

# Effectiveness of Ayurved Siriraj Prasa-Nam-Nom Recipe on Breast Milk Volume in Early Postpartum Women: A Randomized, Double-Blind, Placebo-Controlled Trial

Pharuhas Chanprapaph, M.D.<sup>\*</sup>, Chantanat Thippayacharoentam, B.ATM.<sup>\*\*</sup>, Apirada Iam-am, B.ATM.<sup>\*\*</sup>, Natchagorn Lumlerdkij, Ph.D.<sup>\*\*</sup>, Pravitt Akarasreenont, Ph.D.<sup>\*\*</sup>, Tawee Laohapand, M.D.<sup>\*\*</sup>, Sudarat Bangkha, B.N.S.<sup>\*\*\*</sup>, Nhupat Kumleemak, B.N.S.<sup>\*\*\*</sup>, Sudarat Piyophiprapong, M.D.<sup>\*\*\*\*</sup>, Akarin Nimmannit, M.D.<sup>\*\*\*\*</sup>, Thapthep Thippayacharoentam, M.ATM.<sup>\*\*</sup>

<sup>\*</sup>Breastfeeding Division, Department of Obstetrics and Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, <sup>\*\*</sup>Center of Applied Thai Traditional Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, <sup>\*\*\*</sup>Obstetric and Gynaecological Nursing Unit, Siriraj Hospital, Mahidol University, <sup>\*\*\*\*</sup>Department of Clinical Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, <sup>\*\*\*\*\*</sup>Office for Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, <sup>\*\*\*\*\*</sup>Department of Pharmacology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

## ABSTRACT

**Objective:** To explore the effectiveness of Ayurved Siriraj Prasa-Nam-Nom (ASPNN) recipe on breast milk production in early postpartum women.

**Materials and Methods:** Fifty-four normal vaginal term delivery mothers who had inadequate milk volume were enrolled into this randomized, double-blind, placebo-controlled trial. All participants received ASPNN or placebo 1,500 mg three times/day for 3 days in the hospital and 7 days at home. Primary outcomes, including breast milk volume, %crematocrit, and level of prolactin, were evaluated on day 1 and day 3. Satisfaction scores, adverse effects, and types of breastfeeding were also determined.

**Results:** On day 3, milk volume was increased in both groups. The median volume of ASPNN group was 19 ml, while that of the placebo group was 30 ml. The median %crematocrit of ASPNN and placebo group were 7.17% and 6.98%, respectively. Mean serum prolactin levels of ASPNN and placebo group were  $321.76 \pm 114.23$  ng/ml and  $323.78 \pm 116.68$  ng/ml, respectively. Although the effects were not different from the placebo, the reduction of prolactin in ASPNN was lower. Minor adverse effects included skin rash and mild diarrhea. Exclusive breastfeeding rate on day 11 in ASPNN and placebo group were 92.6 % and 88.5%, respectively.

**Conclusion:** Short term ASPNN supplementation produced no direct effect on breast milk volume, creatatocrit, and serum prolactin. It was safe and might help maintaining serum prolactin. A future trial with more participants and longer period should be conducted to confirm the effect of ASPNN on breast milk quantity and quality.

**Keywords:** Creatatocrit; galactagogue; prolactin; inadequate breast milk volume; Prasa-nam-nom (Siriraj Med J 2022; 74: 11-18)

Corresponding author: Thapthep Thippayacharoentam

E-mail address: thapthep.thi@mahidol.edu

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ORCID ID: <https://orcid.org/0000-0002-6396-3950>

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## INTRODUCTION

Breastfeeding is standard method for infants feeding. Exclusive breastfeeding for at least 6 months has been globally promoted as a standard infant feeding by the United Nations International Children's Emergency Fund (UNICEF) and the World Health Organization (WHO) through a huge campaign "Ten Steps to Successful Breastfeeding". Multiple lines of evidence support that breastfeeding improves health of infants and mothers. It decreases not only the incidence but also the severity of neonatal infections and reduces postnatal mortality rate.<sup>1</sup> However, WHO reported in 2018 that only about 44% of infants worldwide are exclusively breastfed.<sup>2</sup> Breastfeeding failure is a result of multifactorial determinants, including negative reaction toward breastfeeding at work, negative attitude toward colostrum in some societies, fatigue and intensity from work, short maternity leave (<6 weeks), poor advice on breastfeeding position and latching, as well as insufficient supports.<sup>3</sup> Other factors also include short nipple length<sup>4</sup> and perception of babies' dissatisfaction of breastmilk and inadequate milk volume.<sup>5,6</sup>

