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## Expelled effect of single and multiple doses of albendazole against *Trichuris trichiura*

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## Expelled effect of single and multiple doses of albendazole against Trichuris trichiura

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*An average 40% cure rate was obtained in all intensities of Trichuris infections given three days of 400 mg albendazole. Single dose of 400 mg gave cure rates of 30% in light infections only. Worms were expelled from the first day after treatment to the seventh day, with the maximum number of worms expelled in the fourth day of the three-day regimen. In a single dose regimen, worms were expelled on the first day to the sixth day after the treatment with the highest number of worms on the third or the fourth day of collection. The three-day regimen expelled three to seven times more worms than the number of worms expelled with the single dose regimen. The ratio of male to female worm expelled from cured children was 1:2. The overall numbers of eggs per female worm per gram of faeces were 27-2,093 with 229 as the median.*

**Key words:** Treatment, Trichuris trichiura, Albendazole.

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ยาอัลเบนดาโซล ขนาด 400 มิลลิกรัม รับประทานติดต่อกัน 3 วัน ให้ประสิทธิภาพในการรักษาโรคพยาธิไส้เมีในทุกระดับความรุนแรงได้ 40 เปอร์เซ็นต์โดยเฉลี่ย และถ้าให้ยานี้เพียงครั้งเดียวในขนาดที่เท่ากัน ประสิทธิภาพของยาจะเท่ากับ 30 เปอร์เซ็นต์ในกลุ่มที่มีพยาธิเมีอยู่ในระดับความรุนแรงน้อยเท่านั้น การให้ยาต่อเนื่องกัน 3 วัน มีผลให้ตัวพยาธิถูกขับออกมากับอุจจาระตั้งแต่วันแรกจนถึงวันที่ 7 หลังการรับประทานยา จำนวนพยาธิจะสูงสุดในอุจจาระวันที่ 4 ส่วนการให้ยาเพียงครั้งเดียวก็สามารถตรวจพบตัวพยาธิได้ในระหว่างวันที่ 1-6 หลังการให้ยาและจำนวนตัวพยาธิจะมากในช่วงวันที่ 3 และ 4 นอกจากนี้ยังพบว่า จำนวนตัวพยาธิที่ได้จากกลุ่มที่ให้ยานานกว่าจะสูงกว่าอีกกลุ่มหนึ่ง 3-7 เท่า สัดส่วนของพยาธิเพศผู้:เพศเมีย เป็น 1:2 จำนวนไข่พยาธิในอุจจาระ 1 กรัม ต่อพยาธิตัวเมีย 1 ตัว อยู่ระหว่าง 27-2,039 ใบ (ค่ากลาง คือ 229)

Among the common soil-transmitted helminthiases, trichuriasis is the most difficult to control. Being well embedded in the large intestinal wall makes it retracted to most of the anthelmintics available. The benzimidazole compounds, which inhibit worm glucose uptake, were more effective against *Trichuris*, but the result was not consistent. Low intensity infections were more amenable to treatment than high intensity infections and a multiple-dose regimen given over several days yielded more satisfactory therapeutic effect. (Rossinol & Maisonneuve, 1983<sup>(1)</sup>; Kan 1983<sup>(2)</sup> & 1992<sup>(3)</sup>; Anantaphruti *et al.*, 1994.<sup>(4)</sup>)

Bundy *et al.* (1985)<sup>(5)</sup> indicated that albendazole was as effective against *T. trichiura* in a single dose as in a multiple dose regimen and worm expulsion was independent of the dose and duration of the therapy. This study<sup>(5)</sup> disagrees with Hall and Nahar (1994),<sup>(6)</sup> Singhasivanon *et al.* (1993)<sup>(7)</sup> and the above mentioned reports on the effectiveness of single and multiple dose regimens of albendazole. To study this contradiction, the present study measured the number of *Trichuris* worms expelled with a single-dose and a three-dose regimen, and numbers of eggs per female worm per gramme of faeces was also measured when the worms were completely expelled.

