From the Department of Child Health, Medical School, University of Indonesia, Jakarta.

A New Oral Amoebicid (RO 7-0207) in the Treatment of Intestinal Amoebiasis*

by

S.H. PUDJIADI, SUNOTO, SUHARJONO and NARTONO KADRI

Amoebiasis is a widespread disease with the diffusion of the parasite varying more with hygienic than geopraphic conditions. The incidence varies from country to country. Soysa (1971) has estimated that ten per cent of the world-population suffers from amoebiasis. Udani et al. (1971) said that "it will not be an exaggeration to state that everybody in a developing country either had, has or will have amoebic infection". In Indonesia, the incidence varies according to environmental, socio-economic, hygienic and sanitary conditions (Pudjiadi, 1971).

Amoebiasis is rarely seen in the higher sosio-economic classes, but the incidence in rural areas and in the slums of big cities is high. In the Department of Child Health, University of Indonesia, Jakarta, amoebiasis has been conventionally treated with daily injections of HCL-emetine combined with oral antibiotics for five to seven consecutive days. The patient must visit a physician or the clinic daily for this period constituting a financial burden to people of low economic standard.

A survey done on the results of treating vitamin A deficiency with vitamin A injections for five consecutive days showed that treatment could be completed in only 49 per cent of the patients (Pudjiadi and Harmanses, 1965). Oral and low priced anti-amoebic drugs would, therefore, offer the treatment of choice for amoebiasis. In the last few years, several new oral amoebicids became available in the Indonesian market and trials were carried out with some of them, including intestopan — Sandoz (Pudjiadi et al., 1969) Flagyl — Specia (Jo Kian

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Tjay et al., 1971) and Dehydroemetine-Hoffman La Roche (Jo Kian Tjay et al., 1971; Sri Rochani Sudjarwo et al., 1971) Although the results were satisfactory, the relatively high cost of the treatment made them out-of-reach to most patients.

A new amoebicid, RO 7-0207 (Roche), has however shown marked activity against entamoeba histolytica on animal experiments, according to the data sheet provided by Roche Far East Research Foundation, Hong Kong. The investigation described here was aimed at confirming findings on human beings and comparing the drug's efficacy with metronidazole.

Materials and methods

Twenty patients with bloody and frequent diarrhoea, whose stool specimens showed positive amoeba histolytica parasites, were admitted to the Department of Child Health, Medical School University of Indonesia, Jakarta for 15 days. They consisted of 15 boys and five girls, ranging in age from 10 months to 10 years.

Stool examination : Faecal specimens were collected on the day of admission before treatment was started and on every day during hospitalization. As far as possible, a weekly follow-up was continued after discharge. Macroscopic and microscopic examinations of the stool specimens and number of defecations were noticed daily. Eosin (1%) and Lugol's solution (1%) staining of faecal material smears for detecting the E.histolytica parasites were used and examinations were made in triplicates.

Clinical investigations : A daily clinical check-up was carried out with special attention given to possible complications and side-effects of the drug, e.g. abdominal discomfort, loss of appetite, skin rash, neurological signs, etc.

Safety tests: Complete peripheral blood examinations, urine analysis, E.C.G., S.G.P.T. and alkaline phosphatase level determinations were done before, during and after treatment.

Administration of the drug: A double-blind set containing ten bottles of RO 7-0207 125 mg capsules and 10 bottles of metronidazole capsules about 125 mg was supplied by the Roche Far East Research Foundation, Hong Kong. The bottles were numbered 191-210 and contained either RO 7-0207 or metronidazole, unknown to the investigators. The first admitted case was treated with capsules from bottle 191, the second with those from bottle 192, etc.

Dosage: Up to two years 62½ mg, two to six years 125 mg and six to 12 years 250 mg daily, divided into three daily doses for seven consecutive days.

Evaluation: The therapeutic effect was assessed by the clinical evaluation and stool parasitology, Eva-

luation of the results was classified in three categories, as was done previously (Pudjiadi et al., 1969; Sri Rochani Sudjarwo et al., 1971).

a. Excellent: The patient shows very quick response, the clinical symptoms disappear and stools become negative for E.histolytica within three days.
b. Good: Clinical symptoms disappear and stool becomes negative for E.histolytica within four to seven days.
c. Poor: E. histolytica does not disappear after seven days of medication.

Results

The list stating which bottles contained RO 7-0207 or metronidazole was sent by Roche Far East Research Foundation, Hong Kong in a sealed envelope and was only opened after the entire trial was finished.

The group treated with RO 7-0207 (Table 1) consisted of 10 children, eight boys and two girls, varying in age from 15 months to 10 years. The general condition was fair in seven and poor in three children. All of them had frequent defecations with blood and mucus in the faeces. The stools became normal after the treatment was terminated. Clinical improvement was achieved after a period of three to seven days. Faecal parasitological disappearance occurred after two to four days. According to the classification used in this trial, the results in five cases can be categorized as excellent, whereas the remaining cases were good.

In the group treated with metronidazole (Table 2), out of the 10 cases, seven were boys and three were girls, varying in age from 10 months to seven years. The general condition was fair in four and poor in six cases. Frequent defecations with blood and mucus were found in all of them. The faeces became normal after the therapy was finished. Clinicai symptoms disappeared after a period of three to seven days. The faeces became free from E. histolytica parasites after a period of two to four days of treatment. The result of the treatment in this issue can be classified as excellent in two cases and good in eight cases. Out of the 20 cases, nine had fever on admission which subsided after one to four days of treatment. Initial abdominal pain was recorded in four cases, disappearing after two to four days.

