Moringa oleifera (Malunggay) as a Galactagogue for Breastfeeding Mothers: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Background. Moringa oleifera (Malunggay) capsules have been prescribed for years by many physicians in the promotion of breastfeeding. Its efficacy has not been well established due to few, small randomized controlled trials.

Objectives. To perform a meta-analysis of the available data in the medical literature, assessing the effect of intake of Moringa (malunggay) by postpartum women, on breast milk volume and infant’s growth.

Data sources: PubMed, Cochrane Controlled Trials Meta-Register, electronic databases of published, unpublished and non-English language papers; conference proceedings, reference lists, and trial authors.

Selection Criteria. Randomized controlled trials (RCTs) examining the effect of intake of Moringa on breast milk production of postpartum breastfeeding women were eligible for inclusion.

Data Collection. Absolute and relative changes from baseline were calculated for individual studies and pooled using a random effects model.

Main Results. Five RCTs including 366 participants met the inclusion criteria. Of the outcomes reviewed, only breast milk volume showed a statistically significant increase following treatment with moringa capsules on day 4, 5 and 7. The analysis of pooled data demonstrated a statistically significant relative increase on day 4 of 23.09 ml (95% CI 16.85, 29.33 p=.06); day 5 of 31.78 ml (95% CI 24.24, 39.32 p=.00001); and on day 7 of 123.87 ml (95% CI 89.48, 158.26 p=.32) milk volume with moringa capsules treatment compared to placebo. Two RCTs reported an increase in infants’ weight as an outcome with the use of moringa capsules. No adverse events were observed in any of the trials.

Conclusion. Evidence from Randomized Controlled Trials prove that Moringa results in an increase in breast milk volume compared to placebo.

Keywords: Moringa, Moringa oleifera, Malunggay, Galactagogue, Breastfeeding

BACKGROUND

Description of the condition

The most recent National Demographic and Health Survey 2003 of the National Statistics Office showed that of the 7 million children below 5 years old in the Philippines, only 87% were breastfed. This includes infants whose breastfeeding lasted for only one hour, one day or one week. Nearly 3.4 million children (49%) were given complementary feeding within 3 days after birth. Barely 6% were exclusively breastfed. Although 80% of children started breastfeeding within 24 hours from birth, exclusive breastfeeding only lasted for an average of 24 days. Among mothers who did not breastfeed their children, 31% reported that they did not have enough milk. (1) Physicians use several methods to promote breastfeeding; these include maternal education, non-separation policy, and imploring the help of a lactation specialist. To augment the problem in the adequacy of milk volume, clinicians often use galactagogues.

Description of the intervention

Galactagogues are medications or substances believed to assist initiation, maintenance or augmentation of maternal milk production. (2) Common galactagogues include domperidone and metoclopramide. Both are deemed to interact with the dopaminergic system which in turn promotes the release of prolactin. There are several other herbal plants that are said to have lactogenic effects including anise seeds, Bermuda grass, fennel seeds and quinoa. (16)

In the Philippines, Moringa leaves grown in backyards, usually prepared as a vegetable ingredient in chicken soup, have been used by mothers to enhance milk production. (3, 4) It has been encapsulated, marketed and sold com-
commercially to help increase breast milk in lactating mothers.

**How the intervention might work**

Lactogenesis is initiated in the postpartum period by a decrease in plasma progesterone, with corresponding increase of serum prolactin level. According to Hans Selye, each baby's sucking episode is associated with a rise in plasma prolactin. Thus frequent nursing is required to maintain high plasma prolactin level. However, if standard physiologic measures (proper attachment and frequent nursing) are only partially effective, drugs like reserpine, metoclopramide, domperidone, and thyrotropin releasing hormone (TRH) can be utilized to stimulate prolactin production.

In the Philippines moringa leaves have been used to enhance milk production with unclear mechanism of action. Almirante and Lim proposed a mechanism for its lactogenic effects. The study showed that there was a greater increase in maternal prolactin levels among breastfeeding mothers who took the leaves.

