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Dermatology Research

The Effectiveness of Corn Oil Application on Reducing the Risk of Impaired Skin Integrity in Preterm Infants with Parameters Skin Condition Score

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ABSTRACT

Background: *Changes in skin integrity can cause extensive skin damage and become risk factor for infection. This is what makes preterm infants have a higher risk for infection because of the underdeveloped stratum corneum as a barrier. Erythema, scale, prick marks, excoriation, erosion, or crusting may represent barrier impairement. Those condition could be assessed through clinical observation using skin condition score. The application of natural emolient such as corn oil with its antimicrobial properties could be a potentially beneficial topical agent for preterm infants.*

Aim: *proving effectiveness of topical corn oil on reducing the risk of impaired skin integrity of preterm infants with parameters skin condition score.*

Methods: *Searching the electronic database Pubmed-MEDLINE, Scopus, ProQuest, Scopus, Cochrane library, ClinicalTrials.gov, and Google Scholar*

Results: *There are 5 articles included in the qualitative study and 2 articles included in the meta-analysis. The meta-analysis of the effect of topical corn oil compared with control showed the heterogenity test with Tau2=0.16 df=1; p=0.12, I2=58%. The value of the Q statistic was z value = 2,53 (p < 0.01). The results of the overall meta-analysis show that the overall risk ratio value between intervention group compared to control was 0,41[-0.20,-0.82] (p<0.01). It means that the administration of topical corn oil can significantly reduce the risk of impaired skin integrity on preterm infants.*

Conclusions: *The application of corn oil can significantly reduce the risk of impaired skin integrity on preterm infants.*

Keywords

Corn oil, Parameters skin condition score.

Introduction

Indonesia is one of the country with the highest neonates mortality rate, 12.41 per 1,000 births in 2019. According to World Health Organization (WHO), the risk of death in children is mainly faced in the first 28 days of life, where 47% occurs in the neonatal period with infection as one of the causes [1]. Preterm infants have a higher risk of infection due to the risk of impaired skin integrity by the underdeveloped stratum corneum as a skin barrier. The skin is a multifunctional organ that has an important role through its barrier function, such as protection from mechanical trauma, thermoregulation, defense against microbes, and prevention of loss of body fluids. This barrier is formed in the uterus during the third trimester [3]. Early birth in preterm infants causes immaturity of the barrier development, in the form of a thinner stratum corneum, so that the baby's skin becomes incompetent to prevent transepidermal

water loss (TEWL), increased transcutaneous absorption of external agents, microbial invasion, and contains less antimicrobial peptide (AMP) and natural moisturizing factor (NMF). The skin becomes dry and scaly as a result of increased desquamation by the accelerated maturation of the stratum corneum when the baby's skin is in contact with the extrauterine environment. The absence or low amount of vernix caseosa in preterm infants can also reduce skin hydration and be less supportive of acid mantle formation. Changes in skin integrity from dry conditions or traumatic injury can cause extensive skin damage and result in changes in fluid homeostasis, thermoregulation, caloric expenditure, and become risk factors for infection. Some of the factors mentioned above indicate that preterm infants need an extra care to maintain the integrity of their skin so as to prevent infection.

Symptoms that can be an early sign of a risk of infection is an impaired skin integrity, including erythema, erosion, excoriation, or crusting. These can be assessed using skin condition score or its modification obtained from clinical observations of preterm infant's skin. The higher the score for the skin condition, the more severe the impaired skin integrity of preterm infants, which may lead infants to have a more serious infection. Corn oil has been widely used in developing country because it is more affordable and easy to find. Varma SR et al. reported that applying corn oil to the skin can significantly increase the filagrin content in keratinocyte cells so that it can increase skin moisture and improve its function as a barrier [3]. Application of corn oil in preterm infants is expected to reduce the risk of impaired skin integrity on preterm infants.

