

## A SINGLE DOSE OF JONIT IN THE TREATMENT OF SOIL-TRANSMITTED HELMINTHIC INFECTIONS WITH SPECIAL EMPHASIS ON HOOKWORM INFECTION

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### INTRODUCTION

Multiple infections of soil-transmitted helminths are very common in Indonesia, including Yogyakarta, since the environmental conditions are very favourable for their development and transmission. Our recent surveys showed that the prevalence rate is high, although the wormloads are relatively low (Noerhajati, 1973). Hookworm infection is the most debilitating disease and so great is the morbidity in man, that it becomes increasingly important/ to discover newer and better drugs, to fight this problem (Johnson, 1971).

Both species of hookworm: *Ancylostoma duodenale* and *Necator americanus* are found in Yogyakarta and mixed infections do occur, but the dominant species is *N. americanus* (Soenarno & Noerhajati, 1973). Despite a large number of drugs commercially available the treatment of hookworm infections remains unsatisfactory, because none of the drugs is consistently effective against both the common species of hookworm.

Recently bitoscanate (Phenylene-diisothiocyanate 1.4, JONIT), a new drug derived from mustard oil, has been found to be effective in helminthiasis. It has been shown to have action particularly against hookworm regardless of the species, both in animals (Duwel, 1972) and in man (Bunnag & Harinasuta, 1968; Gaitonde *et al.* 1969; Mutalik & Gulati, 1969; Johnson, 1971; Holz *et al.* 1972; O'Holohan & Matthews, 1972; Kosin, 1973).

This paper deals with our experience with Bitoscanate in soil-transmitted helminthic infections with special emphasis on hookworm infection, including the effectiveness and the side-effects of the drug.

### MATERIAL AND METHOD

122 persons of low level group labourers of the milk company «SARI HUSADA», Yogyakarta were examined for hookworm infection in October and Nopember 1973. The fecal specimens were collected and brought to the laboratory of the Parasitology Department Gadjah Mada University, Faculty of Medicine. They had been examined by direct smear and concentration method (zinc sulphate centrifugal floatation method) respectively. From each specimen 6 direct smears and 2 indirect smears by con-

centration method were made. Stools with hookworm ova were cultured to the diagnostic third stage larva (by modified Harada Mori technique).

The Stoll dilution method (Stoll, 1923) for egg counting was done to get a good impression about the degree of intensity of the infection. Before treatment Stoll counts for hookworm ova were made, twice from each specimen. Ova of *Ascaris lumbricoides* and *Trichuris trichiura* were also counted, simultaneously by the same method. All of the patients infected with hookworm were treated with phenylene-diisothiocyanate 1.4, JONIT.

The drug was given by the doctor of the company as a single dose, 150 mg (3 capsules), immediately after the evening meal and was swallowed as a whole with a little water. It was in the form of a gelatin capsule containing 50 mg of the compound.

The treatment after the evening meal was chosen to allow any possible side-effects to be masked by the sleeping hours. Even though, 1 tablet 25 mg Avil was given to the patients to avoid suffering from heavy side-effect reactions.

All patients were carefully observed for a period of 24 to 48 hours after the drug administration and the history of any side-effects was elicited by interrogation.

The follow-up fecal examination was at two and four weeks after treatment, using the same technique, but if the specimen was found negative by the direct smear and concentration method at two weeks, the Stoll count was omitted and recorded as zero, and the examination at four weeks was not carried out.

To evaluate the effectiveness of the treatment we used the criteria of the cure rate as the percentage of the total patients who were completely cleared and the egg reduction rate as the percentage of reduction in egg counts of those who were not completely cleared after treatment. Using the criteria devised by Scott in 1945 (Faust, 1949), heavy infection of hookworm is defined as one in which more than 11,100 eggs occur in one cc. of stool; moderate infection from 2,100 to 11,099 eggs and light infection fewer than 2,099 eggs.

## RESULT

A total of 122 fecal specimens were examined for helminthic infections, and intestinal helminths were found in 105 specimens (86.1%). *A. lumbricoides* ova were found in 56 specimens (45.0%), *T. trichiura* in 96 (78.7%) and hookworm in 54 (44.2%). From 20 patients out of the total 54 hookworm infections treated with JONIT, the follow up fecal examinations were not carried out. These were excluded from the evaluation of the trial, so the total number examined was 34.