**Why it is important to do this review**

Quisumbing 1978 first noted the use of moringa leaves as a galactagogue. This lactation-enhancing effect of moringa leaves was demonstrated in a local study done by Almirante and Lim, wherein moringa leaves in the form of Natalac capsules were given to pregnant term Filipino women immediately after birth. The study showed significantly higher prolactin levels among mothers taking Natalac capsules accompanied by significant weight gain among their babies. A follow up study done by the same authors among hypertensive women mothers showed the same result.

In a randomized controlled trial done by Estrella et al., the administration of Moringa capsules showed an increase in milk production on postpartum day 4 to 5 among mothers who delivered preterm infants, with no reported side effects.

Another study by Balahibo et al. noted that among breastfed newborns, there was a significant increase in weight and length of newborns whose mothers were taking moringa capsules from birth to 2 months. It was also noted that lactation significantly improved in those taking moringa capsules over the 2 month study period.

**OBJECTIVES**

This study aims to perform a meta-analysis of the available data in the medical literature, assessing the effect of intake of Moringa by postpartum women, on volume of milk production, and infant weight gain.

**METHODS**

Criteria for considering studies for this review

**Types of studies**

All randomized controlled trials comparing Moringa versus placebo or any other galactagogues are eligible for inclusion in the review. Search was not limited by date, language or publication status.

**Types of participants**

Post-partum mothers who have taken raw or pharmaceutically compounded drug with *Moringa oleifera* as active ingredient were included. Mothers who had taken Moringa prior to delivery or as prophylaxis were excluded from the study.

**Types of interventions**

Intervention in the included study should use *Moringa oleifera* either as raw or pharmaceutically compounded drug. We excluded studies that used Moringa for any other purpose other than as a galactagogue. Studies where mothers took Moringa for re-lactation or to prior to delivery were also excluded. Control variable had to be a placebo tablet of similar physical characteristic as that of the study drug or any pharmacologic agent deemed to have galactagogue properties.
Types of outcome measures
Primary outcomes
The primary outcome was measured both in-vitro and in-vivo. In-vitro measurement involved measuring the volume of breastmilk in milliliters (mL) or cubic centimeters (cc) obtained through expression by either hand or machine. In-vivo measurement was the adequacy of milk production as evidenced by infant weight gain. This outcome was measured using percentage weight gain (%).

Secondary outcomes
Another outcome that was determined was the level of maternal prolactin production measured in million International Units per liter (mIU/L). Levels of prolactin are said to be related to maternal breastmilk production. Adverse drug events related to use of Moringa were also noted and documented.

Search methods for identification of studies
We searched the following electronic databases using the search terms already described in Appendix 1: Moringa oleifera, Moringa pterygosperma, Moringa, Malungga, Drumstick tree, Horseradish tree and Ben oil tree for the intervention. These search terms were combined with the search terms: breastfeeding, breastmilk and lactation.

Electronic searches
The following electronic databases were searched with uniform search strategy:

- MEDLINE
- CENTRAL
- EMBASE
- Controlled Trials MetaRegister
- HERDIN

Searching other resources
Citations and reference lists of identified articles were examined for additional relevant studies. Conference proceeding and local journals were hand searched for relevant researches. Experts and researchers were queried for ongoing and/or unpublished trials.

DATA COLLECTION AND ANALYSIS
Selection of studies
Two authors independently examined the title, abstracts, and keywords of citations from electronic databases for relevance and subsequently eligibility. The full text of all relevant records were obtained and independently assessed as to whether each met the predefined inclusion criteria. The authors used a form for standardization of appraisal methods. Disagreements were discussed and if consensus was not reached, it was adjudicated upon by the third author. Excluded studies and the reason for exclusion were noted and tabulated.

Data extraction and management
The primary and secondary outcomes were all of continuous variables. The arithmetic means and standard deviations for the two groups were determined from the study and compared. The unit of measurement were ascertained as uniform to ensure consistency.