Material and Methods

Data collection was carried out online using electronic databases including Medline Pubmed, EBSCOhost, Scopus, ProQuest, ScienceDirect, SpringerLink, Elsevier Clinical Key, Cochrane library, ClinicalTrials.gov, as well as hand searching from libraries in Indonesia with a time span until data analysis was carried out. The study sample size was all clinical trials with randomization regarding the administration of corn oil in preterm infant's skin according to the research criteria.

Inclusion Criteria Include

Research using topical corn oil for preterm baby, clinical trials, subjects who were born at 20-37 weeks of gestation and had no pre-existing skin infections, and research outcomes in the form of SCGS or other score assessed against similar clinical criteria.

Exclusion Criteria Studies

Written neither in Indonesian nor English, were case report, serial case, letter, and literature review.

Research Procedures

Information sources and electronic database search strategies include the databases Pubmed-MEDLINE, Scopus, Cambridge Core, Elsevier Clinical Key, ProQuest, Springer Link, Cochrane library, ClinicalTrials.gov, Web of Knowledge, Web of Science, dan World Health Organization international clinical trials registry. Other sources are reference lists, conference proceedings, researchers in the field, and journals. The search for information sources was carried out until the time of data analysis.

The following Medical Subject Headings (MeSH) terms were used to create three subgroups of citations (1) corn oil; (2) virgin corn oil; (3) preterm baby skin. The three subgroups were combined using the Boolean term 'AND' to obtain a subset of citations relevant to the research question. The literature search was performed based on the 2009 PRISMA flowchart. Three researchers conducted an independent literature search and the reference lists of all primary articles and the most recent literature review were checked to identify articles that were not found.

Any disagreements in paper selection and data extraction were resolved by consensus. Using the prepared data extraction forms, data were extracted independently by three researchers. The data recorded were the treatment with corn oil, without intervention, as well as the value of the skin condition score or its modification, such as skin condition grading scale, and skor by Salam et al. (further reffered as Salam score). Study quality was assessed using A revised tool for assessing risk of bias in randomised trials: ROB-2.

