

A Randomized, Double-Blinded Parallel-Controlled Clinical Trial On the Effectiveness of Different Doses of *Moringa oleifera* (Malunggay) in Promoting Growth in Infants of Breastfeeding Mothers from UERMMMCC and Different Hospitals In Metro Manila from June 2000 to January 2001

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Abstract

Malunggay (Moringa oleifera) leaves have long been used in the Philippines as a galactagogue. A controlled, randomized, double-blind study was done to determine the optimum dose of Natalac capsules consisting of 250 mg of dried malunggay leaves. These capsules were given to 60 nursing Filipino mothers for 2 months in an attempt to increase the amount of breast milk.

Sixty Filipino mothers and their newborns were randomly assigned to four trial groups. Within a two-month trial period, group A mothers were given one Natalac capsule OD, group B mothers were given one Natalac capsule BID, group C mothers were given one placebo capsule OD, while group D mothers were given one placebo capsule BID. Increases in both length and weight were obtained every two weeks and compared. An increase of twenty-five percent in length and weight of the newborns were obtained every two weeks and comparisons among the four trial groups were done.

The study found significant increases in the weight and length for both OD and BID Natalac treatment groups. Additional findings showed that BID Natalac significantly improved lactation over OD Natalac group and OD and BID placebo within a study period of eight weeks.

Introduction

Breast-feeding is the best way to feed a newborn (Del Mundo 1990). It is highly recommended by the World Health Organization and the United Nations International Children's Educational Fund for infants until 6 months.

Breast milk contains the right amount of fatty acids, lactose, water and amino acids for human digestion, brain development and growth (Advincula-Diaz et al 1997).

Despite many programs that promote breast-feeding, most infants are given complementary and weaning food before the third month. Even as much as 75% of infants are introduced to weaning food as early as the second month (Yambao et al 1995). Insufficient milk and work are the primary reasons for

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terminating breast-feeding within the first six months (Llanto et al 1991; Mukasa 1992; Yambao et al 1995). Mothers feel their infants need more food and nutrients under the perception that they produce very little milk. Visness and Kennedy (1997) cite that while full-time work has no effect on initiating breast-feeding, it has significant effects on its duration.

Malunggay (*Moringa oleifera*) leaves have long been used in the Philippines as a galactagogue. So far, no adverse effects have been documented in humans. Encapsulated malunggay leaves, in the form of Natalac, have been shown to effectively increase serum prolactin of mothers and percent weight gain of infants (Almirante and Lim, 1996). While Natalac improves lactation, its mechanism of action and most effective dosage has yet to be determined.

Increases in length and weight are attributed to the adequacy of the newborn's nutrition within the first six months. Only after the first six months do genetic factors which determine ultimate height begin to exert their effect (CMDT 1997). In this clinical trial, infants will be fed solely breast milk. Thus, increases in both length and weight may reflect the amount of breast milk the infant receives.

Improving lactation means more available appropriate nutrition for infants. This eliminates the need for milk supplements.

Fewer hospital admissions, cases of ear infection, diarrhea, rash and allergies have been observed in breast-fed babies (Duncan et al 1993). Improved health and decreased morbidity of the newborn would benefit both mother and baby, in light of the increasing cost of health care (Advincula-Diaz et al 1997).

This study aims to determine the effective dosage of encapsulated malunggay leaves. The weight gain and length increase of infants breast-fed by mothers taking Natalac OD and BID, and placebos will be compared.

Methodology

This was a parallel controlled clinical trial of the effective dosage of Natalac, a 250-mg preparation of malunggay leaves, as a galactagogue from June 2000 to January 2001. Respondents from the UERMMMC, Sabater Hospital, De Los Santos Medical Center, and other hospitals were recruited.

Using the Schlesselman's method, a total of 60 Filipino women and their newborns were recruited under several selection criteria. These were 1) that the mothers agreed not to feed their infants any milk formula for 2 months starting from date of birth; 2) that the infants would not be given solid or semi-solid food for the duration of the study; 3) that the infants were healthy, 38-42 weeks AOG, weighed 2500-5000 grams, and not suffering from any illness at birth; 4) that the mothers were not suffering from any illness (i.e. toxemia, hyperthyroidism, diabetes) during gestation and within the duration of the study; 5) that the mothers were nonsmokers and non-alcoholics; and 6) that the mothers did not take any medications during gestation that could affect fetal growth and development.

The mothers were instructed not to feed their infants any milk formula, semi-solid, and solid food during the trial. Their compliance to the regimen was evaluated during each follow-up through a questionnaire.

The doctor and students who took measurements were blinded as to the contents

of the capsules for each trial group, and as to which trial group the respondents belonged. Procedures for obtaining measurements were standardized and measuring instruments were calibrated at each session.