Assessment of risk of bias in included studies
Methodological quality was assessed independently by two review authors using the guidelines in the Cochrane handbook and was assessed for overall quality of evidence using the GRADE approach. The parameters to be used in assessing the risk of bias will included random allocation, concealment allocation, blinding and reporting biases.

Measures of treatment effect
The volume of breastmilk was measured using cubic centimeter (cc) or milliliter (mL). Infant's percent weight gain was expressed in percentage. The level of maternal prolactin was measured in million International Units per liter (mIU/L). A weighted mean difference between treatment and control groups was determined using RevMan 5.1. Analysis was based on mean difference using random effects model.

Dealing with missing data
The authors contacted the original inves-
Data synthesis

Only studies with comparable interventions, populations and outcomes were pooled and analysed. The investigators used RevMan 5.1 for derivation of mean difference of each outcome and subsequently compared, pooled and analyzed studies of comparable interventions and population. Inverse variance was computed via fixed effects method as determined by RevMan 5.1 and reported accordingly.

Subgroup analysis and investigation of heterogeneity

A table of study characteristics was completed by the investigators and was used in assessing the clinical and methodical heterogeneity of each study. Statistical heterogeneity was assessed using Pearson Chi Squared test as determined by RevMan 5.

RESULTS

Description of studies

Results of the search

A total of 32 titles and abstracts were retrieved through searching databases and reference tracking. We obtained the full text of six articles among which one trial was ineligible due to use of intervention prior to delivery (Figure 1). The final trial sample consisted of five randomized trials for the review. The details of included trials are reported in ‘Characteristics of included studies’. The reasons for excluding trials are stated in ‘Characteristics of excluded studies’.

Included studies

Of the five included trials, four trials were done in tertiary hospitals(2,12,13,14) while one was done in the community setting(6). Four trials compared Moringa capsules against placebo(6,12,13,14) while one trial compared Moringa capsules as well as other galactagogues like domperidone and metoclopramide against plain breastfeeding(2) in a randomized manner. A total of 366 postpartum mothers were recruited across all trials. Among the participants, 108 of them were mothers of preterm infants while the rest of them were mothers of term infants not suffering from any illness at birth. An informed consent was obtained from all participants in four trials(2,6,13,14) but it was not explicitly stated in one trial(12). Reporting of inclusion and exclusion criteria was similar across trials.

Of the five pooled trials comparing the efficacy of Moringa as a galactagogue for breastfeeding mothers, three trials(2,13,14) measured milk volume, two trials(6,12) measured infant weight, two trials(2,6) quantified maternal prolactin level, and all trials reported adverse outcomes.
Milk volume measurement varied from day 3 post-partum to 4 months, as well as infant weight taken from birth to 4 months and maternal prolactin level measurement from 6 hours post-partum to 4 months. No adverse effects were noted in four trials.(2,6,13,14)

Excluded studies
One study was excluded because Mor- inga capsules were taken by mothers prior to delivery.(10)

Risk of bias in included studies
Allocation (selection bias)
In only two of the five trials, was randomization done using a controlled block design (2) and table of random numbers (14). Randomization details were not specified in two of the remaining 3 trials(6,12), while in the last trial, randomization was done by the researcher with high risk for bias.(13) Allocation in 3 of the five trials had low risk for bias with treatment assignment concealed using opaque sealed envelopes, identical containers which were coded at the source.(6,13,14) The remaining 2 trials did not specify how allocation concealment was done.(2,12)

Blinding (performance bias and detection bias)
Three of the four trials ensured blinding of participants and personnel (6,12,14) while in the remaining one trial only the participants were blinded.(13) One trial did not specify any blinding done.(2) In all trials, blinded individual assessors were used. For the assessment of milk volume, a standardized, calibrated breast pump and container were used. Milk volume was either recorded by the subjects themselves or by the study personnel. Prolactin level was measured using the ELISA technique while a checklist of adverse symptoms was provided for the subjects. Infants' weight gains were measured by blinded doctors/students but the method was not stated in one trial.(6)

Incomplete outcome data (attrition bias)
The intention-to-treat principle was not mentioned in any of the pooled trials. All trials reported number of dropouts and withdrawals correctly except one trial which did not assess this outcome.(12)

Selective reporting (reporting bias)
All pre-specified outcomes like milk volume, maternal serum prolactin level, infant's weight and adverse effects were reported in all pooled trials.

