

A SINGLE DOSE OF JONIT IN THE TREATMENT OF HUMAN ANCYLOSTOMIASIS

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INTRODUCTION

In 1962 a survey was conducted in the rural regions of Java showing that 82.62 per cent of the population were suffering from hookworm disease and that the average haemoglobin level of these patients was only around 50 per cent (Sahli). It was realized that treatment of this helminthiasis had to be performed, not only for social, but also for economical reasons. Accordingly several drugs against hookworm were tested for their efficiency (Holz, 1963).

In this trial the traditional drugs against hookworm, such as Oil of chenopodium, Carbon tetrachloride, Thymol, Beta-naphthol and Tetrachloroethylene, to a certain extent, proved to be effective. However the organo-toxic properties did not make them suitable for the treatment of people in a poor nutritional condition (Oelkers, 1950).

We commenced treatment with Jonit, a new drug against hookworm infection, introduced by Farbwerke Hoechst A.G., which in previous trials not only revealed a high efficiency against both hookworm species in man, but was also claimed to be free from toxic effects on the vital organs (Rodrigues de Silva and Camillo-Coura, 1968). We began trials with this drug in 1969, which were carried out in several regions of West-Java, by teams of 5 persons from the Institute of Parasitology, University of Padjadjaran.

The study was continued until 1971 and included a total number of 1714 persons out of whom 779 had hookworms.

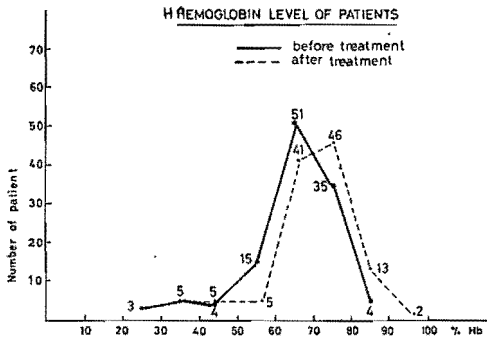
MATERIALS AND METHODS

Our first series of investigations were carried out according to the dosage schedule recommended by the manufacturer, which is 3×100 mg at intervals of 12 hours, altogether a total of 300mg Jonit. The results were extremely satisfactory. To be precise, they resulted in a cure rate of 90 per cent. Nevertheless considering the difficulty of reaching and collecting the patients in our region, it seemed more practical to us to give a single dose treatment. This might also apply to the whole of Southeast Asia (Rockefeller Foundation, 1922). Bearing this in mind we only administered a single dose during our second series of trials.

Drug Jonit : The drug we used is phenylene-di-iso-thiocyanate (1, 4) - generic name : bitoscanate, lab. designation 16,842, trade name : Jonit. The molecular formula is $C_8H_4N_2S_2$. Jonit is insoluble in water, soluble in methanol and ethanol and easily soluble in chloroform. It is a white to yellowish-white crystalline, almost odourless, tasteless powder (Farbwerke Hoechst A.G., 1971). It is presented in sealed capsule form each containing 50 mg. bitoscanate.

Patients : Most of our patients were labourers on rubber and tea estates in the area of Subang (about 60 km north of Bandung, West-Java). All persons were collected and listed by the local health authorities and investigated by our teams for hookworm ova by direct smear, as well as by the Stoll method (Stoll, 1923). It was difficult to collect the patients repeatedly. Therefore we could not

obtain the average number of eggs of each patient by making several counts with the Stoll method. Weight, height, general state of health, and haemoglobin levels (Sahli %) of the patients were determined.



Parasites : The following ova of intestinal helminths were found in the stools of the patients (in order of frequency): *Ascaris*, *Ancylostomatidae*, *Trichuris* and occasionally *Enterobius*.

Ancylostomatidae : Some patients were admitted to hospital and treated with Jonit, to enable us to determine the exact species of the hookworms. In order to recover all the hookworms of a patient, the stools were collected and filtered every day for at least one week or until they were free from hookworm ova. In the course of this procedure we recovered from 11 patients a total of 468

worms out of which 10.8 per cent proved to be *Ancylostoma duodenale* and 89.2 per cent *Necator americanus* (Andajaningsih, 1971). We preferred this method, because the hatching of ova and culturing of larvae from stools under laboratory conditions may lead to inaccurate results as the eggs are frequently damaged (Fülleborn, 1921).

