Efficacy of Mass Treatment for Control of Human Filariasis

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I. INTRODUCTION

Innumerable trials of chemotherapy with various chemicals had been applied to treatment of human filariasis without satisfactory success. Hewett et al in 1947 reported an excellent efficacy of diethylcarbamazine citrate against bacroftian filariasis, and many workers tested the drug on laboratory animals and human cases. The purpose of this study is to evaluate the efficacy of mass treatment with the drug in control of human filariasis on Che Ju Island where was proved to be a suitable area for the study according to the ecological characteristic of the filariasis (Kim et al., 1973)

II. METHODS AND MATERIALS

As reported on the previous article, ecology of filariasis on Che Ju Island, seven villages were selected and 76.6% of all inhabitants were blood smeared in the first year of the three-year study period. To evaluate the efficacy of the mass treatment with diethylcarbamazine and of insecticide spray, these seven areas were divided into five groups: Group I. Placebo and chemotherapy: 6mg of

placebo/kg of body weight was given to mf positives every day for six doses checking side reactions in January 1969. The placebo was made by Tanabe Drug Company which had the same appearance and size to diethylcarbamazine pill. These villages (Tae Hung and Ka Pa) were resurveyed in July 1969 and treated mf positives and clinical filariasis cases with 6 mg of diethylcarbamazine/kg B.W. X12 doses by the same way of placebo administration.

Group II. Chemotherapy only in two courses: 6 mg of diethylcarbamazine/kg B.W. was given to mf positives for six doses in 1968 which was followed by another six doses of the drug in 1969.

Group III. Chemotherapy and insecticide spray: Bi Yang was drug treated and insecticide sprayed. The same dose of the drug for 12 times was given to mf positives and clinical filariasis cases.

Group IV. Placebo and insecticide spray: placebo was given to mf positives and insecticide was sprayed in the next year. The second survey before the insecticide spray was done to set a baseline for the evaluation of the insecticide spray. The third survey

was conducted one year from the second one to get an answer how insecticide spray without mass treatment would affect the endemicity of the disease (Hoengan islet)

Group V. Placebo only without insecticide spray: Ha Yae and Ma Ra were in this category. Two year from the primary survey, resurvey was carried out to have control against the treated group. Placebo was given in January 1969.

In hetrazan treatment, the first six doses were administered by workers by home visits and side reactions were recorded on the charts. Remaining six doses were given to the patients or family with detailed instruction. The vector mosquito, *Aedes togoi* was proved to be sensitive to DDT according to WHO test for insecticide resistance in mosquito adult (Lee and Kim, 1969) and residual spray was done.

III. RESULTS AND DISCUSSION

Over 90% of mf positives were treated with

placebo in selected areas; Table 1 presents the change of mf rate by year, village, and control measures taken, which clearly shows that the placebo treatment did not decrease mf rate as expected. Two placebo treated patients in Tae Hung village complained of headache incriminating the drug. When they were examined, however, there was no positive physical signs, and the complains were not considered to be from the placebo intake.

1. Efficacy of diethylcarbamazine (hetrazan)

A. Percent of mf positives who became mf negative after the drugadministration: 365 of 419 mf positives (81.1%) accepted the treatment and completed full course of the treatment. Some of patients refused to take the medicine because of the side reactions told by others. Most of the mass treatment was given in cold season to avoid reinfection before the resurvey. Table 2 shows the results of the treatment by village: percent turning

