The Comparison Effect of Small-quantity Lipid-based Nutrient Supplements and Biscuit on hemoglobin level of infants in Indonesia

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Abstract
Small-quantity lipid-based nutrient supplements (SQ-LNS) with enriching fat and vitamin and mineral can fill the gap of iron intake and requirement as well as the potential for reducing the prevalence of anemia among childhood. The purpose of the study was to assess the impact of SQ-LNS and biscuit on hemoglobin concentrations and reducing of incidence anemia. A 6-month non-randomized controlled trial was performed among 168 infants who received 20 g of LNS or 3 pieces biscuits or no intervention. Hemoglobin was measured at 0, 3, 6 months of intervention using hemocue autoanalyzer. To compare hemoglobin concentration using Linear Model ANCOVA and logistic regression for the difference in the incidence of anemia. In SQ-LNS group over three-
Month intervention, the adjusted mean hemoglobin concentration increased significantly by 0.73 g/dl ($p < 0.05$), the prevalence of anemia decreased by 19.5% and a significant reduction in the incidence of anemia by 100% ($p < 0.05$). Over six-month intervention, the adjusted mean hemoglobin concentration only increased significantly by 0.15 g/dl, the prevalence decreased by 5.6% with a reduction in the incidence of anemia by 79%. In Biscuit group, over 3-month and 6-month intervention, the hemoglobin concentration decreased by 0.17 g/dl and 0.36 g/dl with the prevalence of anemia was increased by 24.2% and 17.8% as well as reducing in the incidence of anemia by 63% and 27%. SQ-LNS was more effective in improving hemoglobin level and reducing of incidence anemia among infant 6-12 months over three-months intervention than the biscuit.

Key words: SQ-LNS, biscuit, hemoglobin, anemia

INTRODUCTION

In the fact, 270 million children under the age of 5 years (270 million) are affected by anemia with the highest prevalence in developing countries [1]. Anemia during childhood is also a common public health problem in Indonesia. Basic Health Research 2013 reported that the prevalence of anemia among children 12-59 months of age was 42.6% [2]. A survey in Bangkalan district, Indonesia, showed that the prevalence of anemia was 46.7% among children age 6 to 23 months old [3]. The prevalence of anemia decreased from 58.4% to 42.6% among children aged 6-11 months and 12-23 months. Anemia prevalence of 40% or more in any population is considered as a severe public health concern [4].

Anemia as a result of iron deficiency with a low concentration of hemoglobin has adverse functional consequences and may impair cognitive and motor development and cause fatigue and low productivity [5]. The cause of anemia due deficiencies of iron in young children are inadequate intake or poor absorption [6], and requirement is high at the start of life due to rapid growth, while their stores are low [7].

The period 6-24 months is an important phase because of children transition from breast milk to complementary food, as well as require high amounts of micronutrient relatively small quantities of foods to support growth and development. A breastfed infants at 6-8 months of age need more than 4 times of zinc density (per 100 kcal of food) and 9 times of iron density than an adult male needed [8]. Vitta and Dewey (2012) have analyzed using linear programming of unfortified complementary food and indicated that there would be gaps in iron and zinc intakes and will be met with unrealistic amounts of liver that must be consume daily [9].

Currently, home fortification of complementary foods with multiple micronutrient powders (MNP) has been proven as effective as iron drops in improving hemoglobin status and reduction of anemia [10]. Apart from home fortification with MNP, small-quantity lipid-based nutrient supplements providing energy, protein, essential fatty acids, and micronutrients can be used as the food supplement to complement the diet and prevent potential deficiencies. Lipid-based nutrient supplements (LNS), which can be added to complementary food at the time of consumption, are designed to prevent undernutrition and to promote healthy growth and development [11].

