



**PEDIATRIC INFECTIOUS
DISEASE SOCIETY OF THE
PHILIPPINES**

PIDSP JOURNAL

**Vol.10 No.1
January-June 2010**

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**Vol.11 No.1
January-June 2010**

The Antihelminthic Efficacy Of Pineapple Fruit Mebendazole On Soil Transmitted Helminthiases: A Randomized Controlled Trial

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KEYWORDS

pineapple, ascariasis, trichuris, antihelminthic

ABSTRACT

Objectives: The study was performed in order compare the antihelminthic efficacy of pineapple fruit versus mebendazole in schoolchildren.

Design: The study performed was a single, blinded randomized control trial.

Subjects: Ninety subjects aged 5 to 13 years old and positive for soil-transmitted helminthiases were included in the study.

Methods: Eligible participants were subjected to Kato-Katz for diagnosis and quantitative ova count. Those positive for soil-transmitted helminthes were randomized to Group A (pineapple) and Group B (mebendazole). After 7 days of treatment, stool samples were subjected to another Kato Katz for quantitative ova analysis. Seven hundred fifty ml of puree made from one pineapple, with approximate weight of 750g, was given in divided amounts within 24 hours (250 ml 3x a day) for group A.

Results: Majority (77.78%) were infected with *Ascaris lumbricoides*. Pineapple exhibited a significant improvement in egg reduction rate (RR) with a p-value of < 0.001 at 95% CI. This showed 83.5 % egg per gram (epg) of feces reduction and a cure rate of 68.9%. Mebendazole also revealed a significant egg reduction with p-value of < 0.001 at 95% CI. It also showed a remarkable egg per gram reduction rate of 92.25% and cure rate of 88.9%. There were no adverse events reported.

Conclusion: Mebendazole, as an antihelminthic, is a better choice; but pineapple fruit may be beneficial as it had a high egg reduction rate and an acceptable cure rate.

INTRODUCTION

Intestinal parasitism is an important problem in third world countries, including the Philippines. Many studies have been made regarding the incidence of intestinal parasitism. As early as 1963, out of the 169 children examined for parasitism in Caloocan City, 98% of the isolates were *ascaris lumbricoides*, 65% *Trichuris trichuria*, 4% hookworm, and 1% *Giardia lamblia*.⁷ Other studies showed that out of 781 children, 85.1% were *ascaris*, 27.9% were *trichuris*, and 34.4% hookworm. It was also noted that among double parasitism, the most common was the combination of *ascaris* and *trichuris*.⁸

A study was conducted in 40 subjects on the comparison of pineapple and pyrantel pamoate on the treatment of ascariasis. Cure rate was 55% for the pineapple group and 70% for the pyrantel pamoate group.²⁴

OBJECTIVES

The objective of this study is to compare the anti-helminthic efficacy of Pineapple Fruit to Mebendazole among children aged 5 to 13 years old in a community setting. Safety of both regimens will also be investigated.

MATERIALS AND METHODS

Study Design

The study is a single, blinded, Randomized Controlled Trial.

Study Population

Children ages 5 to 13 years old, regardless of sex, who would meet the following criteria: positive of soil-transmitted helminthiasis, e.g. *Ascaris lumbricoides*, *Trichuris trichuria*, and other helminths on the preliminary Kato-Katz; had a normal physical examination prior to the conduct of the study, and those whose parents gave consent for their children to be included in the study.

Patients were excluded if: they had anti-helminthic therapy 2 weeks prior to and during the study period; had a concomitant infection at the time of the study, e.g. cough, colds, fever, diarrhea; had passage of worms 2 weeks

prior to conduct of the study; or had a known allergy to pineapple and/or mebendazole.

Sample Size Calculation

Sample size was computed based on the cure rate of mebendazole at 90%¹⁰ and pineapple at 59.36%. Using the Epi Info version 6, with confidence level of 95% and a power of 80%, 74 participants comprised the sample population. An additional 20% was allocated for drop-outs, thus 90 participants comprised the final sample population at 45 per group.