Table 1. Microfilaria rate by year, village, and control measures

Village	First Survey(1968)			Second Survey (1969)			Third Survey(1970)			Remarks
	No. Exam.	No. of Mf (+)	Mf Rate	No. Exam.	No. of Mf (+)	Mf Rate	No. Exam.	No. of Mf (+)	Mf Rate	Control Measures taken
Tae Hung	381	109	28.6	385	116	30.1	325	14	4.3	Placebo: January, 1969 *Mass treatment: August, 1969 January, 1970
To San	441	120	27.2	396	48	12.4	281	18	6.4	Mass treatment: July, 1968 Nov., 1969
Bi Yang	198	54	27.3	96	17	17.7	113	3	2.7	Mass treatment: January 1969 Nov., 1969 Mosquito control: Summer of 1969
Hoengan	11	20	17.1	91	23	25.2	88	23	26.1	Placebo: Nov., 1968 No. mass treatment but mosquito control for summer of 1969
Ka Pa	662	41	6.2	651	46	7.1	511	5	0.9	Placebo: January, 1969 Mass treatment only: Nov., 1969
Ha Yae	396	53	13.4	—	—	—	33	5	15.2	No control measure: placebo only
Ma Ra	124	3	2.4	—	—	—	74	3	4.1	No control measure: placebo only

* Mass treatment with diethylcarbamazine citrate, hetrazan U. S. P.

Table 2. Result of mass treatment with Hetrazan* (the rate of turning positives to negative) by village

Village	No. Pts. Mf(+) Only	No. Pts. Reexam'd	No. Pts. Staying (+)	No. Pts. Turning (—)	Percent Turning(—)	Remarks
Tae Hung	119	95	6	89	93.7	4 Positives out of 6 had more than 50 Microfilaria
To San	104	82	17	65	79.3	6 dosages (Initial Course)
	114	62	4	58	93.5	Total 12 dosages
Bi Yang	65	51	8	43	84.3	7 Positives out of 8 had more than 100 Mf all of which became less than 10 Mf after 12 doses of the Hetrazan. These positives were treated with 5 more doses and turned to negative.
Ka Pa	46	31	1	30	96.8	This one positive patient had 83 Mf.
Total(12 doses)	344	239	19	220	92.1	

* The full course of treatment is 6mg/kg body weight X 12 either every day or every other day.

to mf negative averaged 92.1% with total 12 doses of diethylcarbamazine citrate. There was tendency of low rate when mf density was high. Table 3 reveals the efficacy of diethylcarbamazine in relation to mf density by village; those patients who had more than 50 mf/20mm³ of blood remained mf positive even after the full course of treatment in 16.5% contrast to 2.1% for low mf density patients. These mf positives were treated with five more doses and turned to mf negative.

B. Change in mf density among mf positives after the treatment: 73.8% showed marked decrease of mf density (Table 4) after the treatment and only 2 out of 42 patients showed some increase compared with 32.2% in untreated group (Kim et al., 1973). When one considers the fact that less than 15 mf/20mm³ of blood can not infect mosquito (Cheng, 1964), the treatment is still effective even when some patients remain mf positive.

C. Change in mosquito infection rate in mass treated villages: on ecological study of

Table 3. The efficacy of the Hetrazan in relation to microfilaria density by village

Village		Microfilaria Density (Mf Count/20mm ³ Blood)	
		More than 50 Mf	Less than 50Mf
	No. Tx & Exam'd	40	55
Tae Hung	No. of Mf(+)	4	2
	% Mf(+)	10.0	3.6
To San	No. Tx & Exam'd	21	41
	No. Mf(+)	4	0
	% Mf(+)	19.0	—
Bi Yang	No. Tx & Exam'd	33	18
	No. Mf(+)	7	1
	% Mf(+)	21.2	5.6
Ka Pa	No. Tx & Exam'd	3	28
	No. Mf(+)	1	0
	% Mf(+)	33.3	—
Total	No. Tx & Exam'd	97	142
	No. Mf(+)	16	3
	% Mf(+)	16.5	2.1

Table 4. Change of microfilaria density in microfilaria positives before and after treatment with Hetrazan

Mf. Count		After Treatment								Total
		1-10	11-20	21-30	31-40	41-50	51-100	101-200	201+	
Before Treatment	1-10	5	—	—	—	—	—	—	—	5
	11-20	2	—	1	—	—	—	—	—	3
	21-30	2	—	1	1	—	—	—	—	4
	31-40	1	—	—	—	—	—	—	—	1
	41-50	3	—	—	—	1	—	—	—	4
	51-100	7	—	—	—	—	—	—	—	7
	101-200	8	—	—	1	—	1	2	—	12
	201+	4	2	—	—	—	—	—	—	6
Total		32	2	2	2	1	1	2	0	42