Other potential sources of bias
Eighty percent of the trials were performed before the year 2005 and 20% before the year 2000. The number of patients per trial ranged between 40 for the smallest(2) and 116 patients for the largest.(6) Only one trial enrolled more than 100 patients (6) and only one trial included information on sample size calculations.(12)

Effects of interventions
Milk Volume
All three trials noted milk volume on day 3 postpartum with intake of Moringa capsules starting on the same day(2,13,14); two trials reported milk volume on day 4 and 5 (13, 14); and two trials on day 7(2,13) I trial each reported milk volume on day 10(13) and day 14.(2) The comparison regarding the outcome milk volume enrolled a total of 171 participants for day 3, 150 participants each for day 4 and 5, and 102 participants for day 7 in the Moringa vs placebo group. The pooled analysis for day 3 showed heterogeneity of effects (Chi2 = 4.59 df=2 12 = 56% p=0.1) and failed to show a significant association of Moringa capsules to increase milk volume against placebo (pooled ratio of the means of 13.58 (95% CI -1.67, 28.83). On days 4 and 5, pooled analysis showed heterogeneity of effects (chi2= 3.5 df =1 12 = 71% p=0.06, chi2= 33.88 df =1 12= 97% p<.00001 respectively), there was significant association of
Moringa capsules with increase milk volume against placebo (day 4 23.09 [95% CI 16.85, 29.33]; day5 31.78 [95% CI 24.24, 39.32]). On day 7, pooled analysis showed homogeneity of effects (chi2= 0.98 df=1 p= 0.32) and significant increase in mean difference of milk volume with Moringa capsules against placebo at 123.87 ml per extraction (95% CI 89.48, 158.26). Fig. 2

<table>
<thead>
<tr>
<th>Experimental Group</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean Difference</th>
<th>N, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>205.58</td>
<td>98.22</td>
<td>30</td>
<td>92.2</td>
<td>76.31</td>
<td>10</td>
<td>19.38</td>
<td>85.58 [10.22, 166.44]</td>
</tr>
<tr>
<td>Moringa A day 1</td>
<td>2480.95</td>
<td>46.60</td>
<td>41</td>
<td>195.6</td>
<td>116.14</td>
<td>41</td>
<td>88.51</td>
<td>122.43 [64.09, 170.70]</td>
</tr>
<tr>
<td>Mean (95% CI)</td>
<td>51</td>
<td>10.04</td>
<td>123.87 [89.48, 158.26]</td>
<td></td>
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<td></td>
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<tr>
<td>Homogeneity Chi2, df = 1 P = 0.32; I2 = 0.0%</td>
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<tr>
<td>Mean total effect 2 = 10.05 (P = 0.00000)</td>
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</table>

Figure 2. Forest plot of comparison: 1 Moringa vs Placebo, outcome: Volume of Breastmilk Day 7

Prolactin Level

Two trials were carried out to assess the efficacy of moringa capsules versus placebo in the increase maternal serum prolactin level.(2,6)

One trial(6) reported on maternal serum prolactin level on 116 patients, 6 hours immediately postpartum (first extraction), 2nd day postpartum (2nd extraction) and 4 months postpartum (3rd extraction). The median prolactin level on the first extraction was 4808 mIU/L in patients who took moringa capsules compared to 5134 mIU/L in patients who took placebo. Prolactin levels were higher in the treatment group on the 2nd and 3rd extraction and was statistically significant yielding a ratio of the medians of 1884.9 (95% CI 1601.8, 2168) and 1838 (95% CI 1073.04, 2602.96), respectively. One trial (2) reported on the prolactin levels on day 3 postpartum, day 7 postpartum and day 14 post partum but did not show any significant difference among all 3 groups. The comparison included a total of 40 patients. (Table 1)