Treatment Assignment and Randomization

Using a computer generated-randomization list, eligible participants were assigned to either the experimental group or the treatment group. The experimental group was designated as group A and was given pineapple. The treatment group was designated as Group B and given mebendazole.

Study Procedures and Activities

All children, whose parents consented, were personally interviewed and examined by the investigator. Age in years, weight in kilograms, and height in centimeters were determined. History of illnesses and other symptoms, intake of antihelminthic drugs, previous history of passage of worms, and allergies to food and medications were asked. Complete physical examinations were also performed. All these data were documented on standardized data collection forms. Eligible participants were subjected to Kato-Katz for diagnosis and quantitative ova count. In addition, participants were classified as to light, moderate, or heavy parasitic infestation according to WHO classification. These procedures were done until the required sample size was reached.

All children positive for *Ascaris lumbricoides*, *Trichuris trichuria*, and other soil-transmitted helminths on Kato-Katz were randomized either to Group A or Group B. After 7 days of treatment, stool samples were again collected from the participants and were coded and subjected to another Kato Katz for quantitative ova analysis. The same medical technologist who did the preliminary Kato Katz

handled the second stool analysis; he was blinded as to which group the stool sample came from.

Fecal Sample Handling and Analysis

Each participant was given sterilized, standard stool specimen containers. Stool samples collected from the participants were subjected to Kato-Katz within one hour of collection.

Study Intervention and Administration

One peeled pineapple, weighing approximately 750 grams, prepared as blended fruit puree was given to each participant in Group A. 750 ml of the puree, sweetened with two tablespoons of sugar, was given to each to be consumed in an entire day. On the other hand, 500 mg mebendazole chewable tablets were given in single doses to each participant in group B. The administration of both interventions was supervised by the investigator to ensure compliance and proper administration.

Study Outcome Measures

Kato-Katz, via microscopy by a trained medical technologist, was used to quantify the number of eggs per sample. The intensity of the helminth infection is defined as eggs per gram (epg) of feces according to the WHO classification. Cure is defined as zero or no ova seen on repeat Kato-Katz after intake of pineapple or administration of mebendazole. In addition, cure rate is defined as the difference in the prevalence rates for each helminth between pre- and post-treatment and is expressed as percentage of the pre-treatment value. The egg reduction rate is expressed as the percentage fall in arithmetic mean egg counts.³¹ These were used to determine whether pineapple fruit is comparable with mebendazole.

All those who had treatment failure in the pineapple group were given the recommended drug, 500 mg of mebendazole chewable tablet as single dose.

Side effects for both the pineapple fruit and mebendazole were also noted. All symptoms

noted by the mother to the child after treatment will be enumerated.

Data Analysis

Data were encoded and an analysis was done on them using SPSS. A paired t-test was used to compare the quantitative ova counts before and after treatment. Logistic regression analysis was used to determine the relationship between the baseline age, weight, height, pre-treatment ova count and the reduction and cure rate of both pineapple and mebendazole.

Outcomes were computed as follows:

$$\text{Cure Rate} = \frac{\text{Number of Subjects Cured}}{\text{Number of Subjects Treated}} \times 100$$

$$\text{Egg per Gram (epg) Reduction Rate} = \frac{\text{Mean egg before treatment} - \text{Mean egg after treatment}}{\text{Mean egg before treatment}} \times 100$$

$$\text{Mean epg} = \frac{\sum \text{epg}}{N}$$

$\sum \text{epg}$ is the sum of each individual epg and is divided by n , the number of subjects treated.

Adverse effects Monitoring

Adverse reactions to both the drug and pineapple were monitored by direct observation by the author during and after administering mebendazole and pineapple. Parents were also advised to report and contact the investigator if any untoward symptoms were noted after the procedures until the time that the second specimen was collected.

Ethical Considerations

This study was performed in accordance with the Principles stated in the Declaration of Helsinki. The Informed Consent form and Information sheet were reviewed and approved by the Bioethics Committee of the De La Salle University Medical Center.