Human milk production can be successfully increased by means of psychological support, stress-relief-techniques and medications.<sup>6</sup> Plasma concentration of prolactin (PRL) plays an important role in human milk production. Dopamine is a physiologic inhibitor of PRL release. Therefore, domperidone which acts as a hypothalamic dopaminergic receptor blocker has been widely used as a galactagogue to promote lactogenesis. The drug was reported to enhance PRL.<sup>7</sup>

Thai traditional medicine (TTM) is a holistic approach to take care of human health. There are several TTM methods used for postpartum women, such as hot salt pot compression, massages, hot herbal charcoal seats and herbal medicines.<sup>8</sup> Prasa-Nam-Nom is a Thai herbal galactagogue mixture which has been traditionally used to improve milk production. This herbal formula helps increasing blood circulation and results in enhancing milk secretion and purifying its content. Prasa-Nam-Nom recipe has been listed in TTM text books as a safe herbal medicine and has been used for more than three decades. Various preparations of Prasa-Nam-Nom are widely described and accepted as a galactagogue, including our Ayurved Siriraj Prasa-Nam-Nom (ASPNN) recipe. The ingredients of ASPNN include garden spurge (*Euphorbia hirta* Linn.), weeping fig (*Ficus benjamina* Linn.), rauwolfia (*Rauwolfia serpentina* Linn. Benth. ex Kurz.), and wild ginger (*Zingiber zerumbet* (L.) Smith.). Among these, *E.hirta* exhibited galactagogue effects in vivo by enhancing milk production, prolactin secretion, and the development of lobuloalveolar system of mammary glands.<sup>9,10</sup>

Despite its increasing popularity, there is limited evidence to support its uses. Tuntratuang (2017) reported that a Prasa-Nam-Nom used in Nong Bua Lamphu Hospital (no detail on its composition) increased breast milk volume of the mothers after caesarean section better than domperidone at 24, 48, and 72 hours.<sup>11</sup> Jankaew and Narumitmontri (2020) reported that a herbal recipe containing *Anthocephalus chinensis* (Lam.) A. Rich ex Walp. and *Diospyros variegata* Kurz administered five grams thrice a day for one week enhanced breast milk flow at 32 and 40 hours after the delivery better than domperidone.<sup>12</sup>

The objectives of this study were to explore the effectiveness of ASPNN recipe on breast milk production in women with inadequate milk volume during early postpartum period. Furthermore, its safety and impact on the level of serum prolactin hormone and the milk quality were also investigated.

## MATERIALS AND METHODS

### Study design

This randomized, double-blind, placebo-controlled study was conducted at the postpartum ward, Department of Obstetrics and Gynaecology, Siriraj Hospital, Mahidol University, Bangkok, Thailand between November 2010 and December 2012. The research protocol was reviewed and approved to be ethical by the Siriraj Institutional Review Board No. 743/2554 (EC3). An informed consent was obtained from each participant before the trial began. The study was registered with Thai Clinical Trials Registry with the project number of TCTR20190218004.

### Participants

Subjects were enrolled if they were eligible to the inclusion criteria: age of  $\geq 18$  years old; first vaginal delivery at term; milk volume at 24-hour after the delivery  $< 49$  ml/breast pump.<sup>13</sup> The exclusion criteria included having medical disorders (hypertension, type 2 diabetes, thyrotoxicosis and hypothyroidism); previous allergy to ASPNN or its ingredients; inability to eat vegetables or spicy food; severe breastfeeding problems (abnormal breast anatomy, short nipples, mastitis, breast abscess and severe fetal tongue-tie); taking other medications (domperidone, metoclopramide, antidepressive drugs, caffeine and alcohol). Subjects were withdrawn if they were unable to take 90% of total drugs or had gastrointestinal unwanted effects.

### Sample size calculation

According to our previous study, normal milk volume on day three after the delivery was  $49 \pm 18$  ml/ breast pump.<sup>13</sup> In this study, an increase in milk production

up to 15 ml was considered to be clinically significant. By setting the probability of 2-sided type I error and the power of test at 0.05 and 80%, respectively, a minimum of 24 subjects in each group was required. To prevent loss to follow-up cases, 10% more of participants was added which resulted in the total number of 54 participants.