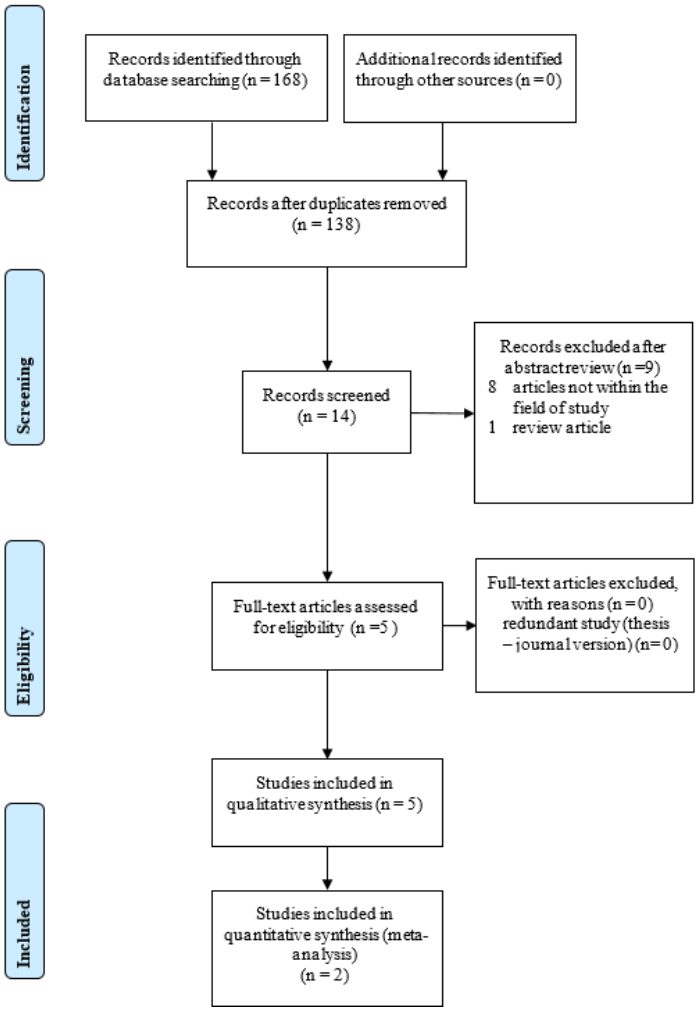
Data Analysis

Prior to data analysis, the collected data will be checked for completeness and correctness of the data. The data will then be entered into the computer. Data on research characteristics such as title and year of research were recorded in the data extraction form. Data in the form of treatment with corn oil, without intervention, as well as the value of the skin condition grading scale and Salam score will be extracted from the research report and entered into the data extraction form. The systematic review assessment and meta-analysis of weighted mean differences between the treatment and control groups will be analyzed using the Cochrane systematic review software (Review Manager (RevMan) [Computer program] Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Result and Discussion

The search for research articles was conducted based on the 2009 Preferred Reporting Items for Systematic Review and Meta Analysis (PRISMA) flowchart (Figure 1).

Data collection was carried out online using electronic databases including Pubmed-MEDLINE, Scopus, ProQuest, Scopus, Cochrane library, ClinicalTrials.gov, and Google Scholar, as well as hand searching from libraries in Indonesia with a time span until the analysis was carried out. The search found 168 articles. After checking the title and removing duplication, there were 14 relevant article titles. The abstracts of these articles were then reviewed, so that 9 articles were excluded, consisting of 8 primary research articles outside the topic of this meta-analysisa and 1 title is a review article. Five articles in the form of complete papers were assessed for eligibility and used in qualitative study, while 2 articles were used in quantitative study to assess the effectiveness of corn oil application on reducing the risk of impaired skin integrity on preterm infants.



Research Characteristics

The locations of these researches were in India (n=2), Pakistan (n=1), Australia (n=1) and Philippines (n=1). The design of these studies are randomized clinical trial. The total sample of 5 studies is 2,750 people. All studies selected a population of preterm newborns as research subjects, with various gestational ages, including 33 weeks with 12 hours of age, ranges >26 and <37 weeks, 37 weeks, <30 weeks, and 34 weeks with age < 72 hours. Two studies used topical corn oil in intervention group compared with the control group, while the other three studies used topical VCO as an emollient given to preterm infants compared to the control group. All studies used a control group that only received routine care for preterm babies in general, without additional treatment. Four out of five studies applied oil with a frequency of 2x a day, while in one study used oil 4x a day. The duration of the treatment was different, where 2 studies gave oil for 28 days, 1 study for 7 days, 1 study for 21 days, and 1 study for 14 days.

Result of Qualitative Data Analysis (Systematic Review)

1. Nangia et al., [4]

This study was conducted on 74 preterm newborns, by comparing the use of topical corn oil (n=37) with the control group (n=37) for 7 days. Gestational age in the corn oil group was 31.89 ± 2.21 weeks and in the control group was 31.00 ± 2.45 weeks. Both groups received standard preterm care. The treatment group was given corn oil spread on the skin starting from under the neck, twice a day, starting at the age of 12-6 hours, while the control group was not given oil. For each session, the nurse on duty will apply 4 ml of corn oil without massaging.

The outcomes assessed in this study were TEWL, skin swab results, and skin condition. The oil group TEWL was checked just before each oil application session using an evaporimeter instrument (VapoMeter®, Delfin Technologies limited, Kuopio, Finland). TEWL in the control group was checked every 12 hours for the first week after birth at the same time as the time of birth. The level of relative humidity and room temperature of the Neonatal Intensive Care Unit (NICU) (RHN and TN) as well as the microenvironmental conditions of the infant (RHB and TB) were also recorded each time the TEWL examination was performed. Skin integrity was evaluated at the end of the first week after birth using SCGS by Lane and Drost, where a score of 0 represented the best skin condition and 9 represented the worst skin condition.