## Materials and methods

The study was conducted on children in Wat Bode Primary School, Tambol Pakpoon, Muang District Nakornsithammarat Province, Southern Thailand. Faecal examination of the school children was performed by a modified thick smear method. The number of eggs per gramme of faeces (epg) was determined and

classified to the degree of infection; Light = 1-1,000, Moderate = 1,001-10,000, Heavy = 10,001\*.

The children were divided into two pair-matched with the number of 100 cases in each group. Twenty-four hour stools were collected the day after the first treatment and continued for seven days. Each day expelled worms were pick up from stool specimens, sexed and counted. Thirty days after the last treatment faecal samples from each child were obtained and examined by the modified thick smear method (Kato-Katz's).

At the end of the study, a lot of children were incompletely submitted stool samples, 86 children (10 heavy, 31 moderate and 45 light infection) were remained in group 1 which were given 400 mg albendazole (Smith Kline and Beecham Pharmaceutical, Thailand) for 3 days and 21 children (2 heavy, 9 moderate and 10 light infection) of group 2 were given a single 400 mg albendazole.

## Results

Of 278 stool samples submitted for examination, 269 specimens or 96.8% were found positive with soil-transmitted helminth eggs. *Trichuris* infection had the highest prevalence of 87.8%. Hookworm infection was 68.7% and *Ascaris* infection was 27.3%.

Table 1 summarizes the results of stool examination on the 30th day after the last treatment of both groups according to degree of *Trichuris* infection. Comparing the two regimens with equal degrees of infection revealed that the three-day regimen gave higher cure rates. In the single dose regimen, cure occurred in light infection cases only.

**Table 1.** Cure rates and egg reduction rates of *Trichuris trichiura* infection with albendazole, determined 30 days after treatment.

Regime	Intensity (median epg*)	No. treated	No. cured	Cure rate	Egg Reduction rate
Multiple dose					
(400mg x3)	Light (351)	45	19	42.2	71.8
	Moderate (2,465)	31	11	35.5	86.4
	Heavy (16,045)	10	4	40.0	78.3
	Total	86	34	39.5	78.8
Single dose					
(400mg)	Light (284)	10	3	30.0	43.2
	Moderate (2,992)	9	0	0	67.2
	Heavy (31,826)	2	0	0	72.2
	Total	21	3	14.3	60.9

\*epg = egg per gm of faeces

Of the children who regularly submitted stool samples for this study, the average number of worms per person per day recovered from 24-hour stool specimens collected from the 1<sup>st</sup> to the 7<sup>th</sup> day after the first dose of treatment showed that the maximum number of worms were expelled on the 4<sup>th</sup> day for the group treated with the three-day regimen. In the group treated with the single dose regimen, the highest number of worms appeared on either the 3<sup>rd</sup> or the 4<sup>th</sup> day after treatment. For both regimens the total numbers of worms expelled were agreeable with the clas-

sified intensity. The maximum numbers of worms were expelled in the heavy infections and the smallest numbers in the light infections (Fig. 1).

Of the cured children who submitted 24-hour stool specimens for seven days after treatment, the number of expelled worms per person was summarized according to pretreatment intensity, and the male to female median ratio was 1:2 (Table 2). Eggs per female worm per gramme of faeces (EPFPG) increased with the intensity (Table 3). The computed interquartile

range of EPFPG suggested that 50% of the female worms in light infection cases laid about 70-200 epg, moderate infection cases laid about 460-

1,300 epg and heavy infection cases laid about 800-2,000 epg. The overall range was 100-800 epg.