### Randomization

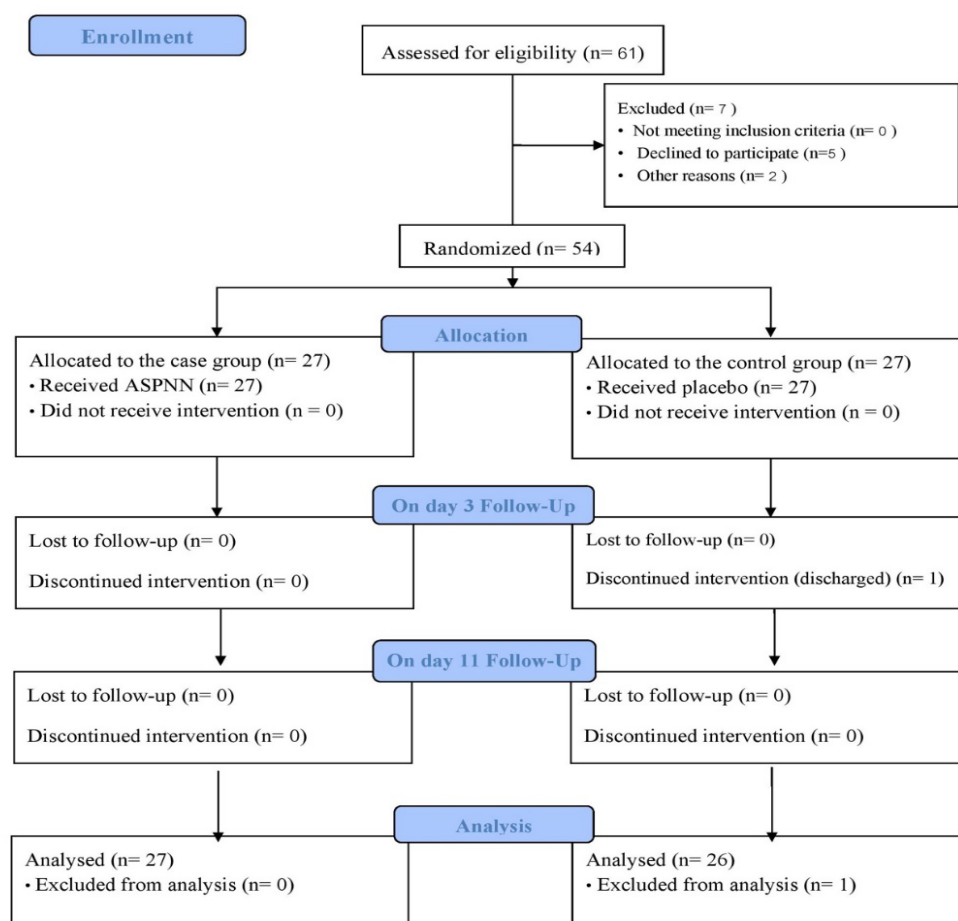
For patient allocation, the treatment codes were randomly generated prior to the trial by a computer software nQuery Advisor® version 7 (Statistical Solutions Ltd., Cork, Ireland, United Kingdom). The codes were block randomized into two groups of the ASPNN group and the placebo group and kept strictly confidential in sequence in sealed opaque envelopes by a research nurse who had no responsibility for patient care in this study. The nurse would open each envelope for the treatment assignment without knowing the identity of the drugs administered by either the physicians or the patients.

### Intervention

This study was conducted in a double-blind fashion. Each participant received three 500-mg capsules of either ASPNN or placebo thrice a day (4,500 mg/day)

30 minutes before meal for three days. All subjects equally obtained three meals and two snacks with total calories of 2,100 kcal daily. On day three, 2 milliliters of breast milk were collected for fat content evaluation and 6 milliliters of blood were taken for PRL level assessment. The volunteers were requested to answer a questionnaire regarding their satisfaction to the taken medication. Prior to the hospital discharge, participants in each group received more medications to continue their treatment for another seven days based on the traditional prescription of Prasa-nam-nom decoction, which is 7 - 10 days. On day eleven, they were interviewed by phone regarding any unwanted effects and type of infant feeding (Fig 1).

Participants' compliance was assessed by interviewing and counting the remaining capsules. Subjects in both groups received the standard postpartum care in the similar environment and were well-supported for breastfeeding by the same lactation consultant nurse. During the study period, they were encouraged to breastfeed every 2-3 hours in proper latch-on position and correct techniques. They also obtained the same amount of food and water in one day while a food and water chart were daily recorded for monitoring.