Table 1. Serum Prolactin Level

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean, mIU/L (n)</th>
<th>SD</th>
<th>Mean, mIU/L (n)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Postpartum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Almirante 1996</td>
<td>4808.0 (58)</td>
<td>2258.4</td>
<td>5134.0 (58)</td>
<td>2304.4</td>
</tr>
<tr>
<td>Day 2</td>
<td>5236.0 (58)</td>
<td>2252.4</td>
<td>3398.0 (58)</td>
<td>1939.5</td>
</tr>
<tr>
<td>Day 3</td>
<td>3149.2 (10)</td>
<td>1312.4</td>
<td>3244.9 (10)</td>
<td>2289.8</td>
</tr>
<tr>
<td>Day 7</td>
<td>2088.7 (10)</td>
<td>2175.3</td>
<td>2812.3 (10)</td>
<td>1968.0</td>
</tr>
<tr>
<td>Day 14</td>
<td>1229.2 (10)</td>
<td>1468.6</td>
<td>2337.2 (10)</td>
<td>2699.9</td>
</tr>
<tr>
<td>4 mos Almirante 1996</td>
<td>2389.0 (58)</td>
<td>1019.7</td>
<td>504.1 (58)</td>
<td>412.6</td>
</tr>
</tbody>
</table>

Infants' Weight

Two trials(6,12) studied the efficacy of moringa capsules versus placebo as a galactagogue by measuring increase in infants' weight. One trial(6) measured the weight at birth, at 2 weeks, at 1 month and at 4 months of age which included 116 participants in the moringa versus placebo group. One trial(12) noted infants' weight at 2 weeks, 4 weeks, 6 weeks and 8 weeks of age in 30 participants. Percentage weight gain was noted in the moringa group for both trials. (Table 2)

Table 2. Percentage Weight Gain

<table>
<thead>
<tr>
<th>Study</th>
<th>Moringa</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean, %</td>
<td>SD</td>
<td>Mean, %</td>
</tr>
<tr>
<td>BW to 1 week</td>
<td>Almirante 1996</td>
<td>-1.300</td>
</tr>
<tr>
<td>BW to 2 weeks</td>
<td>Almirante 1996</td>
<td>7.944</td>
</tr>
<tr>
<td>BW to 4 weeks</td>
<td>Balahibo 2002</td>
<td>27.35</td>
</tr>
<tr>
<td>BW to 6 weeks</td>
<td>Balahibo 2002</td>
<td>30.31</td>
</tr>
<tr>
<td>BW to 8 weeks</td>
<td>Balahibo 2002</td>
<td>72.22</td>
</tr>
<tr>
<td>BW to 16 weeks</td>
<td>Almirante 1996</td>
<td>120.94</td>
</tr>
</tbody>
</table>

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**Adverse Effects**

Only four trials (2, 6, 13, 14) reported on adverse effects in the treatment group. All trials reported no adverse effects. However, in 2 trials (6, 14) the method of reporting adverse effects was not stated. In the remaining two trials (2, 13) a checklist was provided to the participants.

**DISCUSSION**

**Summary of main results**

Galactagogues are often prescribed to breastfeeding mothers to increase the amount of breast milk production. We reviewed efficacy of moringa capsules as a galactagogue by comparing outcomes such as milk volume, maternal serum prolactin level, and infants' weight in breastfeeding mothers.

Three randomized controlled trials (2, 13, 14) reported on increased milk volume with the use of moringa capsules. The data presented in this review demonstrate a significant increasing trend in the volume of milk starting on day 4, 5, and 7. Pooled trials did not show any significant increase of milk volume on day 3 postpartum. This could be attributed to inadequate window of observation from initiation of therapy. Although pooled analysis both showed heterogeneity for day 4 and 5, it is noteworthy that confidence interval of both days are statistically significant favoring the association of intake of Moringa capsules with increase in milk volume.