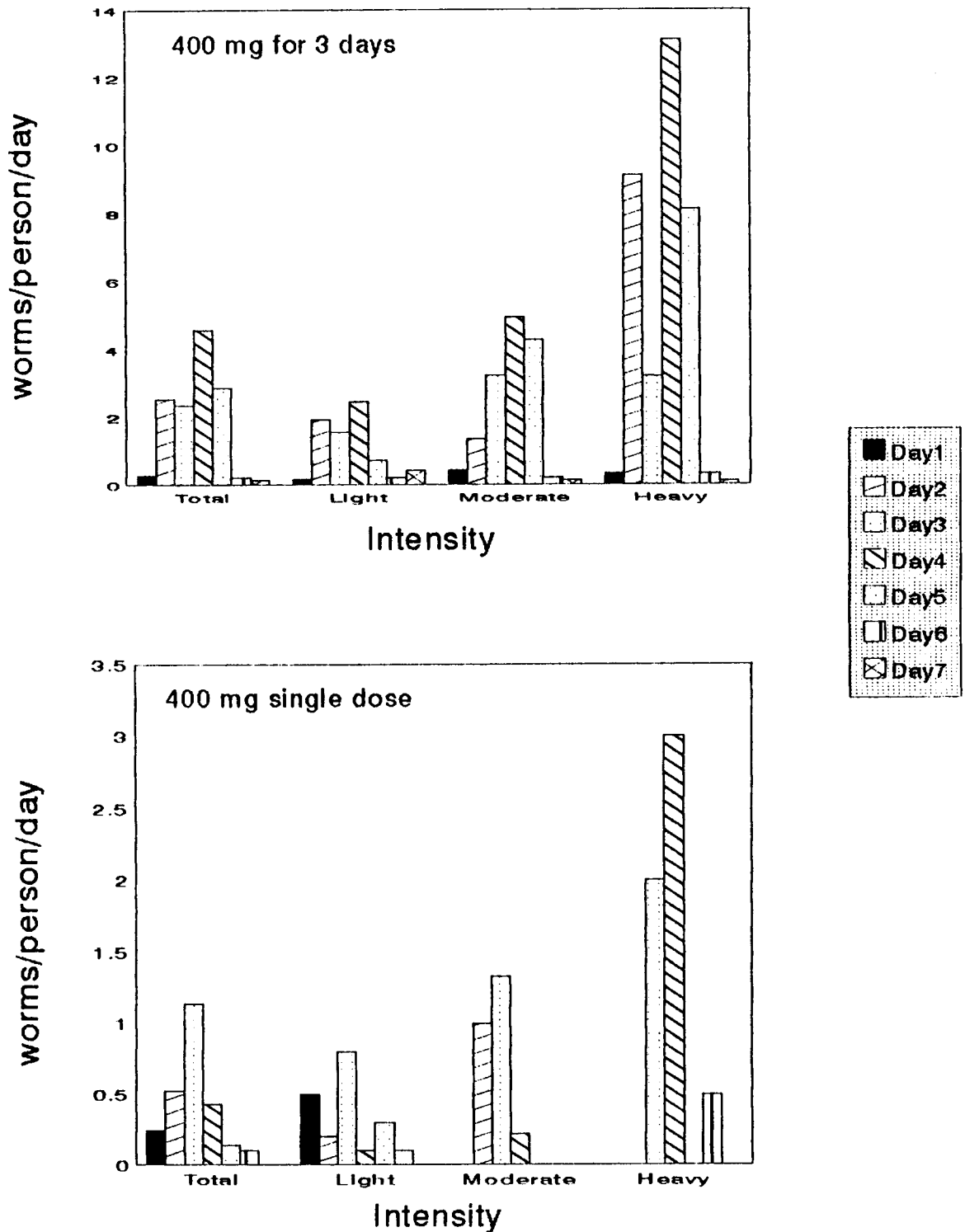


Figure 1. *Trichuris trichiura* worm expelled with two regimens of albendazole grouping by its intensity of infections

**Table 2.** Number and sex ratio of *Trichuris trichiura* worm expelled from cure cases who submitted 24 hours stool for 7 days after treatment with both regimes of albendazole.