Culture examination of skin swab samples was performed at the end of the first week after birth to evaluate bacterial colonization in the skin. The officers who examined the skin scores, the microbiologist, and the officers who analyzed the data were not aware of the division of the study groups. The oil group showed significantly lower TEWL values at all measurement points from 12 to 168 hours of age. The mean value of TEWL of the corn oil group showed a significantly lower result, 15.67 ± 8.67, than the control group, which was 25.64 ± 26.43. The skin condition showed good results in both groups, with the worst score obtained as much as 3, where the skin score was significantly better in the group that received oil. The highest score of skin conditions in infants after treatment in the oil group was 1 (54.05%), followed by a score of 2 (43.24%), and the least was a score of 3 (2.7%). The highest score in the control group was a score of 2 (70.27%), a score of 3 (18.92%), and a score of 1 (10.81%). Culture examination of skin swab samples showed sterile results in 81% of infants in the oil group and in 43% of infants in the control group. Seven infants in the oil group showed growth of gram-positive coccus bacteria, while in the control group, growth of gram-positive coccus bacteria was found in 16 infants, gram-negative bacilli in 4 infants, and mixed colonization in 1 infant.

2. Salam et al., [5]

This study was conducted on 258 preterm babies born at Aga Khan University Hospital (AKUH), Karachi, Pakistan, with a gestational age range of >26 and <37 weeks for 28 days. The subjects were divided into two groups, the intervention group with corn oil application and the control group. The treatment group was given 5 mL/kg of corn oil, twice a day in all over the body surface (other than the face, scalp, and the location of the intravenous infusion line) for 2-3 minutes. All neonates in the treatment and control groups underwent the same routine care for premature infants.

The study was conducted for 28 days. Neonates in both study

groups were monitored once a week after discharge from hospital until 28 days of age. Mothers of neonates in the intervention group were trained to apply corn oil twice a day at home until the baby was 28 days old and given a new supply of corn oil in a sterile container once a week upon arrival for a control examination. Compliance with oil use was evaluated at each control visit by checking the volume of oil required to refill the previously supplied container to the brim.

The main assessment in this study is the incidence of hospital-acquired blood stream infection (HABSI), which is defined as the presence of a positive blood culture for any pathogenic organism. A blood culture is performed whenever the doctor suspects a systemic infection based on clinical signs, including lethargy, poor peripheral perfusion, fever or unstable body temperature, increased oxygen demand, abdominal distension, inability to eat, bradycardia, or apnea. The secondary outcomes evaluated included weight gain and skin condition, which were assessed daily by the nurse after the baby was bathed using a sponge in both study groups. The skin condition of the neonates was assessed based on the criteria used by Salam et al., where the scores were 0: Skin intact; 1: Reddish skin; 2: Visible peeling skin and appearance of red spots; and 3: if there are bruises and abrasions. Mortality rates were also recorded at 28 days of age.

The incidence of HABSI was found to be greater in the control group than the treatment at the end of the study. A total of 38 neonates were recorded as having HABSI, with the most common etiologies being coagulase negative Staphylococcus spp and Acinetobacter spp. Four neonates were known to be infected by Klebsiella pneumoniae, 3 neonates each by Pseudomonas spp and Staphylococcus aureus, 2 neonates each by Enterococcus spp and Candida albicans, and 1 neonate by Streptococcus spp. The treatment group showed lower HABSI overall, in which only 22 neonates developed infection. Three of them were caused by Acinetobacter spp, 2 by Klebsiella pneumoniae, while the other 4 were caused by coagulase negative Staphylococcus spp, Enterococcus spp, Candida albicans, and Staphylococcus aureus, respectively.

The use of corn oil was proven to significantly improve skin integrity ($p<0.0001$), where 31% or 40 of 128 neonates in the control group showed impaired skin integrity with different degrees of severity; as many as 3 neonates were known to have a score of 3, 20 neonates showed a score of 2, 17 neonates with a score of 1, and 90 others with a score of 0. The treatment group showed fewer skin integrity disorders, namely only in 11% or 15 of 130 neonates, where 2 neonates showed a score of 3, 4 neonates with a score of 2, 9 neonates with a score of 1, and as many as 113 neonates (88.3%) showed a score of 0 or no skin disorders. The length of hospitalization was about 7 days in both groups, where the treatment group was 7.0 days, while the control group was 7.7 days ($p=0.416$). Undesirable side effects due to the use of corn oil in the form of skin reactions, phototherapy burns or other types of infection, were not found in the treatment group.