Identifications of the L3 stage from the modified Harada Mori culture of all stools positive with hookworm ova, showed that most of them were single infections of *N. americanus* (79.41%). *A. duodenale* was found in a very small amount as single infections (2.94%) and in mixed infections with *N. americanus* (17.65%) (Table 1).

TABLE 1. - Comparison of single infections of *N. americanus*, *A. duodenale* and mixed infections in 34 patients positive for hookworms

Hookworm	Number Found Infected	% Found Infected
<i>N. americanus</i>	27	79.41
<i>A. duodenale</i>	1	2.94
<i>N. americanus</i> and <i>A. duodenale</i>	6	17.65
Total	34	100

The cure rate for hookworm infection was evaluated with the Stoll egg counting method and the modified Harada Mori culture technique. The results were relatively good as can be seen in Tables 2 and 3.

The cure rates were 82.35%, 84.84% and 85.71% for hookworm, *N. americanus* and *A. duodenale* respectively. All cases of moderate hookworm infection cleared after treatment. Heavy infections were not found.

TABLE 2. - Cure rates and egg reduction rates one month after treatment for hookworm

G r o u p	Stoll Egg Count Be- fore Treat- ment	No. of Subjects	% Indivi- duals	Average e.p.g. Mean of 2 Counts		No. of In- dividuals 100% Cleared	Cure Rate in %	
				Before Treat- ment	After Treat- ment			Egg Re- duction Rate in %
1	- 1000	28	82.35	256	28	89.06	22	78.57
2	1 - 2000	3	8.82	1.366	0	100	3	100
3	2 - 3000	1	2.94	2.350	0	100	1	100
4	3 - 4000	—	—	—	—	—	—	—
5	4 - 5000	1	2.94	4.000	0	100	1	100
6	5 - 6000	—	—	—	—	—	—	—
7	6 - 7000	1	2.94	6.500	0	100	1	100
Total		34	100				28	82.35

Overall egg reduction rate = 96.76%.

TABLE 3. - Cure rates for *N. americanus* and *N. duodenale* in 34 patients positive with hookworm, one month after treatment

Hookworm	Number of Cases		Cure Rate in %
	Before	After	
<i>Necator americanus</i>	33	9	84.81
<i>Ancylostoma duodenale</i>	7	1	85.71

*N. americanus* and *A. duodenale* as single and mixed infections.

17 cases of the total patients treated with JONIT were found infected with *Ascaris lumbricoides*. The cure rate for *A. lumbricoides* was 47.05% and the egg reduction rate was 81.09% (Table 4).

TABLE 4. - Cure rates and egg reduction rates one month after treatment for *A. lumbricoides*

G r o u p	Stoll Count Be- fore Treat- ment	Egg Count	No. of Subject	% Indi- viduals	Average e.p.g. Mean of 2 Counts			No. of In- dividuals 100% Cleared	Cure Rate in %
					Before Treat- ment	After Treat- ment	Egg Re- duction Rate in %		
1	—	1.000	8	47.05	149	12	91.95	7	87.5
2	1	5.000	2	11.77	2875	2300	20.0	—	—
3	5	10.000	2	11.77	7975	2050	74.29	1	50.0
4	10	15.000	1	5.88	14600	3950	72.95	—	—
5	15	20.000	—	—	—	—	—	—	—
6	20	25.000	2	11.77	21500	800	96.28	—	—
7	25	30.000	2	11.77	27075	5550	79.50	—	—
Total			17	100				8	47.05

Overall egg reduction rate = 81.09%.

All 34 hookworm infected persons were also positive with *Trichuris trichiura*. Against *T. trichiura* Jonit was not very effective. It indicated a cure rate of only 26.47% and an egg reduction rate of 62.19% (Table 5).

For both *A. lumbricoides* and *T. trichiura*, in cases with an average egg count less than 1000, the drug was more effective. The cure rates were 87.5% and 36.36% for *A. lumbricoides* and *T. trichiura* respectively (Table 4 and 5).

TABLE 5. - Cure rates and egg reduction rates one month after treatment for *T. trichiura*

G r o u p	Stoll Count Be- fore Treat- ment	Egg Count	No. of Subjects	% Indi- viduals	Average e.p.g. Mean of 2 Counts			No. of In- dividuals 100% Cleared	Cure Rate in %
					Before Treat- ment	After Treat- ment	Egg Re- duction Rate in %		
1	—	1000	22	64.71	263	247	6.08	8	36.36
2	1	2000	9	26.47	1444	433	70.00	1	11.11
3	2	3000	1	2.94	2400	100	95.83	0	0
4	3	4000	2	5.88	3350	550	83.58	0	0
Total			34	100				9	26.47

Overall egg reduction rate = 62.20%.