**Fig 1.** Study flow diagram based on the CONSORT 2010 flow diagram

## Drug preparation

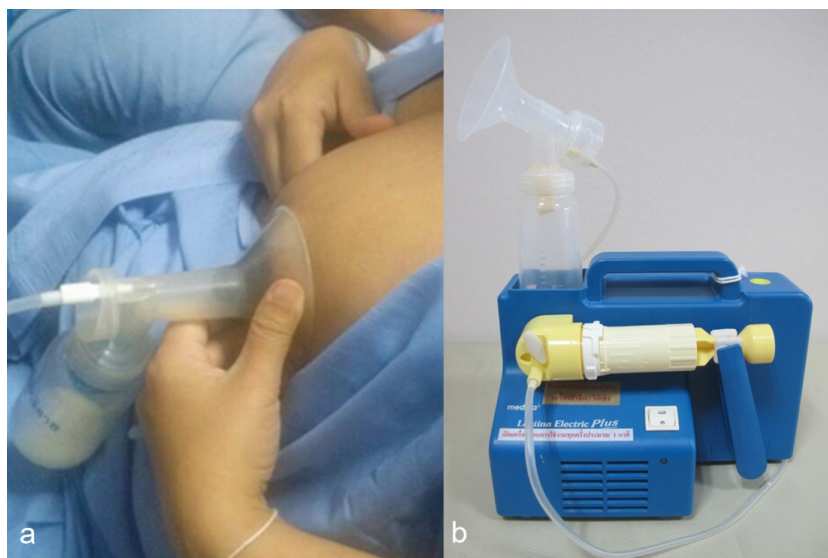
The 500-mg of ASPNN and identical-looking placebo capsules were prepared under the good manufacturing practice by Ayurved Siriraj Manufacturing Unit of Herbal Medicine and Products, Center of Applied Thai Traditional Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University (Bangkok, Thailand). All herbal ingredients were selected, washed and oven-dried at 45-55 °C for 6-8 hours. Then, they were chopped, grounded and filtered into brown fine powder. The mixtures were weighed and filled into 500-mg green opaque capsules using a capsule filling machine. Placebo capsules were made with green opaque capsule shells with the same appearance with those used to make ASPNN, but filled with fine granular flour, magnesium stearate and talcum. Both ASPNN and placebo capsules were similarly packed in sealed opaque envelopes. Then the capsules were tested for weight variation and disintegration to ensure that they met with the specification. To ensure the similarity of the given medications, all herbal and placebo capsules were sufficiently produced for the whole study within the same batch. All capsules were stored in a cool dry place at room temperature during the study period.

## Breast milk volume collection and measurement

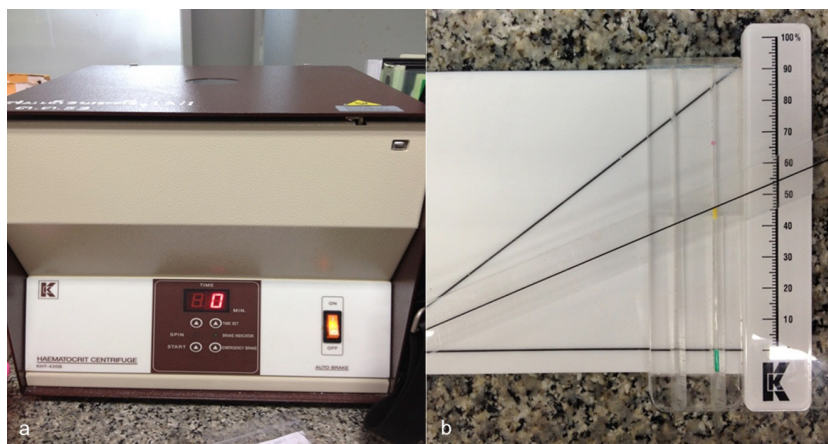
Breast milk was collected on day 1 before the drug administration and on day 3 before discharge using an electrical breast pump (Lactina Electric Plus breastpump by Medela CO. Switzerland) with moderate pumping power for 15 minutes on each side. The milk volume was presented as mL of breastmilk from both sides per pump (Fig 2). The collected breast milk was later brought to the infants.