Table 5. Mosquito infection rate by village, year, and human mf rate

Village	1 9 6 8			1 9 6 9			1 9 7 0		
	Mf rate	Mosquito		Mf rate	Mosquito		Mf rate	Mosquito	
		Inf. Rate	Ave. No. Larv.		Inf. Rate	Ave. No. Larv.		Inf. Rate	Ave. No. Larv.
**Tae Hung	28.6(%)	6.4(%)	3.3/inf. mosq.	30.1(%)	7.1(%)	2.8/inf. mo.	4.3(%)	0	0
*To San	27.2	—	—	12.4	3.2	2.7	6.4	0	0
*Bi Yang	27.3	8.5	4.7	17.7	4.1	2.0	2.7	0	0
Hoengan	17.1	—	—	25.2	7.7	3.8	26.1	10.7	3.5
Ha Yae	13.4	3.6	1.8	—	—	—	15.2	—	—
Ka Pa	6.2	—	—	7.1	1.4	2.0	0.9	0	0

** Please refer to Table 1 to see the time when control measures were applied.

filariasis, it was found that human was the only reservoir in these study areas (Kim et al., 1973). Because of this reason mosquito infection rate with the human filaria was used as one of measure sticks in evaluating mass chemotherapy. The mosquito infection rate dropped almost proportionately to decreased human mf rate and finally to zero when human mf rate became less than 7% as shown in Table 5. The average number of filarial larva/infected mosquito, however, was not so related to mf rate.

2. Side reactions produced by diethylcarbamazine

Side reactions were checked carefully for

every patient for first seven days until they disappeared completely. During the first three days, the patients were examined for existing diseases other than filariasis, blood pressure, pulse, body temperature, and body weight. The side reaction was relatively severe for the first three doses after which it was gradually diminished either spontaneously or by symptomatic treatment with A.P.C. The symptoms of side reaction was very similar to clinical symptoms of febrile fit of filariasis suggesting that the reaction may be due to an allergic response of host provoked by destruction of the parasite. The rate of side reaction among treated patients ranged from

Table 6. The rate of side reaction among all patients treated with Hetrazan by village

Village	No. of Pts. with S. R.	No. of Pts. without S. R.	Total	Percent of Pts. with S. R.
Tae Hung	87	32	119	73.1
To San	102	12	114	89.5
Bi Yang	45	20	65	69.2
Ka Pa	32	18	50	64.0
Total	266	82	348	76.4

Table 7. Symptoms of the side reaction induced by Hetrazan on 266 patients

Symptoms	No. of Sympt.	Percent* Total Pts.
Chill	44	16.5
Headache	188	70.6
Fever	141	53.0
Joint Pain	67	25.2
Generalized Muscle Pain	56	21.1
Abdominal Pain	30	11.3
Lymphangitis & Lymphadenitis	23	8.6
Backache	21	7.9
Nausea and Vomiting	48	18.0
Diarrhea	15	5.6
Respiratory Difficulty	4	1.5
Skin Rash	1	0.4
Swelling of Face	1	0.4

* No. of symptoms/No. of total patients with side reaction.

64% to 90% by village (Table 6). The most frequent symptom was fever and headache which was followed by joint pain and generalized muscle pain (Table 7). Nausea and vomiting was not infrequent. Lymphangitis with or without lymphadenitis appeared quite often in the middle of treatment. The physical check up before and after the drug administration did not show any significant change except in body temperature and pulse; the average increase of temperature was about

1-3°C in the first 3-4 days, and the increased pulse rate secondary to elevated temperature. Further analysis of side reaction data by Chi Square test showed that the side reaction was associated with daily dosage of the drug rather than mf density suggesting minimized daily dosage even for heavy person may decrease side reaction in frequency and severity.