Results of the study were subjected to statistical tests to determine significance. A twenty-five percent increase in length and weight were considered significant as indirect measures of increased milk production. The Wilcoxon Rank Sum Test and the Kruskal-Wallis Test were then used in comparing the significance of the results.

Results

Table 1. describes the sample population based on the parity, manner of delivery, educational attainment, age, employment status,

Table 1. Demographic characteristics of the sample population

Characteristic	Count (%)
Parity	Primipara 30 (50%)
	Multipara 30 (50%)
Manner of Delivery	NSD 41 (68%)
	CS 19 (32%)
Educational Attainment of Mother	College Graduate 36 (60%)
	High school graduate 20 (33%)
	Elementary 2 (3%)
	NA 2 (3%)
Age of Mother	19-24 19 (32%)
	25-30 24 (40%)
	31-37 13 (22%)
	38-43 4 (7%)
Employment Status of Mother	Working 25 (42%)
	Unemployed 35 (58%)
History of Breastfeeding	Yes 25 (42%)
	No 35 (58%)
Average Monthly Family Income	P50-550 24 (40%)
	P600-1000 17 (29%)
	NA 19 (32%)
Vitamin Intake of Mother	Yes 48 (80%)
	No 8 (13%)
	Antibiotics 4 (7%)

history of breastfeeding, average monthly income and vitamin supplement intake of mothers. The median age of the sample population is 27 years old and the mode is 33 years old. Majority of the respondents had normal spontaneous delivery, were college graduates, unemployed, without history of breastfeeding, have average monthly incomes below P600 and are taking vitamin supplements.

The four study groups are compared according to average monthly income of the family in Table 2.

In all study groups, the percentage of families with a monthly income of P600 to P1000 was lower than those of mothers with lower than P50-P550.

Table 2. Comparison of Treatment Groups According to Average Monthly Family Income

Treatment	Average Monthly Family Income		
	P50-550	P600-1000	NA
OD Natalac	Row% 44.4	38.9	16.7
BID Natalac	Row% 35.7	21.4	42.9
OD Placebo	Row% 38.5	25.1	38.5
BID Placebo	Row% 40.0	26.7	33.3

Table 3 shows mean percent weight gain of infants in the OD groups. This table shows that the percent weight gain from birth until 8 weeks is larger in patients' whose mothers are taking Natalac, with the biggest difference between treatment and placebo at 8th week. Wilcoxon Rank Sum Test Comparing OD Placebo and OD Natalac Groups revealed that the percent weight gain of patients receiving OD dose of Natalac are significantly greater than placebo from 6 to 8 weeks.

Table 3. Weight mean percentage of infants who are in the OD Groups

	Treatment	Placebo	Difference	Wilcoxon
Birth to 2 Weeks	20.20	19.46	0.74	$\mu=120, cv=75, NS$
Birth to 4 Weeks	51.29	42.83	8.46	$\mu=80, cv=50, NS$
Birth to 6 Weeks	91.01	65.61	25.40	$\mu=37, cv=77, S$
Birth to 8 Weeks	134.95	93.50	41.80	$\mu=30, cv=31, S$

Table 4 shows that the percent length increase in the OD groups of infants in the Treatment Group is bigger than that in the Placebo Group. Wilcoxon Rank Sum Test showed no significant difference between the Treatment and the Placebo Group, receiving OD dosages, except in the 2nd week.

Table 4. Mean percent length increase of infants who are in the OD Groups

	Treatment	Placebo	Difference	Wilcoxon
Birth to 2 Weeks	3.24	2.65	0.59	$\mu=74, cv=75, S$
Birth to 4 Weeks	6.49	6.07	0.42	$\mu=55, cv=50, NS$
Birth to 6 Weeks	10.06	8.90	1.15	$\mu=40, cv=34, NS$
Birth to 8 Weeks	12.38	11.95	0.43	$\mu=44.5, cv=31, NS$

Table 5 shows that the mean percent weight gain of infants in the BID Groups is greater in the Treatment than in the Placebo Group. The BID Natalac Group is significantly higher than the BID Placebo Group based on the Wilcoxon Rank Sum Test.

Table 5. Mean percent weight gain of infants who are in the BID groups.

	Treatment	Placebo	Difference	Wilcoxon
Birth to 2 Weeks	27.35	18.35	9.0	$\mu=78, cv=66, NS$
Birth to 4 Weeks	72.22	44.56	27.62	$\mu=47, cv=61, S$
Birth to 6 Weeks	120.94	75.36	45.58	$\mu=40, cv=51, S$
Birth to 8 Weeks	156.46	110.41	46.05	$\mu=30, cv=47, S$

Table 6 shows that among the BID groups, the percent length increase of infants in the Treatment Group is larger than that in the Placebo Group. Wilcoxon Rank Sum Test shows that the BID Natalac is statistically higher than BID Placebo in all four measurements.

