



The Effect of Katuk (*Sauvagesia androgynus* (L) Merr) Leaf Biscuit on Increasing Prolactin Levels of Breastfeeding Mother

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Abstract

Prolactin is one of the important hormones for increasing the synthesis and secretion of breast milk. Katuk (*Sauvagesia androgynus* (L) Merr) leaf biscuits are standardized and practical processed food products that are substituted with katuk leaf extract and have met the requirements as additional food for breastfeeding mothers. In addition to nutritional content, katuk leaf biscuits also contain phytochemical compounds, namely steroids and alkaloids. The purpose of this study was to determine the effect of katuk leaf biscuits on increasing serum prolactin levels of breastfeeding mothers. This research was conducted in the city of Bandung. The design used was a randomized controlled trial. The sample was 45 primiparous postpartum mothers who gave birth at the public health center for Obstetrics and Neonatal Basic Emergency Services (Puskesmas PONED) in Bandung City, consisting of 22 treatment groups and 23 control groups. Sampling is conducted by block randomization. Data were analyzed using the Independent T-test. The results showed that there was an effect of katuk leaf biscuits on increasing serum prolactin levels in breastfeeding mothers. It is suggested that katuk leaf biscuits be used as an alternative as an effort to increase breast milk production so that it can support the success of exclusive breastfeeding.

Introduction

Breastfeeding is a physiological process to provide optimal nutrition to babies. Breast milk (ASI) is the best nutrition for babies because it contains all the nutrients, antibodies, hormones, and immune factors as well as antioxidants that babies need to grow and develop especially during the first six months of life. Breastfeeding is the main source of nutrition for babies to achieve normal growth, development and immunological protection, (Eidelman et al., 2012). UNICEF in 2005 reported that there were 30,000 infant deaths in Indonesia and 10 million toddler deaths in the world every year but this could be prevented by exclusive breastfeeding, (Yulidasari et al.,

2017). Optimal breastfeeding has been shown to be effective in reducing the risk of infectious diseases and preventing the death of infants and toddlers. Infants who are exclusively breastfed have been shown to have a lower risk of various infectious diseases such as diarrhea, respiratory infections, ear infections, pneumonia, urinary tract infections and other diseases such as obesity, diabetes, allergies, inflammatory gastrointestinal diseases, and cancer in the future, (Eidelman et al., 2012). Meanwhile, babies who do not get breast milk, they have a greater risk of death from diarrhea compared to babies who get exclusive breastfeeding, (Lamberti et al., 2011).

The problem that often occurs in

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breastfeeding mothers and is a predictor of decreasing exclusive breastfeeding is the lack of milk production. This problem of breastfeeding mostly occurs in primiparous, women who give birth to babies for the first time (Gunanegara et al., 2012). Inadequate milk production is caused by various factors such as nutritional and non-nutritional factors including hormonal problems, parity, pregnancy, age and psychological factors. Nutritional factors are required by breastfeeding mothers. Nutrients are required for the synthesis of milk and for stimulating the production of hormones that play a role in the production and secretion of milk. The hormones that play a role in this process are the hormones prolactin and oxytocin (Penagos Tabares et al., 2014, Zuppa, 2010).

One of the main hormones that plays a role in the process of lactation is the hormone prolactin. The hormone prolactin is needed to build and maintain lactation. In the mammary gland, the hormone prolactin specifically stimulates DNA synthesis and epithelial cell proliferation as well as the synthesis of milk proteins (casein, lactalbumin), free fatty acids, and lactose. The prolactin hormone specifically stimulates the transcription rate of the milk protein gene, (Hall, 2010). Low levels of the hormone prolactin can inhibit the synthesis and secretion of milk. This has been proven by a study from Hill et al which states that the secretion of milk in mothers stops within three to four days after a decrease in prolactin levels (Hill et al., 2009), whereas an increase in the hormone prolactin occurs during the first week of the puerperium that triggers it. increased milk production (Mortel and Mehta, 2013). Thus, the hormone prolactin is essential for the initiation and secretion of milk at the beginning of lactation and for the maintenance of milk production during lactation. Increased levels of the hormone prolactin are influenced by several factors such as frequency of breastfeeding, previous breastfeeding experience, milk production, and pharmacological drugs including the use of *galactagogues*, (Srinivas et al., 2014). *Galaktogogue* is a synthetic substance or plant molecule that is used to induce, maintain and increase milk production through a complex process involving the interaction of

physical and physiological factors. The most important factor in the lactation process is the prolactin hormone (Mortel and Mehta, 2013, Srinivas et al., 2014).