Ascaris lumbricoides eggs were found in the faeces of six cases and remained present in five out of the six cases after the treatment were finished.

Trichuris trichiura eggs were also found in six cases; the faeces became negative after treatment in only one case.

No significant changes were noted in the urine of any patient during and after treatment with either RO 7-0207 or metronidazole.

TABLE 1 : *Amoebicidc activity of RO 7-0207 (Roche) in intestinal amoebiasis*

Case	Age (years)	Sex	General condition	Duration of onset (days) before admission	Daily frequency of defecation		Clinical improvement is achieved (days)	Disappearance of faecal parasites (days)	Result	Drug code
					Before treatm.	After treatm.				
1. (Marni)	3½	f	poor	10	10	1	5	4	good	194 = A
2. (Hidajat)	8	m	poor	30	6	1	7	4	good	192 = A
3. (Surjadi)	4	m	fair	7	8	1	5	3	good	197 = A
4. (Mardiani)	1 3/12	f	fair	7	6	2	4	2	excellent	198 = A
5. (Eka P)	5	m	fair	7	6	1	5	4	good	199 = A
6. (Sukmadi)	10	m	fair	7	5	1	4	2	excellent	201 = A
7. (Ratno)	5	m	poor	12	10	1	6	4	good	204 = A
8. (Urip)	3	m	fair	7	10	1	3	2	excellent	205 = A
9. (Tarmidi)	5	m	fair	5	8	1	4	2	excellent	206 = A
10. (Mardi)	4	m	fair	30	4	1	3	3	excellent	208 = A

TABLE 2 : *Amoebicide activity of metronidazole in intestinal amoebiasis.*

Case	Age (years)	Sex	General condition	Duration of onset (days) before admission	Daily frequency of defecation		Clinical improvement is achieved (days)	Disappearance of faecal parasites (days)	Result	Drug Code
					Before treatm.	After treatm.				
1. (Hendra)	2½	m	poor	30	15	1	5	4	good	191 = B
2. (Ngadiono)	11/12	m	fair	20	7	1	6	3	good	193 = B
3. (Supardi)	7	m	fair	7	10	1	6	3	good	195 = B
4. (Budi Utomo)	10/12	m	poor	7	10	1	7	4	good	196 = B
5. (Sri S)	4½	f	poor	75	10	1	3	3	excellent	200 = B
6. (Farida)	3½	f	poor	10	6	1	6	4	good	202 = B
7. (Rusmiati)	5	f	poor	7	7	1	7	4	good	203 = B
8. (Torik)	3	m	fair	21	6	1	7	2	good	207 = B
9. (Djaenal)	3	m	fair	7	15	1	3	2	excellent	209 = B
10. (Darmito)	6½	m	poor	5	4	1	3	4	good	210 = B

No trend of abnormality of values for serum alkaline phosphatase, S.G.P.T., haemoglobin, BUN was observed during and after treatment, E.C.G.s were normal in all cases during and after treatment. No clinical side-effects — e.g. nausea, loss of appetite, neurological signs — were observed in any of the cases.

Discussion

Patients suffering from intestinal amoebiasis are in general not severely ill. Their parents, too, are reluctant to allow hospitalization particularly if it requires several weeks. However, to be sure that the drug will be given properly and to avoid possible re-infection from the patient's surroundings, we only used inpatients in our study. Also due to an overloaded bed occupancy, only 20 patients could be collected during a six-month period.

Metronidazole is regarded by many authors as the drug of choice for the treatment of intestinal amoebiasis (Jo Kian Tjay, 1971; Soysa, 1971; W.H.O., 1969) and RO7-0207 had similar results — a 100 per cent cure rate. Out of the 10 cases, five could be categorized as having an excellent result, whereas in the metronidazole group, only two out of the 10 cases could be categorized as such. However, the difference in results between the two groups is statistically not significant at the five percent level. The two month follow-up study after discharge carried out on seven out of the entire group showed no signs of clinical nor parasitological relapse.

No side-effects were encountered in either groups. The safety tests showed that no abnormality was found in all the patients treated with both drugs.

Previous studies done in the same hospital with the same method of evaluation on oral intestopan (30-40 mg/kg b.w. daily for seven consecutive days) showed a cure-rate as follow: 39.1 per cent excellent, 47.8 per cent good and 13.1 per cent poor (Pudjiadi, 1969), whereas on oral dehydro-emetine (1mg/kg b.w. daily for seven to 10 days), 48.4 per cent were excellent, 41.9 per cent were good and 9.7 per cent were poor (Sri Rochani Sudjarwo, 1971). The material used in this study is too small to draw any decisive conclusion. However, the results suggest that RO 7-0207 is a useful and effective amoebicid in the treatment of intestinal amoebiasis.

If RO 7-0207 could be produced inexpensively to be within the reach of the masses, it would compete favourably with other oral amoebicides for mass treatment of intestinal amoebiasis, still endemic in many parts of the world, including Indonesia.

Summary

A double blind controlled study was conducted on the efficacy of two oral drugs, RO 7-0207 (Roche)

and metronidazole in the treatment of intestinal amoebiasis in 20 children. The patients who were up to two years old, received 62½ mg, the two to six year group 125 mg and the six to 12 years old 250 mg daily in three divided doses for seven consecutive days.

The results show that both drugs achieved a 100 per cent cure rate as evaluated by the clinical evaluation and stool parasitology. No side-effects or signs of drug toxicity were observed. No sign of clinical or parasitological relapse was seen on seven patients followed up for eight weeks after discharge.

The results of the study suggest that RO 7-0207 is as effective as the currently available oral amoebicides.

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