## Creamatocrit measurement

Creamatocrit is a method widely used in lactation research. It is used to determine lipid content and energy content in breast milk.<sup>14</sup> The assessment technique requires a hematocrit centrifuge machine, a standard glass capillary tube and a hematocrit reader. 75 µl of collected milk was transferred into a glass capillary tube which was sealed one end by clay and centrifuged for 30 minutes at a speed of 3,000 rpm. The creamatocrit value was evaluated on day 1 before the drug administration and on day 3 before discharge and demonstrated by a percentage of the length of the cream layer to the length of the milk column in the tube (Fig 3).



**Fig 2.** (a) breast milk volume was measured before the drug administration and on day 3 and (b) an electrical breast pump



**Fig 3.** Creamatocrit measurement (a) a hematocrit centrifuge machine and (b) a hematocrit reader.



### Prolactin level assessment

Serum prolactin levels (PRL) were determined on day 1 before the drug administration and on day 3 before discharge using Prolactin II assay (Roche Diagnostic) and analyzed by Modular Analytics E170 module (Roche Diagnostic, Mannheim, Germany). This technique was an electrochemiluminescence immunoassay based on the sandwich principle.

### Satisfaction scores, adverse effects, and types of breastfeeding

Satisfaction scores and adverse effects were determined on day 3. After a discharge from the hospital, the participants continued the intervention for another 7 days at home. Then satisfaction scores, adverse events, and types of breastfeeding were assessed on day 11 by a telephone interview. The participants rated their satisfaction with odor and flavor of the intervention on a scale of 1-5, where 1 = very unsatisfied, 2 = unsatisfied, 3 = neutral, 4 = satisfied, and 5 = very satisfied. The participants were asked with an open-ended question for self-report adverse effects. Lastly, they were asked for types of breastfeeding whether they fed the baby with only breast milk (exclusive breastfeeding) or combine with formula supplementation (partial breastfeeding).

### Statistical analysis

All statistical analyses were performed using SPSS version 18 for Windows software (SPSS, Inc., Chicago, IL). All data were presented as mean  $\pm$  SD or median (min, max). Independent t- test or Mann-Whitney U test were used to compare these values between two groups. Paired t-test or Wilcoxon Signed Rank test were used to compared results before - after of each group. Satisfaction scores and adverse effects were presented as

case number and percentage. The comparison between two groups was performed using Pearson Chi- square. Breastfeeding types on day 11 were presented as case number and percentage. The comparison was performed with Fisher's exact test. The statistical significance was set at  $p < 0.05$ .

## RESULTS

From the total enrolled 61 women, there were 54 eligible women who were randomly allocated into the placebo group or the ASPNN group. On day three, one case in the placebo group dropped out. Therefore, the data from only 53 cases were used for statistical analysis (Fig 1).

At the beginning, maternal age, body mass index, total gestational weight gain, baby birth weight, pumped milk volume, creatatocrit and serum PRL level in both groups were similar (Table 1).

After three days of the interventions, the median milk volume in both groups remarkably improved from 0.15 to 19 ml in the ASPNN group and 0.3 to 30 ml in the placebo group (Table 2). Maximum milk volume of the ASPNN group was higher than that of the placebo group. Breast milk volume, increased milk volume, creatatocrit and PRL of both groups were not difference. Serum PRL of the ASPNN group on day 3 was not different from day 1 ( $p = 0.31$ ), while that of the placebo group significantly reduced ( $p = 0.03$ ).

ASPNN drug was highly accepted by the women in terms of its odor and flavor (Table 3). Minor adverse effects were reported, including skin rash and mild diarrhea, with spontaneous recovery (Table 4). The percentage of exclusive breastfeeding on day 11 of the ASPNN group was 92.6%, whereas that of the placebo group was 88.5%.