Katuk is a *galactagogue* that is trusted by the public to increase breast milk production. Katuk (*Sauvopus androgynus* (L) Merr) is a shrub that belongs to the Euphorbiaceae family. Katuk contains nutrients and several compounds that are useful for the synthesis and production of breast milk. Katuk contains nutrients and several useful compounds. The nutritional content of katuk leaves can increase milk production by increasing glucose metabolism for lactose synthesis, (Suprayogi, 2012). In addition, the phytosterol levels in katuk leaves are higher than other types of vegetables (Arista, 2013). Phytosterols have hormonal effects that are estrogenic so that they can increase prolactin and milk production (Penagos Tabares et al., 2014). Another component contained in katuk leaves is papaverine. Papaverin can stimulate the release of prolactin. The papaverine content of old katuk leaves has the effect of relaxing smooth muscle and widening blood vessels, causing an increase in circulating oxytocin and prolactin hormones in the bloodstream (Susan Soka, 2011). A study showed that giving katuk leaf extract was proven to increase the expression of prolactin and oxytocin genes in breastfeeding mice (Soka et al., 2010). Inappropriate processing of katuk leaves can reduce the beneficial effects of katuk leaves, even if too much use or incorrect processing can cause side effects (Bunawan et al., 2015). Therefore, it is necessary to develop alternative preparations for processed katuk leaves which are more practical and standardized with proper and permanent processing so that they can provide beneficial effects without causing side effects.

Katuk can be processed in various forms of processed foods that are more practical and standardized. There are many studies on processed katuk such as biscuits or plain bread without reducing nutritional content and can be accepted by the community (Setyaningsih DN, 2014). Biscuits are snacks which are usually made from wheat flour or other types of flour. Usually, in the process of making biscuits, it is necessary to add fat or oil which functions

to soften or make it crispy so that it becomes more delicious, (Pangaribuan, 2013). Katuk leaf biscuits are standardized and practical processed food products that are substituted with 900 mg of katuk leaf extract. These katuk leaf biscuits have been tested for the quality of biscuits and the results have met the requirements of the Indonesian National Standard (SNI) for biscuits. In addition, organoleptic tests have been carried out on katuk leaf biscuits so that they are suitable for consumption by nursing mothers. Apart from having protein, fat and carbohydrate nutritional content, these katuk leaf biscuits also contain phytochemical compounds (steroid and alkaloid compounds). Research from Mutiara 2016 shows that giving katuk leaf biscuits to mice has proven that katuk leaves can increase the volume of breast milk, (Mutiara, 2016). This study aims to determine the effect of katuk leaf biscuits on serum prolactin levels of breastfeeding mothers.

Method

This research was conducted at the public health center for Obstetrics and Neonatal Basic Emergency Services (Puskesmas PONED) in Bandung City. These locations are Puskesmas Garuda, Puskesmas Pagarsih, Puskesmas Puter, Puskesmas Padasuka, and Puskesmas Ibrahim Adjie and were conducted from March to May 2016. The population in the study were all postpartum mothers in those five public health center (Puskesmas PONED) in Bandung City. The samples were postpartum mothers who fulfilled the inclusion and exclusion criteria. The sample in this study were 45 people, consisting of 22 people in the treatment group and 23 people in the control group. The inclusion criteria in this study were mothers who gave birth for the first time (primiparous), did not use other drugs to increase milk production, exclusively breastfed their babies, their babies were full-term, single babies, healthy, birth weight babies around ≥ 2500 grams, and willing to be a respondent. Meanwhile, the exclusion criteria were mothers who had breast problems such as drowning nipples, a history of breast surgery, diabetes mellitus and / or hypertension, smoking and or drinking alcohol, mothers and / or babies who had severe complications and needed treatment and babies with congenital abnormalities. Research subjects will be

excluded from the study (dropout) if during the study they experience one or more of the following criteria, namely the mother does not consume the recommended biscuits for at least two consecutive days and / or the baby is given formula milk and / or nutritional intake other than breast milk.