3. Strunk et al., [6]

This study was conducted in Australia on 72 preterm infants with gestational age <30 weeks and 24 hours postpartum. Subjects were divided into two groups, where 36 neonates in the treatment group received topical VCO, while 36 neonates in the control group did not receive the oil. Gestational age ranged from 23.7–29.9 weeks for the treatment group and 23.0–29.9 weeks for the control group. VCO was given twice a day at 5 mL/kg for 21 days by trained nurses, starting within 24 hours after birth. The oil is applied to the entire surface of the skin, except for the face, scalp, and the site of insertion of a catheter or drain, and is given with gentle strokes without massage. The process of giving corn oil is done within 2-3 minutes. Both groups received routine care for neonates according to the latest guidelines in the NICU, where topical VCO was applied to the treatment group at the same time as routine care to avoid excessive contact with the baby.

The main results assessed in this study were the feasibility of using corn oil in infants who were used as research subjects according to the study protocol, safety or incidence of skin irritation or local infection, and effectiveness in improving the skin condition of preterm infants assessed using NSCS by two independent examiners before the intervention, as well as on days 7, 14, and 21. Secondary outcomes in the form of mortality rates and the incidence of late onset sepsis (LOS) will also be discussed in this chapter, while other results include weight gain, the incidence of body temperature instability, intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, and chronic lung disease will not be discussed further because they are not related to skin integrity.

The median value (IQR) of neonates in the treatment group, which was 1.312 (1.085-1.502) grams, showed better results than the control group, which was 1.296 (1.066-1.492) grams on day 21. Mortality in the treatment group was 0 (0), while the control group is 4 (11,1).

Median (IQR) NSCS in the control group showed a decrease from a score of 3 (3–4) on the first day, to 4 (4–4) on day 21, while neonates in the intervention showed a stable median value from birth until the end of intervention period, 3 (3-3); $p = 0.01$.

The use of corn oil twice a day was considered very feasible. Undesirable events due to the use of corn oil were not found in this study. The incidence of skin irritation showed equal results in both groups, where the treatment group got 9 events (25%), while the control group got 8 events (22.2%); $p = 0.779$. This study showed that the use of topical VCO as prophylaxis on the skin of preterm infants can result in significantly better skin integrity without any unwanted events.

4. Konar et al., [7]

This study was conducted on 2,294 preterm newborns who were divided into two groups randomly using a computer program. Groups A and B consisted of 1146 and 1148 preterm newborn, respectively, with gestational age <37 weeks. The mean gestational

age of the study population was 31.9 ± 3.4 weeks, of which 50.4% of the infants were male. Neonates who were included in group A received 5 ml of VCO, four times a day. Corn oil is applied with gentle massage by the nurse on duty (during hospitalization) and by the mother/family member (after discharge) to all body surfaces other than the face and scalp, after they wash their hands thoroughly. Neonates included in group B received treatment in the form of gentle massage by the nurse on duty (during hospitalization) and by the mother/family member (after being discharged) without applying oil to the skin.

The results assessed in this study that related to skin integrity including skin condition scores and clinical conditions, which were assessed for the presence or absence of sepsis. Other outcomes such as weight gain, serum vitamin D3 level, and neurologic development were not discussed further because they were not related to skin integrity. Skin condition or integrity was evaluated using NSCS at 7, 14, 21 and 28 days of age. The score is determined based on three main parameters: dry skin, erythema, and damage or impaired skin integrity. The NSCS score is obtained by adding up the three scores.

No significant difference in mean NSCS was found between the two groups at study entry (4.9 ± 1.1 compared with 5.0 ± 1.0, p>0.01). However, during the study period it was found that there was a significantly better NSCS score in Group A compared to Group B on days 7, 14, 21 and 28 (p<0.01). The mean score of NSCS on day 28 of group A was 3.9 ± 0.7, while group B was 4.8 ± 1.0.