3. Efficacy of insecticidespray in control of filariasis

DDT was sprayed to two islets, Bi Yang and Hoengan in the early summer of 1969; Bi Yang combined with mass treatment, and Hoengan DDT spray only. There was no effect on both mf rate and mosquito infection rate as seen in Table 1 and 5.

IV. SUMMARY

This study was carried out for three years from 1968 to 1970. Three coastal villages and four remote islets of Che Ju Island were surveyed and 90% of all inhabitants were blood smeared. These study areas were grouped into five according to its characteristic for evaluation of mass treatment with diethyl-carbamazine citrate (Hetrazan U. S. P.) and insecticide spray in control of human filariasis. To set baseline up for control group, placebo was administered. Followings are the results obtained:

1. 81.1% of all mf positives accepted and completed the mass chemotherapy; main reason for refusal was side reactions told by neighboring villagers who experienced them.
2. 6mg of hetrazan/kg B.W. X 12 doses given every day turned mf positives to mf negative in 92.1%. The patients who had high mf density remained mf positive in 16.5% whereas only 2.1% for low mf density.
3. 73.8% of mf positives after the treatment

showed marked decrease in mf density. most of them to less than 15mg/20mm³ of blood that can not infect mosquito effectively.

4. Mosquito infection rates were also dropped markedly in areas where mf positives were mass treated.

5. Side reaction induced by diethylcarbamazine was frequent(64%-90%) and various. The most frequent symptom was headache and fever.

6. DDT spray did not influence human mf rate and mosquito infection rate.

ACKNOWLEDGEMENT

This study was supported by U.S. Army Research and Development Group (Far East).

We would like to thank health workers in Sogwipo Health Center who made the study possible.

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絲狀蟲症管理를 위한 集團治療의 效果

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本研究는 濟州道の 7個 部落을 對象으로 全住民의 90%를 夜間血液塗沫에 依한 仔虫陽性者를 索出하여 그 地域別 特性에 따라 5群으로 分類 各各 該當 管理法을 適用하였다. 對照群을 設定하여 placebo를 投與하였고 WHO基準에 依한 모기의 殺虫劑에 對한 感受性을 試驗한 후 DDT를 殺虫劑로 選定하여 該當地域에 散布하였다. 다음은 本研究 結果를 要約한 것이다.

1. 仔虫陽性者의 81.1%가 集團治療에 參與하여 끝까지 藥을 服用했다. 集團治療을 拒絶한 大部分의 患者들은 이 옷동리 사람들로부터 藥에 依한 副作用을 들었기 때문이라고 했다.

2. 體重 kg 당 6mg diethylcarbamazine citrate의 12回 投藥은 係虫陽性者의 92.1%를 陰轉시켰으며 仔虫密度 50마리/20mm³ 血液以上인 사람들 16.5%가, 50마리 以下인 사람들 2.1%가 治療後에도 仔虫陽性을 나타내어 仔虫密度와 仔虫陰轉率과는 連關性을 갖고 있었다.

3. 治療後에도 仔虫陽性인 사람들中 73.8%가 顯著한 仔虫密度의 減少를 가져왔으며 이들 大部分이 모기에게 感染을 일으키지 못하는 15마리/20mm³血液에 屬하여 비록 陰轉化는 못해도 모기의 傳播率을 低下시키는데는 큰 意義가 있었다.

4. 集團治療後의 모기 感染率도 현저히 減少되고 사람의 仔虫陽性率이 7% 以下로 된後에는 其感染率이 零으로 되었다.

5. Diethylcarbamazine에 作한 副作用은 比較的 甚하고 頻番하여 投藥者 64%~90%에서 볼수 있었고 그 때문에 投藥과 再調査에 不應하는 原因中에 하나가 되었다.

6. 殺虫劑 散布는 住民들의 仔虫陽性率이나 모기 感染率에 別 影響을 주지 못했다.