Small-quantity lipid-based nutrient supplements (SQ-LNS) can fill gap iron intake and high needed as well as the potential for reducing the prevalence of anemia among childhood. In Indonesia, the provision biscuit MP-ASI used in supplementary feeding programs for children younger than five years old and still not yet for evaluating of effect both growth and anemia.
The purpose of the study was to compare the effect of supplementation with SQ-LNS and fortified biscuits on the hemoglobin concentration among infants in a rural area, Indonesia. Sub-objectives included describing changes in the prevalence and incidence of anemia in the participants.

METHODS

Study Design

The study was conducted in 50 villages of eight sub-districts in Bangka-lan Districts, West Madura Island, East Java Province, Indonesia between October 2014 and August 2015. A community-based, non-randomized, controlled intervention was selected for the study design.

The study design was chosen due to the different type of product of intervention i.e., food supplement using peanut paste with multiple vitamin and mineral fortified and biscuit.

The study compared the effects of three groups schemes with small-quantity lipid-based nutrient supplements (SQ-LNS) in the form of fortified peanut-paste, Biscuit MP-ASI, and a control group. Infants in the control group were not provided with any complementary food supplement during the study period, but they received supplementation with biscuits for one-month consumption after the end of study. In the SQ-LNS group, infants received SQ-LNS 20 g per day in 1 sachet (energy ~118 kcal, protein, essential fat acid, 22 vitamins and minerals) for six months. SQ-LNS were provided by Nutriset SAS (Malaunay, France). In another treatment group, infants received biscuits in 3 pieces per day @30 g (energy ~35 kcal, protein, 16 vitamins, and minerals) for six months. The biscuit was donated by Ministry of Health, Indonesia and was developed for a national supplementary feeding program. The energy and nutrient contents of a daily ration SQ-LNS and biscuit was reported in the previous article [12]. The child’s caregiver was advised to feed mixed in complementary food and divided into two daily doses (@10 g).

SQ-LNS and biscuit were delivered by a field team to home respondents’ every month for six-month’s intervention period. The field team distributed 30 sachets of SQ-LNS or 8 packages of biscuits (96 pieces) per infant and collected information on the use and possible complaints or adverse events. The field team distributed 30 sachets LNS or 8 package biscuit (96 pieces) per infants and collect information on the use and possible complaint or adverse events.

Sources of data

The primary variable in the study was the change of hemoglobin concentration, prevalence, and incidence of anemia after 3 months and 6 months intervention.

The other variables were child characteristic (sex, age, nutritional status), maternal characteristic (age, length of education, occupation, nutrition education), and household characteristics (household food security status, household dietary diversity), adherence to SQ-LNS and biscuits and morbidity status.

Participants

Potentially age-eligible children were identified from infant cohort data from midwives. The inclusion criteria included infant more than 6.0 months of age who had consumed complementary food, resided in the study area, and had the signed informed consent from a legal guardian. The exclusion criteria were severe stunting (LAZ <-3 SD), acute infectious disease (i.e., TBC), the presence of edema, history of peanut allergy, severe illness requiring hospitalization, and concurrent participation in another clinical trial.

The sample size was calculated on the basis expected values of hemoglobin change. In the previous study, the mean
hemoglobin change 0.88 (10.57 g/dl and 11.45 g/dl), [13]. Assuming a standard deviation of 1.35 with a power test of 80% (1-β=0.84) and a 95% confidence interval with a one-sided test of 1.645. The minimum sample required was 30 infants per group. The total samples are 168 infants for three group based on the calculation sample size with another variable (length gain).

**Data Collection**

The child’s, maternal, and household characteristics were collected at baseline using a structured questionnaire. The instrument of nutrition knowledge was using a questionnaire, which has with 10 questions on breastfeeding and complementary feeding. Based on validity analysis, using product moment testing showed significant correlations (p<0.01) and reliability of the instrument to assess nutritional knowledge (Cronbach’s alpha = 0.222). Household category based on food security status was assessed using nine questions on the household’s food access [14]. The adherence of SQ-LNS and biscuit and morbidity status was collected at monthly monitoring using questionnaire by field enumerators.

