังต้องได้รับการรักษาต่อเนื่องเป็นรอบ ๆ การลดลงของปริมาณเชื้อหนอนพยาธิในกลุ่มแรงงานชาวพม่าที่ขึ้นทะเบียนแรงงานสามารถใช้เป็นตัวบ่งชี้ในการกำกับ ติดตาม และประเมินประสิทธิผลของการรักษากลุ่มด้วยยา DEC/ABZ ในระดับจังหวัด*