**TABLE 1.** Demographic data (before the treatment)

Characteristic	ASPNN (n = 27)	Placebo (n = 26)	P-value
Age (years), mean $\pm$ SD	23.74 $\pm$ 4.95	24.27 $\pm$ 5.38	0.36
Body mass index (kg/m <sup>2</sup> ), mean $\pm$ SD	20.57 $\pm$ 2.91	20.53 $\pm$ 2.52	0.48
Total gestational weight gain (kg), mean $\pm$ SD	12.54 $\pm$ 3.96	12.89 $\pm$ 3.43	0.37
Baby birth weight (g), mean $\pm$ SD	3,013.33 $\pm$ 288. 42	2,981.15 $\pm$ 311.58	0.35
Day-1 breast milk volume (ml), median (min, max)	0.15 (0, 5)	0.3 (0, 4.1)	0.94
Day-1 creatatocrit (%), median (min, max)	7.25 (2.58, 14.23)	6.03 (2.13, 12.34)	0.47
Day-1 prolactin (ng/mL), mean $\pm$ SD	339.18 $\pm$ 164. 21	386.54 $\pm$ 192.61	0.17

**TABLE 2.** Breast milk volume, creatatocrit and serum prolactin level on day 3 in each group and the changes

Data	ASPNN (n=27)	Placebo (n=26)	p-value
Day-3 breast milk volume (ml), median (min, max)	19 (0, 139)	30 (0.01, 110)	0.53
Breast milk volume changes (ml) <sup>#</sup> , median (min, max)	18.55 (0, 137.3)	29.75 (0.01, 110)	0.58
Day-3 creatatocrit (%), median (min, max)	7.17 (3.94, 10.71)	6.98 (2.52, 11.52)	0.28
Creatatocrit changes (%) <sup>#</sup> , median (min, max)	-0.07 (-7.8, 8.13)	0.37 (-4.31, 4.94)	0.49
Day-3 prolactin (ng/mL), mean ± SD	321.76 ± 114.23	323.78 ± 116.68	0.47
Prolactin changes (ng/mL) <sup>#</sup> , mean ± SD	- 17.42 ± 92.95	- 62.77 ± 169.62	0.12

<sup>#</sup> compared to the baseline

**TABLE 3.** Satisfaction with odor and flavor of the interventions (day 3)

Topics	ASPNN (n = 27)	Placebo (n = 26)	p-value
<b>Satisfaction</b>			
Excellent	17 (63.0%)	23 (88.5%)	0.031
Delight	10 (37.0%)	3 (11.5%)	
<b>Odor</b>			
Very satisfied	14 (51.9%)	12 (46.2%)	0.408
Satisfied	11 (40.7%)	8 (30.8%)	
neutral	2 (7.4%)	5 (19.2%)	
Unsatisfied	0 (0%)	1 (3.8%)	
<b>Flavor</b>			
Very satisfied	13 (48.2%)	15 (57.7%)	0.557
Satisfied	11 (40.7%)	10 (38.5%)	
neutral	3 (11.1%)	1 (3.8%)	

Value is presented by number of cases (%)

**TABLE 4.** Self - reported adverse effects

Adverse Effects	ASPNN (n = 27)		Placebo (n = 26)		p-value
	Day 3	Day 11	Day 3	Day 11	
None	25 (92.6%)	27 (100%)	26 (100%)	26 (100%)	0.368
Skin rash	1 (3.7%)	0 (0%)	0 (0%)	0 (0%)	
Mild diarrhea	1 (3.7%)	0 (0%)	0 (0%)	0 (0%)	

Value is presented as number of cases (%)

(The is no p-value on day 11 because the adverse effect is a constant)

## DISCUSSION

Compromised lactation is originated from several factors, including preglandular, glandular or postglandular problems.<sup>15</sup> Phase II lactogenesis occurs 3 - 7 days after the delivery. In this phase, the quantity of breast milk becomes higher at the end of the first week after the delivery. However, many early-postpartum women perceive that they might have insufficient breastmilk and this leads them to stop breastfeeding. Therefore, it is necessary to initiate a successful breastfeeding as soon as possible to encourage exclusive breastfeeding later.<sup>16</sup> In this study, we focused on the implementation of ASPNN, which has been used to stimulate breast milk production in Thai traditional medicine, in order to help early-postpartum women initiating breastfeeding.

ASPNN administration for 3 days showed no statistically significant effect to breast milk volume compared to the placebo. This might due to the short duration of the intervention, which was limited by the usual hospital stay. Galactagogues, such as domperidone or metoclopramide, are usually prescribed for 5 - 28 days.<sup>17</sup> A study from Nong Bua Lamphu Hospital showed that Prasa-Nam-Nom could increase milk volume in 72 hours.<sup>11</sup> However, this study measured the 24 - hour milk volume, while our study measured milk volume from only one pump in a day.