Our results are in accordance with similar investigations on materials gained during post-mortem dissections.

Method of Treatment : Since Jonit has to be taken after a meal, all patients were given 100 gm of boiled rice mixed with 15 gm beef, which had to be taken in the presence of one of the investigators. Thereafter three capsules, each containing 50 mg Jonit, had to be swallowed with some water.

RESULTS

No. of patients treated	117
No. of patients cured	92 = 79%
No. of patients showing an egg reduction of more than 70%	7 = 6%
No. of patients showing an egg reduction of less than 70% and failures	18 = 15%

On the day of the check-up, four weeks after the first treatment, the 25 persons not

Table 1
Egg reduction after 24 hours.

Number of eggs	Number of patients	First Treatment					Second Treatment				
		0 -69%	70% -79%	80% -89%	90% -99%	100%	0 -69%	70% -79%	80% -89%	90% -99%	100%
1 - 1000	60	1	-	-	-	49	2	-	-	-	9
1001 - 5000	47	3	3	2	-	36	-	-	-	1	4
5001 - or more	10	1	-	-	1	7	1	-	-	-	1
Total	117	5	3	2	1	92	3	-	-	1	14

cured were given a second course of treatment with a single dose of 150 mg Jonit. The results of the follow-up treatment was the following:

No. of patients treated for the second time	25
Out of this number 2 did not reappear for check-up, leaving us for evaluation	23
No. of patients cured after second treatment	14 = 61 %
No. of patients showing an egg reduction of more than 70% after the second treatment	1 = 4 %
No. of patients showing an egg reduction of less than 70% and failures after the second treatment	8 = 35 %

DISCUSSION

Ancylostomiasis is one of the major health problems in rural areas of Indonesia. So far this fact has been neglected to a great extent and it seems that the time has come to be aware of these conditions. To be able to take the necessary steps to overcome this health problem, first of all data, dealing with epidemiology and prevalence of these parasites and their effects on their hosts have to be studied. Furthermore it is of general interest to assess the loss caused by the decrease of working power of the people infected with hookworms. This has to be done in order to convince the economically minded authorities that expenses for eradication of hookworm disease will be financially profitable.

At present the well known classic anthelmintics are commonly used for therapy. Unfortunately they have a high rate of toxicity not only on the hookworms, but also on the cell systems of their hosts. For this reason their use in tropical regions is limited

to patients, who are under permanent medical observation, but they are not suitable for mass treatment, where individual supervision is impossible. It is therefore justified to search for new drugs, which are safe and effective in their administration and well tolerated even by people in poor health or nutritional conditions.

Jonit, seems to fulfill all these requirements. It is easy to take, eliminates hookworms with a single dose of 150 mg, with a cure rate of 79 per cent, in both species of hookworm. Although in 39 per cent we observed side effects (nausea, late vomiting, diarrhoea, vertigo), the patients were still ready to undergo a second treatment voluntarily. This was especially seen during our course with the triple dose treatment, when patients came back to swallow the capsule for the second and third time. We had observed that 39 per cent of the patients had side effects, a rate which considerably exceeds the percentage seen by other investigators. To this we would like to add the following: Those people who experienced side effects were allowed to stay away from work by their employers. Taking into consideration human nature, many might have utilized this offer without having any side effects at all. The actual rate might therefore have been much lower.

After our excellent experience with Jonit we contacted the World Food Program in Rome to start a joint action for eradication of hookworms. It can be expected that with single dose treatment, given in three half-yearly intervals, not only the people will be cured, but that due to the reduction in hookworm eggs, the reinfection rate will be so low that we practically can speak of an eradication.

The World Food Program was requested to contribute to this scheme by supplying food free of charge in order to speed up

recovery and to attract people to come forward for treatment.

SUMMARY

Bitoscanate (Jonit) proved to be a reliable and effective drug for the treatment of ancylostomiasis in agricultural areas of Java. The most suitable dosage of Bitoscanate is a single dose of 150 mg given orally. The cure rate was 79 per cent irrespective of whether the persons were infected by *Ancylostoma duodenale* or *Necator americanus*. Side effects did not prove to be an obstacle in the treatment of 1714 persons (including 581 control cases). Since persons do not have to be examined individually before treatment, Bitoscanate is suitable for eradication programmes in tropical regions.

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