The measurement of blood hemoglobin concentration was using Photo-meter Hemocue haemoglobinimeter, Angelholm, Sweden) by trained field enumerators at 0, 3, 6 months of intervention. The HemoCue® and the cyanmethemoglobin are the methods recommended for uses in surveys to determine the population prevalence of anemia. The HemoCue® is based on the cyanmethemoglobin methods and can be fix since be stable and durable in field setting [15]. The prevalence and incidence of anemia (Hb<11 g/dl).

**Data Management and Analysis**

Multilevel checked by the self-enumerators, other field workers, and field supervisors were done in the field to assurance quality data. Statistical analysis was done using IBM® SPSS®, version 20.0 (IBM Corp., NY, USA). Statistical significance was defined as p<0.05.

The distribution of data was checked for normality by using Kolmogorov-Smirnov test and homogeneity of data variance by using Levene test. Adjusted for covariate was performed using Linear Model ANCOVA to compare hemoglobin concentration. A difference in the incidence of anemia was compared with logistic regression adjusting for respective baseline value.

The study was approved by the Ethical Committee of Faculty of Public Health, University of Diponegoro (Certificate No. 146/EC/FGM/2014). Eligible infants were enrolled in the study after collecting informed consent from at least one parent or caregiver.

**RESULTS**

Of the 324 infants screened, 269 of them were enrolled. At the end of the study were 67 infants (24.9%) dropped out of the study and 34 infants were excluded from data analysis due to age < 6.0 months. Reasons for dropping out were: migration to other areas temporarily (n=43), not receiving supplementation for more than 3 months (n=18), refusal to continue participating in the study due to the child not liking SQ-LNS or biscuits or vomiting (n=4), mother being busy (n=1), and the child having severe illness requiring hospitalization (n=1). The dropout rate among the study groups was not significantly different with 27.4%, 27.8%, and 20.2% for the Control, SQ-LNS, and Biscuit groups, respectively. Potential biases associated with loss to follow-up were assessed.

The flowchart of participation, baseline characteristic, and adherence to SQ-LNS and Biscuit as well as morbidity status have presented in the previous article [12].
The adherence of SQ-LNS and biscuit and associated factors have been shown in the previous article [16].

**Effect of SQ-LNS and Biscuit on Blood Hemoglobin**

At baseline, there was no significant difference between groups for mean Hb values (10.27 g/dl, 10.32 g/dl, 10.43 g/dl for Control group, SQ-LNS group, and Biscuit group), shown in Table 1. Over 3-month intervention period, hemoglobin levels were 9.93 g/dl, 11.05 g/dl, 10.26 g/dl for Control group, SQ-LNS group, and Biscuit group, respectively (p=0.018). The mean hemoglobin concentration increased significantly by 0.73 g/dl in SQ-LNS group and decreased by -0.17 g/dl in Biscuit group and -0.34 g/dl in Control group.

At the end intervention, over 6-month intervention period, hemoglobin levels were 9.98 g/dl, 10.47 g/dl, 10.07, for Control group, SQ-LNS group, and Biscuit group, respectively (p=0.035). The mean hemoglobin concentration increased by -0.15 g/dl in SQ-LNS group and decreased by -0.36 g/dl in Biscuit group and -0.29 g/dl in Control group.

**Effect of SQ-LNS and Biscuit on Prevalence Anemia**

There was no significant difference in the prevalence of anemia at baseline, after the 3-month and 6-month intervention periods (p>0.05), Table 2. At baseline, participants in Control group (63.3%) had the prevalence of anemia was lower than SQ-LNS (79.5%) and Biscuit group (75.5%), (p>0.05).

Over three-month intervention period, the significant hemoglobin level greater and resulted in the lowest prevalence of anemia in SQ-LNS with 60.0%, compared with 80.0% of children in Biscuit group and 87.5% in Control group. Prevalence of anemia in SQ-LNS decreased by 19.5 percentage point, whereas in Biscuit and Control group increased to 24.2% and 15.5%, respectively. Compared to the control, children in SQ-LNS group had a relative risk (RR) (95% CI) of 0.21 (0.04-1.30, p=0.095) of being anemia at 3-month intervention. Meanwhile, in Biscuit group had an RR of being anemia was 0.57 (0.07-4.87, p=0.609).