The investigator coordinated with the members of the community to present the study and get an approval. A meeting with the barangay health workers, barangay officials and parents was done to explain the study and all

its procedures. The adverse effects which may be encountered, the persons and hospital where they could seek medical attention was explained to the parents and the members of the community. A permit was secured from the municipal mayor and municipal health officer prior to the conduct of the study.

On the screening visit (Day 0), informed consent was obtained from the parents or guardian.

RESULTS

Demographic and Clinical Characteristics

Table 1 shows that there were significant differences in some clinical characteristics of the subjects in the two treatment groups. Mean weight and height were significantly lower and mean pre-treatment ova count was significantly higher in the control group compared to the pineapple group.

Most of the subjects in the pineapple group had no wasting or had mild wasting (31.10 %). On the other hand, the mebendazole group is mostly composed of subjects with no wasting (35.60%). Most of the subjects have mild stunting on both the pineapple and mebendazole group with 53.30 % and 57.80 %, respectively (Table 2).

Among the 102 stool samples examined, 90 were positive for helminths. *Ascaris lumbricoides* was the most common helminth infection upon enrollment in the study. All infections were of light intensity according to the WHO classification. Majority had single infection and 2.22% had mixed infections. *Ascaris lumbricoides* and *Trichuris trichuria* is the only dual infection noted among those who had mixed infection at 2.22%.

Moreover, among those treated with pineapple, *Ascaris lumbricoides* was the most common cause of single infection (73.33%). A similar observation was noted in the mebendazole group. No hookworm was noted as a cause of single infection.

Study Outcome Measures

Ova Count

Before the administration of medications both groups had a significant difference in terms of ova count. However, after treatment the ova counts were significantly reduced (Table 4).

Table 1. Baseline Characteristics of the Subjects.

	Pineapple (n = 45)	Mebendazole (n = 45)	p value
Sex n (%)			
Male	22 (48.9%)	15 (33.3%)	0.135
Female	23 (51.1%)	30 (66.7%)	
Age			
Mean \pm SD ¹	8.7333 \pm 2.10411	7.0444 \pm 2.64537	0.098
Weight			
Mean \pm SD	21.1111 \pm 4.71931	18.5667 \pm 6.64773	0.019
Height			
Mean \pm SD	120.1333 \pm 11.37301	107.0667 \pm 21.91450	0.013
Pre Treatment Ova Count Mean \pm SD	4.4222 \pm 1.49983	6.3778 \pm 3.32545	0.001

¹ Standard Deviation

Table 2. Clinical Characteristics of the Subjects.

Clinical	Pineapple (n = 45)	Mebendazole (n = 45)
Wasting according to Waterlowes Classification		
Normal	14 (31.10%)	16 (35.60%)
Mild	14 (31.10%)	15 (33.30%)
Moderate	11 (24.40%)	10 (22.20%)
Severe	6 (13.30%)	4 (8.900%)
Total	45 (100%)	45 (100%)
Stunting according to Waterlowes Classification:		
Normal	10 (22.00%)	10 (22.20%)
Mild	24 (53.30%)	26 (57.80%)
Moderate	9 (20.00%)	3 (6.700%)
Severe	2 (4.400%)	6 (13.30%)
Total	45 (100%)	45 (100%)

Table 3. Parasites Found According to the WHO Classification on Intensity of Helminthiasis On Baseline Kato-Katz.

Intensity of Infection	Parasite	Pineapple N = 45 (%)	Mebendazole N= 45 (%)	Total N (%)
Light	Ascaris (As)	33 (73.33%)	37 (82.22%)	70 (77.78%)
	Trichuris (Tr)	11 (24.44%)	7 (15.56%)	18 (20.0%)
	As and Tr	1 (2.22%)	1 (2.22%)	2 (2.22%)
Moderate	Ascaris	0	0	0
	Trichuris trichuria	0	0	0
	As and Tr	0	0	0
	As, Tr and Hookworm	0	0	0
Heavy	Ascaris	0	0	0
	Trichuris	0	0	0
	As and Tr	0	0	0
	As, Tr and Hookworm	0	0	0
TOTAL		(100%)	(100%)	(100%)

Table 4. Comparison of the Ova Count before and After Administration of Medication.