## SIDE-EFFECTS OF JONIT

9 out of the total patients who received the drug did not reappear for the side-effects examination. The total number examined was therefore only 45.

### Vomiting

20 patients (44%) vomited; three (3) vomited immediately after taking the drug; four (4) vomited during the night; three (3) during the night and followed on rising in the morning and 10 (ten) patients vomited on the following day.

### Nausea

34 patients (76%) complained of nausea. The nausea in 5 patients started immediately after ingestion of the drug; in most of the patients it started during the night and persisted until morning. Only 11 patients felt nausea on the next morning. In many cases nausea was accompanied or followed by vomiting.

### Giddiness or headache

29 patients (64%) had sensation of giddiness, in 5 cases not very late in the evening; 17 patients seemed to have headache and dizziness during the night and some of them persisted on a rising in the morning. Only 8 patients felt the sensation on the next day.

### Diarrhoea

There was no diarrhoea which occurred immediately after the treatment, but 15 patients had diarrhoea during the night until the following day and 21 began just on the next day. The total 36 patients (80%) who complained diarrhoea had between 2 and loose motions while the highest frequency was 15 motions.

They did not receive any medication for this.

### Others

28 patients had transient abdominal discomfort, such as abdominal pain and colic which disappeared after defecation.

## DISCUSSION

All the previous reports on the use of bitoscanate or phenylene-diisothiocyanate 1.4 JONIT, in a single dose of 150 mg was found to be effective against hookworm infection. Many investigators reported the result of JONIT comparing with other anthelmintics in hookworm infection. In this trial it was desired to find out the efficacy of JONIT in hookworm infection compared with other soil-transmitted helminthic infections.

Using the criteria of a cure rate as a percentage of the number of patients showing reduction above 70 percent in egg count/g of faeces, Gaitonde *et al.* (1969) found a cure rate of 63% for hookworm and 25% for *A. lumbricoides*. He reported that the prominent side-effects were vomiting and dizziness which were comparatively mild, not needing any treatment.

In the investigation of Holz *et al.* (1972), 92 out of the total 117 hookworm patients treated with JONIT cleared after treatment. This indicated a cure rate of 79%.

O'Holohan & Matthews (1972) used single dose regimens of JONIT in 50 patients with hookworm. There was an average reduction of the hookworm egg count after treatment by 94% and for *T. trichiura* by 61%. But for *A. lumbricoides* it was not effective. The side-effects as occurred did not require treatment or interfere with their daily activities or cause loss of work. Diarrhoea was a common accompaniment.

Bunnag & Harinasuta (1968), using two doses of 150 mg JONIT each at 12 hours interval after meal, found a mean reduction in egg count of 89% in *N. americanus* infection. Mild and transient toxic effects were present in approximately 20% of patients and more severe toxic effects were present in only 5%. They included anorexia, vomiting, retching, abdominal pains and weakness.

Kosin (1973) showed a cure rate of 84.5% in hookworm infection, but it was ineffective against *A. lumbricoides*. The effectiveness of JONIT against *T. trichiura* was not reported.

In our trial we found that a single dose of JONIT proved to be effective against hookworm infections. The cure rate was 82.35% and the egg reduction rate was 96.76%. It seemed that the drug was even effective against *N. americanus* or *A. duodenale*. The cure rates were 84.84% and 85.71% for *N. americanus* and *A. duodenale* respectively. It was not very effective against *A. lumbricoides* and *T. trichiura*, since the cure rates were only 47.05% and 26.47%.

The side-effects experienced by the patients were commonly gastrointestinal complains. Diarrhoea was the most frequent accompaniment of this drug (80%), but it ceased without any treatment.

## SUMMARY

Phenelyne-diisothiocyanate 1.4 (JONIT) or Bitoscanate in a single dose of 150 mg was given to 34 patients infected with hookworm. Besides hookworm, they also harboured the common species of soil-transmitted helminths, such as *Ascaris lumbricoides* and *Trichuris trichiura*.

The result of the study showed that the drug was effective against hookworm and less effective against *A. lumbricoides* and *T. trichiura* infections. The cure rates were 82.35%, 47.05% and 26.47% for hookworm, *A. lumbricoides* and *T. trichiura* respectively.

The side effects, including nausea, vomiting, diarrhoea, giddiness or headache and abdominal discomfort were mild and transient which did not require any treatment.

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