At the end of the study, the significant hemoglobin level greater and resulted in the lowest prevalence of anemia in SQ-LNS with 73.9%, compared 93.3% of children in Biscuit group and 83.3% in Control group. Over 6-month intervention, the prevalence of anemia in SQ-LNS decreased by 5.6 percentage point, whereas in Biscuit and Control group increased to 17.8% and 20.0%, respectively. Compared to the control, children in SQ-LNS group had a relative risk (RR) (95% CI) of 0.57 (0.19-1.66, p=0.310) of being anemia at 6-month intervention. Meanwhile, in Biscuit group had a RR of being anemia was 2.80 (0.65-12.09, p=0.168).

**Effect of SQ-LNS and Biscuit on Incidence Anemia**

The incidence of anemia over 3-month intervention period was 40 events (4/10), 0, and 20.0 events (2/10) in Control group, SQ-LNS group, and Biscuit group. The incidence of anemia over 6-month intervention period was 34.8 events (8/23), 10.0 events (3/30), and 27.9 events (12/43) in Control group, SQ-LNS group, and Biscuit group.

A provision SQ-LNS resulted in 100% (p=0.011) reduction in the incidence of anemia after 3-months intervention period and 79% (p=0.029) after 6-months intervention. In Biscuit group, thus resulted in 63% (p=0.342) reduction in incidence anemia after 3-months intervention and 27% (p=0.565) after 6-months intervention period.
### Table 1. The hemoglobin concentration among participants by study group

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Control</th>
<th>SQ-LNS</th>
<th>Biscuit</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin, g/dl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>10.27±1.06</td>
<td>10.32±0.86</td>
<td>10.43±1.30</td>
<td>0.806</td>
</tr>
<tr>
<td>(95% CI: 9.87-10.67)</td>
<td>(95% CI: 10.04-10.60)</td>
<td>(95% CI: 10.07-10.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid intervention</td>
<td>9.93±0.86(^a)</td>
<td>11.05±1.26(^b)</td>
<td>10.26±1.02(^a)</td>
<td>0.018</td>
</tr>
<tr>
<td>(95% CI: 9.47-10.38)</td>
<td>(95% CI: 10.35-11.75)</td>
<td>(95% CI: 9.53-10.99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End</td>
<td>9.98±0.97(^a)</td>
<td>10.47±1.09(^b)</td>
<td>10.07±0.60(^a)</td>
<td>0.035</td>
</tr>
<tr>
<td>(95% CI: 9.65-10.31)</td>
<td>(95% CI: 9.89-10.25)</td>
<td>(95% CI: 9.89-10.25)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SQ-LNS: small-quantity lipid-based nutrient supplement.
Data are mean±SD. Values in the same row with different superscript letters are significantly different (p<0.05).
Analysis with ANOVA adjusted for baseline.

### Table 2. Point prevalence and incidence anemia among participants by study group

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Control</th>
<th>SQ-LNS</th>
<th>Biscuit</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Point Prevalence Anemia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>63.3%</td>
<td>79.5%</td>
<td>75.5%</td>
<td>0.297</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>1.0 (ref)</td>
<td>2.24 (0.77-6.57)</td>
<td>1.78 (0.67-4.70)</td>
<td></td>
</tr>
<tr>
<td>Midline</td>
<td>87.5%</td>
<td>60.0%</td>
<td>80.0%</td>
<td>0.191</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>1.0 (ref)</td>
<td>0.21 (0.04-1.30)</td>
<td>0.57 (0.07-4.87)</td>
<td></td>
</tr>
<tr>
<td>Endline</td>
<td>83.3% (30)(^{a,b})</td>
<td>73.9% (34)(^b)</td>
<td>93.3% (42)(^a)</td>
<td>0.045</td>
</tr>
<tr>
<td>RR (95% CI)</td>
<td>1.0 (ref)</td>
<td>0.57 (0.19-1.66)</td>
<td>2.80 (0.65-12.09)</td>
<td></td>
</tr>
</tbody>
</table>