This study used a Randomized Controlled Trial (RCT) design. The independent variable was the provision of katuk leaf biscuits while the dependent variable was the serum prolactin level. The sampling technique used block randomization, to determine each sample in the treatment and control groups. Randomization was performed by the enumerator and was unknown to the researcher. The treatment group was given katuk leaf biscuits while the control group was given katuk leaf biscuits. The treatment was given for 14 days and research subjects had to eat 9 biscuits a day. The data obtained are primary data based on the measurement results of basal prolactin hormone levels of breastfeeding mothers using the ELISA (Enzyme-linked Immunosorbent Assay) method which was conducted at the Molecular Genetics Laboratory of the Faculty of Medicine, Padjadjaran University. The basal prolactin hormone is obtained within 3-4 hours after the patient wakes up, which is around 8-10 am. This time is the most accurate sampling time for the hormone prolactin.

The research procedure was started by selecting the research subjects according to the inclusion and exclusion criteria. After that, the researcher provides information by explaining the objectives and research procedures to the research subjects. Then, ask for consent to be a research subject in the form of a signature on the informed consent sheet provided. The next step, researchers took blood samples which were carried out at a time span of 07-10 AM to obtain basal serum prolactin levels for nursing mothers. Blood was drawn on the median cubital vein with 3 cc. The researcher coordinated with the enumerator to give biscuits based on randomization results. The types of biscuits provided by the enumerators were not known by the research subjects or researchers. Enumerators provided counseling on how to eat biscuits and told the research subjects to record the number of biscuits

consumed each day. This is recorded in the form posted on the research subject's house provided by the researcher. The research subjects had to consume one packet of biscuits containing the nine biscuits within 24 hours during the 14 days of the puerperium. Biscuits were given by the enumerator every two days and then monitoring was carried out including health conditions, frequency of breastfeeding, complaints experienced by research subjects, and compliance with biscuits. On the 15th day, researchers took back a venous blood sample with 3 cc to measure the basal serum prolactin levels of the mother after giving biscuits for 14 consecutive days.

After the data was collected, the researcher performed data processing including editing, scoring, data normality testing and coding. In this study, data analysis using the help of a computerized program includes univariate and bivariate analysis. Univariate analysis was performed to describe the characteristics of the variables studied. Bivariate analysis to test the effect of katuk leaf biscuits on increasing serum prolactin levels of breastfeeding mothers using

the Independent T-test statistical test is a form of statistical test used to test the comparative test hypothesis of numerical categories. The significance value or indication that there is a difference in serum prolactin levels in the treatment group and the control group is shown if the p value is <0.05 .

Result and Discussion

Table 1. below provides an overview of the characteristics of the research subjects who participated in this study. The results showed that there were no differences in terms of education, occupation, nutritional status, age, frequency of breastfeeding, stress levels, and compliance between the katuk leaf biscuit group and the control biscuit group ($p > 0.05$). In this study, all respondents were primiparous with an average age of 21 years and an age range of 16-28 years. Breastfeeding problems such as milk production are less common in primiparous. The results of previous studies showed that 56.4% of delayed lactogenesis occurred in primiparous (Larasati, 2014). Respondents in the treatment group and the control group had no differences in terms of age, education,

Table 1. Characteristics of respondents

Characteristics	Group		P
	Treatment (%) (n=22)	Control (%) (n=23)	
Education Level			0.956 ^a
Primary School	2 (9.1)	2 (8.7)	
Junior High School	7 (31.8)	7 (30.4)	
Senior High School	9 (40.9)	11(47.8)	
University	4 (18.2)	3(13.0)	
Occupation			0.722 ^b
Work	4 (18.2)	6 (26.1)	
Don't work	18 (81.8)	17 (73.9)	
Nutritional Status			0.559 ^a
Low	5 (22.7)	7 (30.4)	
Medium	17 (77.3)	16 (69.6)	
High	0	0	
Obesity	0	0	
Frequency of breastfeeding			0.626 ^a
< 8x	0	0	
8-12	14 (63.6)	13 (56.5)	
>12	8 (36.4)	10 (43.5)	
Stress			0.672 ^a
Light	9 (40.9)	8 (34.8)	
Moderate	13 (59.1)	15 (65.2)	
Weight	0	0	
Age			0.850 ^c
x (SD)	21.7(3.4)	21.9(3.2)	
Range	17-28	16-28	
Compliance			0.978 ^d
Median	100	100	
Range	92.9-100	92.9-100	