Table 6. Mean percent length increase of infants who are in the BID groups

	Treatment	Placebo	Difference	Wilcoxon
Birth to 2 Weeks	3.24	2.65	0.59	$\mu=74, cv=75, S$
Birth to 4 Weeks	6.49	6.07	0.42	$\mu=55, cv=50, NS$
Birth to 6 Weeks	10.06	8.90	1.15	$\mu=40, cv=34, NS$

Table 7 compares the differences between the Treatment and Placebo Groups in the different dosage regimens. Treatment and Placebo Groups in the different dosage regimens.

The results of the Kruskal-Wallis Test comparing the four study groups based on percent weight gain and length increase are presented in Table 8.

Table 7a. Mean percent weight gain difference between treatment and placebo groups

	OD	BID	Difference
Birth to 2 Weeks	0.74	9.0	8.26
Birth to 4 Weeks	8.46	27.62	19.16
Birth to 6 Weeks	25.40	45.58	20.18
Birth to 8 Weeks	41.80	46.05	4.25

Table 7b. Mean percent length increase between treatment and placebo groups

	OD	BID	Difference
Birth to 2 Weeks	0.59	0.83	0.24
Birth to 4 Weeks	0.42	3.20	2.78
Birth to 6 Weeks	1.15	6.21	5.06
Birth to 8 Weeks	0.43	8.25	7.82

Table 8a shows that the percent weight gain from birth to 2 weeks of the four treatment groups were similar, while the rest was statistically significant at 95% level of confidence.

Percent length increases of the four study groups are significantly varied at 95% level of confidence, as shown by Table 8b, from 2 weeks to 8 weeks.

Table 8a. Kruskal-Wallis Test of percent weight gain, and length increase of the four Treatment Groups

	p value*
Birth to 2 Weeks	0.599
Birth to 4 Weeks	0.042
Birth to 6 Weeks	0.028
Birth to 8 Weeks	0.071

*The null hypothesis that the four study groups are equal, is rejected if the p value is less than 0.05.

Table 8b. Kruskal-Wallis Test of length increase of the four Treatment Groups

	pvalue*
Birth to 2 Weeks	0.003
Birth to 4 Weeks	0.000
Birth to 6 Weeks	0.000
Birth to 8 Weeks	0.000

*The null hypothesis that the four study groups are equal, is rejected if the p value is less than 0.05.

Discussion

The study population has a small sample size (Appendix A) that does not result in a normal frequency distribution; hence, non-parametric tests, such as Kruskal-Wallis and Wilcoxon Rank Sum Test were used. Comparability of the four study groups were determined and are presented in Appendix B.

In one month, the average weight increase in the OD Natalac Group is 59.29%, while that in BID is 72.22%.

Kruskal-Wallis Test was used to analyze if the four study groups have the equivalent percent weight increase and length gain. Since the study groups were found to be unequal at 95% level of significance, we must see which

study group results in the highest percent increase in weight and length of infants.

Wilcoxon Rank Sum Test allows comparison of study groups, two at a time. Using this statistical test we can determine if OD Natalac or BID Natalac results in higher percent length increase or weight gain.

Table 9a shows that at 4 weeks, percent weight gain is significantly higher in Group B (BID Natalac) than both Groups C and D (placebo groups) from birth to four weeks, to six weeks, and to eight weeks. This table also shows that in comparing percent weight gain, Group BID Natalac is not significantly higher than OD Natalac, BID placebo is not significantly higher than OD placebo, and OD Natalac may be significantly better than OD placebo.

Table 9b shows the result of the Wilcoxon Rank Sum Test comparing the study groups in terms of percent length increase of infants. Based on increasing length, OD Natalac is not better than OD Placebo but is significantly better than BID placebo; BID

Table 9a. Wilcoxon rank sum test of percent weight gain

Treatment	Birth to 2 wks	Birth to 4 wks	Birth to 6 wks	Birth to 8 wks
A&B	$\mu=99$ CV=82 NS	$\mu=67$ CV=66 NS	$\mu=58$ CV=51 NS	$\mu=59$ CV=42 NS
A&C	$\mu=99$ CV=75 NS	$\mu=67$ CV=50 NS	$\mu=58$ CV=37 Significant	$\mu=59$ CV=31 Significant
A&D	$\mu=122$ CV=88 NS	$\mu=83$ CV=66 NS	$\mu=65.5$ CV=51 NS	$\mu=43$ CV=39 NS
B&C	$\mu=71.5$ CV=56 NS	$\mu=34$ CV=46 Significant	$\mu=25$ CV=37 Significant	$\mu=28$ CV=37 Significant
B&D	$\mu=78$ CV=66 NS	$\mu=47$ CV=61 Significant	$\mu=40$ CV=51 Significant	$\mu=30$ CV=47 Significant
C&D	$\mu=87.5$ CV=61 NS	$\mu=81$ CV=46 NS	$\mu=51$ CV=37 NS	$\mu=44$ CV=34 NS