Lipid is a crucial component of breast milk which provides energy to infants. Creamatocrit measurement is simple, inexpensive, and effective to determine lipid content and calories in breast milk. There was also a strong relationship between the creatatocrit value and the infants' body weight increment.<sup>14</sup> The percentage of fat component in breast milk was improved in both groups (25 - 38%). Interestingly, there was a trend of increased creatatocrit in the ASPNN group compared to the placebo group. According to the TTM knowledge, ASPNN has been prescribed in order to promote milk production and to purify the milk. Therefore, further investigation should be conducted to explore the effect of ASPNN on quality of breast milk.

PRL is among reproductive hormones that are responsible for milk production and secretion and becomes a pharmacological target for galactagogues.<sup>17</sup> Although ASPNN showed no statistically significant effect on PRL concentrations, there was a trend that the herbal medicine could maintain PRL level which is important for a successful breastfeeding. The level of PRL is high in the first two hours after delivery and declines after that. Infant suckling stimulates PRL.<sup>17</sup> In our study, the participants were encouraged to breastfeed their babies every 2-3 hours and this should help maintaining PRL

level. However, the placebo group showed a significant reduction in PRL. This suggests that ASPNN might be beneficial for lactogenesis by its impact on PRL.

After discharged, all participants continued their treatment for another week and were interviewed by phone regarding any adverse effects and types of infant feeding. This study shows that short term use of ASPNN is safe for lactating women with only minor and recoverable adverse effects. Its safety for longer period of use is still needed to monitor. The rates of exclusive breastfeeding in both groups were high, which might due to the effectiveness of overall lactation program that could initiate breastfeeding in early postpartum phase.

Traditionally, Prasa-Nam-Nom decoction in conjunction with other treatments, including body massages, hot salt pot, hot charcoal seat, herbal hot spa (Yu-fai) are given to nursing mother for 4 - 6 weeks. This holistic care approach aims to relieve muscle pain, restore the body balance, improve blood circulation, promote perineum wound healing and uterine involution.<sup>8</sup> ASPNN decoction has been used in Ayurved Siriraj Clinic of Applied Thai Traditional Medicine. However, the decoction is inconvenient and difficult to drink. The preparation process is also difficult to control when the participants were at home. Therefore, ASPNN capsule was used in this study instead to ensure that every participant in ASPNN group receive similar intervention. According to the satisfaction survey, the capsule was well-accepted similarly to the placebo.

The advantage of this study was that we designed the experiment to minimize interference to the participants. The breastfeeding was encouraged but voluntarily performed. The milk collection was done only once a day to avoid disturbing baby suckling. Maternal food and water intake were monitored as these affects milk production. Not only the quantity of breast milk, the quality was also assessed. Although the results were not significant, the information can be used in future research.

The limitation of this study was that the main outcomes were determined on day 3 but ASPNN may produce significant benefits later. Although many factors affecting breast milk production and other outcomes were controlled or monitored in the current study (eg. frequency of infant suckling, proper latch-on techniques, monitoring of food and water intake), some uncontrollable factors still exist, such as maternal stress, exact food and water intake, and exact times of milk and blood collection. Future clinical trials should be performed with larger sample size and evaluate outcomes on day 7 afterward. The milk and blood collection times should be similar in all participants. Even though management of maternal

stress was routinely performed in the postpartum ward, it should also be assessed.

## CONCLUSION

Short term supplementation of ASPNN produce no direct effect on breast milk volume, creatumocrit, and serum prolactin. It was safe and might help maintaining serum prolactin. A future trial with more participants and longer period should be conducted to confirm the effect of ASPNN on breast milk quantity and quality.

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## Abbreviations

ASPNN: Ayurved Siriraj Prasa-Nam-Nom; PRL: Prolactin level; TTM: Thai traditional medicine

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## Authors' contributions

PC : analyzed and interpreted the data and contributed in writing the manuscript.

CT : collected the data and performed creatumocrit measurement.

AI : collected the data and performed creatumocrit measurement.

NL : conducted the production of medicines, analyzed the data and contributed in writing the manuscript.

PA : contributed in planning the study protocol and provided information for data analysis.

TL : contributed in planning and development of this research.

SB : recruited the participants, collected blood and breast milk, and gave the treatment.

NK : recruited the participants, collected blood and breast milk, and gave the treatment.

SP : performed Prolactin level assessment.

AN : contributed in planning and development of this research.

TT : analyzed the data and contributed in planning the study protocol and in writing the manuscript.

All : authors read and approved the final manuscript.

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