	Pineapple	Mebendazole	P Value	95% CI
Before Treatment Mean \pm SD	4.4222 \pm 1.49983	6.3778 \pm 3.32545	0.001	-3.03627 – -0.87484
After Treatment Mean \pm SD	0.6444 \pm 1.04785	0.2889 \pm 0.92004	0.091	-0.05754- 0.76865

Table 5. Comparison of the Ova Count In Terms of the Treatment Group before and After Administration of Medication.

Treatment Group	Before Treatment	After Treatment	P value	95% CI
Pineapple Mean \pm SD	4.4222 \pm 1.49983	0.6444 \pm 1.04785	< 0.001	3.20170 – 4.35386
Mebendazole Mean \pm SD	6.3778 \pm 3.32545	0.2889 \pm 0.92004	< 0.001	5.01551 – 7.16227

There was significant ova reduction in each of the treatment groups. Both pineapple and mebendazole had p values of less than 0.001 and with a 95% confidence interval. (Table 5).

Reduction and Cure Rates

There was a cure rate of 68.9 % for pineapple fruit as compared to 88.9% for mebendazole. In terms of the egg per gram of feces, there was a reduction rate of 83.52 % for pineapple and 92.3 % for mebendazole (Table 6). No adverse effects were noted for any of the treatment groups.

Table 6. The Efficacy Measures of Pineapple Fruit and Mebendazole.

Treatment	Cure Rate	epg ¹ reduction rate
Pineapple	68.9%	83.52%
Mebendazole	88.9%	92.3%

¹eggs per gram of feces

Table 7 shows that the significant difference in the baseline data (age, weight, height, and pre treatment ova count) did not affect the reduction and cure rates of both pineapple and mebendazole.

Table 7. Logistic Regression Analysis of the Factors associated with the reduction and cure rates of pineapple fruit and mebendazole.

VARIABLES	SLOPE B	SIG P VALUE
Ova Count	.137	.371
Group2	- 1.466	.059
Age	0.048	.858
Weight	.322	.100
Height	-.071	.286
Constant	3.125	0.027

Adverse Effects Monitoring

None of the parents or subjects complained of any problems related to the administration of both the medicine and the fruit.

DISCUSSION

Demographic and Clinical Characteristics

Based on the Waterlowes' classification on wasting and stunting, most of the participants included in this study had normal to mild wasting and with mild stunting. In a study done in 2001 by Andrade, et. al., mean age was noted at 8.9 years old; children included in his study were below the third percentile and were noted to be stunted and wasted.³²

Majority of the children included in the study were infected with *Ascaris lumbricoides* only, followed by *Trichuris trichuria*. If combined, *Ascaris* and *Trichuris* was the most common co infection. Same results were noted by Akbar, et. al. with regard to frequency of ascaris and trichuris infestation.³³ A study done in Zamboanga (2004) revealed that the most prevalent parasite was *Ascaris lumbricoides*.³⁴

All parasitic infections noted in this study were of light intensity according to the WHO classification. A study by Albonico likewise noted that most of the children included in his study had light helminth infestation.³⁵

The baseline, clinical characteristics of weight, height, and pretreatment ova count were significantly different in the two groups. This implies that randomization was not able to distribute these known variables, more or less, equally to the two groups; thus there is a possibility that the outcomes could be affected by bias. However, statistical analysis revealed that these factors did not affect the reduction and cure rate in both groups.