* μ is the Wilcoxon Rank Value and is SIGNIFICANT if it is less than or equal to the critical value (CV); CV is the critical values at alpha = 0.05 of the Wilcoxon Rank Sum Test; NS means non-significant.

Table 9b. Wilcoxon rank sum test of percent length increase

Treatment	Birth to 2 wks	Birth to 4 wks	Birth to 6 wks	Birth to 8 wks
A&B	$\mu=92.5$ CV=82 NS	$\mu=57.5$ CV=66 Significant	$\mu=30.5$ CV=47 Significant	$\mu=12$ CV=42 Significant
A&C	$\mu=74$ CV=75 Significant	$\mu=55$ CV=50 NS	$\mu=40.5$ CV=34 NS	$\mu=44.5$ CV=31 NS
A&D	$\mu=59.5$ CV=88 Significant	$\mu=35$ CV=66 Significant	$\mu=40.5$ CV=47 Significant	$\mu=44.5$ CV=38 Significant
B&C	$\mu=40$ CV=56 Significant	$\mu=29$ CV=46 Significant	$\mu=10.5$ CV=37 Significant	$\mu=11.5$ CV=37 Significant
B&D	$\mu=39$ CV=72 Significant	$\mu=32$ CV=61 Significant	$\mu=1$ CV=51 Significant	$\mu=2$ CV=47 Significant
C&D	$\mu=69$ CV=61 NS	$\mu=124$ CV=46 NS	$\mu=115$ CV=37 NS	$\mu=80.5$ CV=34 NS

* μ is the Wilcoxon Rank Value and is SIGNIFICANT if it is less than or equal to the critical value (CV); CV is the critical values at alpha = 0.05 of the Wilcoxon Rank Sum Test; NS means non-significant.

Natalac is significantly better than OD Natalac, OD Placebo, and BID Placebo Groups; while BID Placebo is not better than OD Placebo.

Stratifying our data based on average monthly income, (Appendix C) we found out that the effectiveness of BID Natalac in increasing weight and length of infants is better appreciated among those who have 600 to 1000 pesos average monthly income than those with less than 600 pesos monthly income. Even with data stratification, BID dose of Natalac is still the dosage that resulted in better percent weight gain and length.

Conclusion

Natalac OD significantly increased length and weight over an OD placebo. BID Natalac significantly increased length and weight over a BID placebo. The BID Natalac significantly increased length and weight over OD Natalac. Thus, 250-mg malunggay leaves, in The form of Natalac, given twice a day significantly improved lactation over Natalac given once a day.

Limitations of the Study

The mothers' diet within the duration of the trial should have been controlled. Given the economic limitations of the majority of the respondents, a diet plan was not practical.

Prolactin assays may have been used as direct measures of improvement in lactation. Due to financial constraints, expensive assays were far beyond the reach of this study.

Appendices

Appendix A

Sample Size Computation

Schlesselman's Equation:

$$n = \frac{2(z\alpha + b)^2 (SD)^2}{E^2}$$

A study conducted by Almirante and Lim on the effectiveness of Moringa as a galactagogue showed that twice daily dosing of 250 mg capsules of Natalac resulted in 31% increase in weight of infants in one month with a standard deviation of 22.76. This study considered a 25% increase in weight in both OD and BID dosage of Natalac in 4 weeks using 95% level of significance and power of 80.

$$n = \frac{2(2.48)^2 (22.76)^2}{(25)^2}$$

$$n = 10.20$$

To allow for noncompliance of patients to treatment regimen, incidence of sickness of the infant or mother during the study, or failure to follow-up, we increased the sample size to 20 in each of the four study groups, for a total of 80 patients.

$$n = 20$$

$$N = 80$$

Appendix B

Tables comparing the demographic characteristics of the four study groups

Table 1. Comparison of treatment groups according to parity

Treatment Group		Parity	
		Primipara	Multipara
OD Natalac	Row%	50.0	50.0
BID Natalac	Row%	57.1	42.9
OD Placebo	Row%	38.5	61.5
BID Placebo	Row%	53.3	46.7