Intensity	No. cured case	worm per case range	Male worm per case median (range)	Female worm per case median (range)	Sex ratio M:F (median)
Light	21	1-9	1(0-4)	2(1-5)	1 : 2
Moderate	11	1-21	2(0-7)	3(1-14)	1 : 1.5
Heavy	3	15-32	11(8-12)	13(7-20)	1 : 1.2
Total	35	1-32	1(0-12)	2(1-20)	1 : 2

**Table 3.** Egg per female worm per gram of faeces (EPFPG) of *Trichuris trichiura* calculated from the data of cured cases who submitted 24 hours stool for 7 days after treatment with both regimes of albendazole.

Intensity	Number cured case	expelled female worm/person (range)	EPFPG median (range)	EPFPG interquartile range
Light	21	1-5	122 (27-459)	71-208
Moderate	11	1-14	824 (98-2,039)	467-1,330
Heavy	3	7-20	1,112 (777-2,012)	777-2,012
Total	35	1-20	229 (27-2,039)	94-782

## Discussion

This study was conducted at the school in the endemic area where prevalence of Trichuriasis was high. At the beginning of the study, children in both groups of treatment were equal in number. But unfortunately, drop out rate of children in single dose regimen was higher than

in multiple dose. The children in moderate and heavy infection of single dose regime were very few and the result may not represent the real value of the anthelmintic efficacy.

Based on the results of the faecal examinations carried out on the 30th day after the treatment, in light infection cases a similar cure



rate was observed from both regimens. But in higher intensities the cure was observed in the multiple dose regimen only. The cure rates of this study were lower than the results obtained by Rossignol and Maisonneuve (1983),<sup>(1)</sup> Bundy *et al.* (1985 a)<sup>(5)</sup> and Setasuban *et al.* (1991),<sup>(6)</sup> but more or less agreed with the results of Ow-Yang and Hanjeet (1986).<sup>(9)</sup>

Egg reduction rates (ERR) of this study were also lower than in the other studies mentioned above, and multiple doses induced higher ERR than single doses.

Expelled worms were analysed from the children who were both completely submitted faecal sample the whole seven day period of collection and 30th day post treatment faeces free of *Trichuris* egg.

Comparing worm expulsion between single and multiple dose regimens showed that the single dose gave lower numbers of worms expelled, a little shorter period of expulsion (6 days) and on irregular expulsion pattern. The highest number of worms appeared on day 3 in light and moderate infection cases and day 4 in heavy infection cases. The worms were not expelled every day during the collecting period as in the first and second day in heavy infection cases. In the multiple dose regimen, worms were expelled every day during the 7 days of collection, and the maximum number of worms were expelled on day 4 in all intensities.

Bundy *et al.* (1985 a)<sup>(5)</sup> reported that single and double doses of albendazole gave the same result in expelling worms, but our study showed a marked difference between single and triple doses, especially in moderate and heavy infection cases.

The sex ratio of *T. trichiura* in this study was in the range of previous studies summarized by Bundy *et al.* (1985 b).<sup>(10)</sup> The overall EPFPG range in this study was very wide, 50% of the central tendency was between 100-800 epg while the median EPFPG of worms classified in light infection cases was in the lower range, the moderate infection in the EPFPG was higher than the interquartile value. Though the number of worms expelled increased with the intensity of infection, they were not markedly different. It seemed that the intensity of infection classify in this study was influenced by the egg laying capacity of the individual females aggregated in the person. Calculated from the overall EPFPG range (Table 3), one of the highest capacity female laid eggs per gram equal to 75 females of the lowest capacity. The infections with the same actual worm loads may be classified in differently intensity according to the capacity of female worms. This phenomenon indicates that the classification of egg intensity of *Trichuris* infection should be readjusted, and further studies on actual worm load and EPFPG are still needed.

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