Recently, a study was conducted on the comparison of pineapple and pyrantel pamoate on the treatment of ascariasis. Said study used 3 slices of pineapple, 2 centimeters thick, to be eaten after meals and for 7 days; this was compared to a single dose of pyrantel pamoate at 11 mg/kg/dose. The efficacy was measured by comparing the cure rates: it is a complete cure if the stool exam turned out negative or if there is a reduction rate of >50% after one week of treatment. The results of the stool exam showed that one week of treatment noted a 55% complete cure for pineapple fruit

and a 70% cure rate for pyrantel pamoate. However, the study was limited to 40 subjects.²⁴

For this study, both treatment groups had significant improvements in the reduction of ova count after 7 days of treatment. Moreover, in each of the treatment groups, pineapple fruit had a notable egg reduction rate of 83.52%, 7 days after its administration. These findings are also noted in the study of Adriano, which claimed an egg reduction rate of greater than 50% in 17 out of 20 subjects.²⁵ In other studies, pineapple leaves were also used—noting a dramatic reduced egg counts of greater than 90% after 10 days of administration.⁶ However, it is to be noted that the reduction rate in this study is based only on light infection according to WHO classification.

On the other hand, mebendazole has an egg reduction rate of 92.25% after 7 days of its administration. A high egg reduction rate of 99.1 % with mebendazole was likewise noted by Albonico in 1994.³⁵

In another study conducted by Legese, et. al.³⁶, mebendazole was shown to have a cure rate of 96%. According to the WHO, mebendazole has a cure rate of 60% to 89 % against *Trichuris*, and more than 90 % cure rate for *Ascaris*.³⁷

No adverse events or complications were noted in both treatment groups, which implied that both interventions were well tolerated and safe.

Active Ingredients in Pineapple

Pineapples have proteolytic enzyme—bromelain, that aids in digestion.²² In 1989 at MCU Manila, isolation of the enzyme bromelain from pineapple fruit was made. This study noted that the percent yield of bromelain from pineapple juice was 0.1965%. The anti-helminthic products, which were compounded in the form of suspension gave an acceptable quality when used to kill the ascaris worms.²³ However, this study did not mention whether the pineapple juice used was commercially made or was fresh. Another study was done in

UPLB on the anti-helminthic property of pineapple. In this study, pineapple leaves were used; it demonstrated reduced egg counts in nematode-infected cattle. The egg count reduction after 10 days was as good as 90%, compared to the control group treatment, which was a broad spectrum commercial product.⁶

Bromelain's primary component is sulfhydryl proteolytic fraction. It also contains peroxidase, acid phosphatase, and several protease inhibitors. It is not heat-stable and it exhibits its activity over a pH range of 4.5 to 9.8.²⁶

Bromelain has a very low toxicity, with an LD50 greater than 10g/kg body weight. Dosages of 1.5g/kg/day administered to rats showed no carcinogenic or teratogenic effect.²⁷ In humans, side effects have not been observed. Dosage of up to 460 mg revealed no effect on heart rate or blood pressure. However, in doses above 700mg, palpitations and subjective discomfort have been reported.²⁸ It is also a potential allergen particularly in IgE-mediated respiratory allergies.²⁹ It has been shown to have therapeutic benefits in doses of as low as 160mg/day and had best results when given in doses above 500mg/day.

CONCLUSIONS

This study shows that the mean age of parasitism in children was 8 years old; with normal to mild wasting and with mild stunting: all infections were of light intensity according to the WHO classification. Of the 90 infected subjects, 97.78 % were singly infected with *Ascaris lumbricoides*, 2.22 % had mixed infections of *Ascaris lumbricoides* and *Trichuris trichuria*. The cure rate of pineapple fruit is 68.9 % as compared to 88.9% for mebendazole. In terms of the egg per gram of feces, there is a reduction rate of 83.5 % and 92.25 % for pineapple and mebendazole, respectively. No adverse effects were noted after administration of both pineapple and mebendazole.

Mebendazole is a better choice as an antihelminthic drug because it is more efficacious. However, the pineapple fruit may also be beneficial since it has a relatively high egg reduction rate and an acceptable cure rate.

RECOMMENDATIONS

The following recommendations are made to improve the results in terms of cure rate and egg reduction rate:

1. To obtain the Bromelain content of one pineapple fruit for proper dosaging.
2. To use different preparations and dosages of pineapple fruit to obtain better cure rate and reduction rate.
3. To apply pineapple fruit to subjects with moderate to heavy intensity for a better assessment of its antihelminthic property.

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