Test description: ^a Chi Square, ^b Fisher Exact, ^c Independent T-test ^d Mann Whitney

Table 2. The relationship between katuk leaf biscuits and prolactin levels

Characteristics	Group		p
	Treatment (n=22)	Control (n=23)	
Prolactin levels - Pre			
x (SD)	139.7 (46.6)	143.3 (40.45)	0.394 ^c
Prolactin levels - Post			
x (SD)	149.1 (44.9)	118.5 (50.5)	0.019 ^c
Increase Prolactin			
x (SD)	9.37(51.2)	-24.73 (67.3)	0.032 ^c

Test description: ^c Independent T-test

occupation, nutritional status, frequency of breastfeeding, stress levels and compliance with biscuits. Thus, the research subjects in this study were homogeneous. The following is a table of respondent characteristics. While the results of research on differences in prolactin levels in the treatment and control groups can be seen in Table 2.

Table 2 shows that on the first day of the puerperium, before the intervention administration, there was no significant difference in serum prolactin levels between the two groups (the katuk leaf biscuit group and control biscuits) but after the end of the study, the 15th day of the puerperium or after administration. The intervention showed that there was a difference in serum prolactin levels between the group given katuk leaf biscuits and the control biscuit group ($p < 0.05$) and there was a significant difference in the increase in serum prolactin levels between the katuk leaf biscuit group and the control biscuit group. The result of statistical test shows that the value is $p < 0.05$. After 14 days of giving katuk leaf biscuits, the treatment group experienced an increase in prolactin levels by 9.37 ng / ml while the control group experienced a decrease in serum prolactin levels by 24.73 ng / ml. Based on the statistical test, it shows that there is a significant difference in the increase in serum prolactin levels between the katuk leaf biscuit group and the control biscuit ($p < 0.05$), it can be concluded that the provision of katuk leaf biscuits has an effect on the increase in serum prolactin levels for breastfeeding mothers. This is consistent with the results of research by Soka (2013) which showed that giving 173.6 mg / kg of katuk leaf extract to lactating wistar rats for 12 days increased 14.65 times the expression of the prolactin gene and 22.2 times the expression of the oxytocin gene compared to the group

control, (Soka et al., 2010).

Prolactin hormone levels in breastfeeding mothers fall by around 50 percent during the first week after giving birth. The basal level of the hormone prolactin in nursing mothers averaged 90 ng / ml at 10 days after delivery. This level slowly decreases over the 180 postpartum days, 44.3 ng / ml. Thus, to maintain breast milk production, it is necessary to have high levels of the hormone prolactin. Basal prolactin hormone levels need to be increased within the first week of breastfeeding to stimulate the initiation and secretion of milk. It is proven that in the case of mothers with premature babies with gestational age ≤ 36 weeks, there is no milk production and it turns out that the basal prolactin hormone level is 45 ng / ml. Whereas for mothers who deliver term babies and are able to express breast milk, it turns out that the level of the hormone prolactin reaches 90-110 ng / ml. Thus, giving galactogogue to mothers who give birth preterm is very useful to induce an increase in prolactin hormone levels up to the equivalent of mothers who give birth at term so that this can increase milk production (Hill et al., 2009). This is in line with research conducted by Mortel et al. Which shows that galactogogue herbs can increase serum levels of the hormone prolactin, oxytocin, breast milk volume, infant weight, and breast milk composition (Mortel and Mehta, 2013).