**Incidence Anemia**

**3-months follow up**

| Ever developed anemia | 40.0\(^a\) | 0\(^b\) | 20.0\(^{a,b}\) | 0.039   |
| RR (95% CI)           | 1.0 (ref)| 0      | 0.37 (0.38-0.05) |         |
| Ever developed moderate anemia | 30.0     | 0      | 10.0          | 0.078   |

SQ-LNS: small-quantity lipid-based nutrient supplement.
Data are mean±SD. Values in the same row with different superscript letters are significantly different (p<0.05).
Analysis with ANOVA adjusted for baseline.
DISCUSSION

The study was carried out to study the effect of a daily provision small-quantity lipid-based nutrient supplement on hemoglobin concentration and reducing anemia. We compared the effect on biscuit developed by Minister of Health for supplementary food program. The interventions of complementary food supplement are small-quantity lipid-based nutrient supplement with 20 g daily portion and biscuit with 3 pieces (30 g) daily portion.

Prevalence of anemia was more than 50% in all study groups at baseline and confirmed that anemia is the major public health problem in infants and young children in Indonesia. That was in accordance with data from another study showing an anemia prevalence of 58.4% among infants 6-11 months and 42.6% among children 12-23 months of age [3]. The data showed that an intervention was needed for infant and childhood to combat anemia.

The provision small-quantity lipid-based nutrient supplement with 20g daily doses for children aged 6-12 months showed mean hemoglobin values increased significantly by 0.65 g/dl (p<0.05) after 3 months of intervention. In another study in Peru, the effect of LNS on children aged six to eleven months old increased 0.67 g/dl (p<0.05), [17]. Intervention home fortification with micronutrient nutrient powder (MNP) in Dhaka informed that intervention MNP for four-month to children under two years also had significant 2.5% points enhancement of hemoglobin level [18].

Provision of small-quantity lipid-based nutrition (SQ-LNS) in the study could significant reducing of 19.5% of proportion anemia and of 100% of incidence anemia for three-month intervention. Moreover, SQ-LNS can reduce the proportion of anemia by 27 percent point in Peru [17]. In another study, intervention with Nutributer showed reducing prevalence anemia by 22% for six months intervention [13]. The result of this study has the impact on reducing the prevalence of
anemia was greater than finding in Dhaka with MNP which statistically significant reduction of 9% in the 2 months MNP group and 12% in the 4 months MNP group [18]. The analysis of effect MNP can reduce anemia by 31% and iron deficiency by 51% in infants and young children [10].

The hemoglobin and vitamin C content of the daily serving of SQ-LNS was higher than the biscuit. A 20 g of SQ-LNS per day, provided 6 mg Fe, equal to 85.7% of recommended dietary allowance (RDA) and 30 mg vitamin C (60% of RDA). 3 pieces of biscuit per day, provided 4.8 mg Fe (25.7% of RDA) and no vitamin C.

The strength of the study was similar to characteristic participants and those who dropped out. The distribution and measure of compliance by field team every month and could support the caregiver to regularly giving SQ-LNS or biscuits and also discuss to resolve any adverse events due to consumption of SQ-LNS or biscuits. Trained field team selected with nutrition backgrounds and educations performed the measurement of anthropometric data, interviews using structured questionnaires and conduct a 24-hour recall. The limitations of the study were that the study design was not a randomized control trial because of the different type of product intervention (peanut paste and biscuit), no randomization for allocation of participants; there was no blinding of group allocation and no masking mothers or field workers to who received SQ-LNS or biscuits.

CONCLUSION

In conclusion, the study showed that small-quantity LNS (SQ-LNS) was more effective in improving hemoglobin level and reducing prevalence and incidence anemia in children 6-12 months over three-months intervention.

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