The quality of reporting of the milk volume trials showed some methodological deficiencies and had small sample size of less than 100. None mentioned an intention to treat analysis. Methodological quality was moderate in one trial where the method of random sequence, concealment of random allocation, double blinding and number of dropouts were reported (14). The two remaining trials showed methodological deficiencies. One trial had high risk of randomization bias and single blinding (13) while the remaining trial did not state allocation and blinding procedure.

Increased prolactin production is the prevailing theory on how Moringa produces its lactogenic effects. Two randomized controlled trials (2, 6) reported on increase in maternal serum prolactin level with the use of moringa capsules. However, both trials reported measurement of prolactin level on different times, such that no pooling of data cannot be done for comparison. Moreover, both studies showed conflicting results. One trial (6) stated that there is significant increase in maternal serum prolactin level with the use of moringa capsules while another trial (2) stated otherwise. However, both trials showed methodological deficiencies. Both trials did not specify method of randomization. In one trial, allocation concealment and double blinding were done (6) and in the remaining trial, no allocation concealment and blinding were stated (2). Both however, noted blinding of assessors by using the ELISA technique to measure maternal serum prolactin levels. Reporting of withdrawals was noted in both trials. One trial had a small sample size of 40.

Two randomized controlled trials (6, 12) reported an increase in infants' weight as an outcome with the use of moringa capsules. Both trials had moderate methodological quality. Except for reporting of double-blinding, none of the trials properly reported the requested quality criteria. Although percentage weight gain was noted in both trials; no pooled analysis was available for comparison. In one study (12) standard deviation was not specified, such that no confidence interval could be derived. Taken singly, both trials reported increase in percentage weight gain with moringa capsules compared to placebo. However, with no pooled analysis available, it is unverifiable to report as such.

Overall, evidence from five small RCTs unanimously concluded that Moringa produces an increase in breast milk volume compared to placebo.

**Overall completeness and applicability of evidence**

The evidence provided by the review appears to be widely applicable. Moringa leaves are easily accessible in the Philippines as it is found in many backyards. It is commer-
cally available in capsule form. Outcomes such as milk volume, prolactin level and infants' weight are also measurable in our setting. As a galactagogue, it is also well received by Philippine medical societies, in its efforts at promotes breastfeeding.

Quality of the evidence

Many important aspects of moringa capsules as a galactagogue cannot be addressed with the current evidence. It would be interesting, for example, to know whether differential drug efficacy exits in term and preterm infants, primigravid and multigravid mothers. Such subgroup analyses, however, need adequate power or specific research questions and can not be answered by this meta-analysis.

Potential biases in the review process

Most included trials are of small size and therefore prone to effect overestimation due to publication bias. Since the number of trials per comparison was usually very limited, formal assessment of publication bias was not possible.

AUTHORS' CONCLUSIONS

Implications for practice

Moringa is commonly used in the Philippines as a galactagogue to help breastfeeding mothers increase milk production. This study has proven its efficacy in increasing milk volume. This conclusion is based on small trials with limited methodological quality compromising the robustness of its quality. Nevertheless, it is important to recognize that all studies favor the experimental (Moringa) group over the placebo group.

More pharmacodynamic studies need to be done and other theories need to be explored to provide information on the mechanism of its lactogenic effects. Available data on this is also based on small trials with limited quality of methodology.

Moringa is safe with minimal to no adverse effects as reported by all five studies.

Implications for research

Further studies should provide sufficient transparent reporting of allocation, randomization, and blinding. Follow up duration should be adequate and studies should also use uniform endpoint reporting of outcomes. In addition, Moringa can be compared with other galactagogues using a range of doses. Other surrogate outcomes can be investigated such as decreased incidence of acute gastroenteritis and respiratory infections.

DECLARATION OF INTEREST

The authors have no affiliations with any drug companies. This research was not funded by any institution. The authors are members of a pediatrics department that is a key player in the promotion of breastfeeding.

References