Katuk is a galactogogue herb that is trusted by the people of West Java to increase breast milk production. This is supported by the results of research which show that giving katuk leaf extract to wistar rats for 12 days can increase prolactin gene expression by 14.6 times compared to the group without katuk leaf extract (Soka et al., 2010). This happens because katuk leaves contain the alkaloid papaverine which has a relaxing effect on

smooth muscle and dilates blood vessels. It also causes the circulating hormone oxytocin and prolactin to increase blood flow. In addition, the phytosterols contained in katuk leaves have a hormonal effect from chemical sterols which are estrogenic. This molecule induces the expression of the prolactin hormone receptor. A study explains that phytoestrogens are compounds that can increase the hormone prolactin and milk production. Phytoestrogens are one of the phytosterols. Phytoestrogens have an action similar to estrogen (E2). This triggers the expression of the prolactin gene through 2 independent pathways and an unknown pathway in the pituitary lactotrophic cells as a producer of the prolactin hormone. The first pathway through the intracellular receptor E2 (E2R) which ultimately increases prolactin gene expression and increases milk secretion. This effect is mediated by the triggering pathway of the α isoform of the estrogen receptor membrane (mE2R). The second pathway is blocking the activation pathway by dopamine D2R receptors, stimulating the production of the hormone prolactin, proliferation of lactotrophic cells in the pituitary by increasing the cAMP pathway in PKA phosphorylase which triggers expression of the prolactin gene. Therefore, the secretion of the prolactin hormone into the vasculature increases and affects the mammary alveoli cells which contain lots of prolactin receptors and ultimately can increase milk production (Penagos Tabares et al., 2014, Susan Soka, 2011). This is also supported by Setyaningsih's research which states that the katuk plant can increase breast milk production, presumably based on the hormonal effect of chemical sterols which are estrogenic. Katuk leaves contain steroids and polyphenols which can increase prolactin levels and the content of other micronutrients found in katuk. 100 g of katuk leaves contain 204 mg of calcium and 200 mg of vitamin C, in addition to fiber and other nutrients such as protein, carotene, vitamins A and B and chlorophyll, (Setyaningsih et al., 2017).

Although katuk leaf biscuits had an effect on increasing serum prolactin levels, in this study there were still research subjects in the treatment group who experienced a decrease in serum prolactin levels and conversely, there

were research subjects who experienced an increase in serum prolactin levels in the control group. This happens because many factors can influence this. This is because each individual has different biological characteristics so that the response to stimuli is different even though in this study it was limited that the research subjects were primiparous who had never breastfed before. It is expected that the research subjects have the same prolactin receptors so that the number of prolactin receptors circulating in the blood is not much different. Another condition that causes this is the baby suction during each breastfeeding (duration of breastfeeding). The strength of the babies' suction was different, although in this study the frequency of breastfeeding in the control and treatment groups was not different. This has limitations because only the quantity of suction is assessed without considering the strength of the suction which describes the quality of the baby's suction. In addition, the secretion of the hormone prolactin is very complex, which is influenced by other hormones and may have different characteristics for each individual. Based on related sources, the secretion of the prolactin hormone is also controlled by Prolactin-Releasing Factors (PRF) such as Thyrotropin-Releasing Hormone (TRH), Vasoactive Intestinal Peptide (VIP), oxytocin, angiotensin II and serotonin, (Hall, 2010). In this study, the hormones involved in the secretion of the hormone prolactin were not examined so that it could not explain in detail the relation of these hormones to the secretion of the hormone prolactin. Further research is required to explore the exact mechanism of action at the molecular level in relation to the factors that influence the increase in prolactin.

This study has a research limitation, namely the examination of prolactin hormone levels is only conducted twice at the pre and post time which is conducted on the first day of childbirth and the 15th day of the puerperium. In this study, no midterm observation of prolactin levels was carried out so that it could not assess the trend of the increasing pattern of prolactin hormone in breastfeeding mothers.

Conclusion

Based on the results of the study, it can be concluded that there is an effect of giving

katuk leaf biscuits during the first 14 days of the puerperium in primipara on an increase in serum prolactin levels. Suggestions in this study are the provision of katuk leaf biscuits is expected to be used as an alternative to increase milk production so that it can support the success of exclusive breastfeeding.

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