Earlier maturation was found in the skin of the neonates in Group A. The neonates in Group A were 0.31 times less likely (95% CI: 0.24–0.39) to have decreased skin maturity. Group A also showed a 0.45 times lower (95% CI: 0.39–0.53) probability of developing hypothermia and 0.62 times lower (95% CI: 0.58–0.67) of developing hypothermia. apnea. All of these observations were statistically significant (p<0.01). The incidence of late-onset sepsis (2.7% compared with 3.2%, p>0.01) and the incidence of rash (1.8% compared with 2.0%, p>0.01) were not significantly different between Group A and Group A. Group B. No significant side effects were found due to the use of corn oil. This study shows that the use of corn oil on the skin of neonates can help the process of skin maturity and prevent hypothermia in preterm neonates.

5. Bautista et al., 2005

This study was conducted on 52 preterm infants with gestational age at birth 34 weeks, aged <72 hours to determine the effectiveness of topical VCO administration compared to the control group. The treatment group consisted of 24 infants, while the control group consisted of 28 infants. Infants in the treatment group received topical VCO twice a day for 14 days after being included as study subjects, at a dose of 4 g/kg body weight per session. Patients in the control group received routine skin care according to standards in the NICU, with minimal or no use of topical emollients. Both groups received the same general care.

The main outcome assessed was the incidence of nosocomial infections in the form of sepsis, both clinically diagnosed and supported by bacteriological examination results, pneumonia, meningitis, necrotizing enterocolitis, and urinary tract infections. Other secondary outcomes were not discussed further because they were not related to the skin integrity of preterm infants.

All patients underwent routine blood cultures at the start of the study within 48 hours of starting treatment. The results obtained were then compared with the results of blood and cerebrospinal fluid culture examinations performed on patients suspected of having sepsis. If the culture performed on a patient suspected of having sepsis showed the same type of organism as the initial culture, the patient was considered to have persistent congenital infection and was excluded from analysis for nosocomial infection. Infants who are research subjects will be observed their development until the age of 28 days or until the patient is discharged. The frequency of incidence of nosocomial sepsis in the control group showed higher results when compared to the intervention group, 12 of 28 (43%) compared to 9 of 24 infants (38%). However, this difference was not statistically significant (P=0.695). The mortality rate showed relatively similar results between the two study groups; where the group that received routine skin care showed a mortality rate of 14% and the topical VCO therapy group showed a mortality rate of 12%, P= 0.851.

Quantitative Data result (Meta-Analysis)

Meta-Analysis of the Effect of Virgin Corn Oil on Skin Integrity of Preterm Infant

Meta-Analysis of the Effect of Corn Oil on Skin Integrity of Preterm Infant

The research group of Nangia and Salam was divided into 2 groups, the group of preterm infants with mild and moderate-severe skin disorders. The meta-analysis of the effects of corn oil on the skin integrity of preterm infants in these two studies was assessed by the magnitude of the risk of developing moderate-to-severe skin disorders seen at the end of the study. The number of preterm infants with moderate-severe skin integrity disorders in the treatment and control groups is shown in the following table.

Table 1: The impaired skin integrity of preterm infants in intervention group compared to control.

Study or Subgroup	Corn oil		Control	
	Preterm infants with moderate to severe skin integrity disorders	(n)	Preterm infants with moderate to severe skin integrity disorders	(n)
Nangia dkk, 2015	17/37	37	33/37	37
Salam dkk, 2015	6/128	128	23/130	130

Table 1 shows that the number of preterm infants with moderate to severe skin integrity disorders in the study of Nangia et al. was found to be higher in the control group, which was 33 infants, while in the group that received corn oil only 17 infants. Salam et al. study also showed that infants with moderate-severe skin integrity disorders were found to be 23 babies in the control group,

while the treatment group only had 6 babies.

The results of the meta-analysis of the effectiveness of topical corn oil on the skin integrity of preterm infants seen from the risk of moderate to severe skin integrity disorders are shown in the table 2.

Meta-analysis showed significant heterogeneity test (p=0.12) with I^2=58%. The data processing is carried out using a random-effect model by assessing the risk ratio. Test for overall effect showed that the incidence of moderate-to-severe skin disorders in premature infants in the group receiving corn oil was lower than the control group overall with a significant difference (p=0.01). The results of the meta-analysis showed that topical administration of ordinary corn oil had a significant effect on reducing impaired skin integrity in preterm infants.

Risk of Bias from the Included Studies

The research articles included in the meta-analysis were 4 studies; Konar et al., 2014-2018 [7]; Strunk et al., 2017 [6] reported data with outcomes in the form of pre and post NSCS treatment using topical VCO. Two other studies by Nangia et al., 2015 [4]; and Salam et al., 2015 [5] with data in the form of skin condition scores using SCGS and Salam scores, which were assessed post-treatment using topical corn oil. The results of both studies were classified into two groups; the group of preterm infants with mild or moderate-severe skin integrity disorders.

The risk of bias from studies included in the analysis, both qualitative and quantitative, was assessed using The Cochrane Collecting data - form for RCTs only and The Cochrane Collaboration's tool for assessing risk of bias in randomized trials, including randomization, allocation concealment, blinding of study subjects, blinding outcomes, incomplete outcome data, selection of reported outcomes, and other biases. The risk assessment of bias from each of these aspects is then converted according to Agency for Healthcare Research and Quality (AHRQ) standards. Every conducted study has a high risk for it to be biased for blinding personnel. The clinical-care team understands the division of each research group tp avoid any intervention which may resulted in blinding. Another reason was the lack of the ability in developing proper placebo formulation to make a comparison of its effect with corn oil, hence it is unlikely to blind the doctors and nurses during the process of administering emollients. As a result, these studies can be categorized as medium quality of evidence. The risk assessment for bias is shown in table 3.

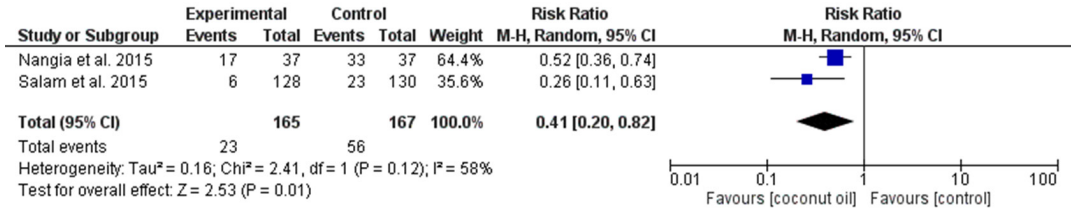


Table 2: The meta-analysis of the effectiveness of topical corn oil on the skin integrity of preterm infants.

	Random Sequence Generation	*Allocation oncealment*	*Selective Reporting*	*Other Bias*	*Blinding arpicipants and Personnel*	*Blinding of Outcome Assesment*	*Incomplete Outcome Data*	**Standard AHRQ**
Strunk dkk, 2017	Low	Low	Low	Low	High	Low	Low	*Fair*
Konar dkk, 2019	Low	Low	Low	Low	High	Low	Low	*Fair*
Nangia dkk, 2015	Low	Low	Low	Low	High	Low	Low	*Fair*
Salam dkk, 2015	Low	Low	Low	Low	High	Low	Low	*Fair*

Table 3: Risk of bias in studies used for systematic reviews and meta analyses.

Discussion

The method used in this study is a meta-analytic observational study, a systematic review and meta-analysis on the effectiveness of using corn oil to reduce the risk of impaired skin integrity for preterm infants using skin condition score as parameters, in which is obtained from visual observations, as well as SCGS and Salam scores.

All studies has shown a better result in terms of score for the oil group at the end of this study. Strunk et al., and Konar et al., [6,7], both used VCO in the intervention group and assessed skin condition at the beginning and end of the study using NSCS. Neonatal skin condition score in the study of Strunk showed the same median value in the treatment and control groups at the beginning of the study, but at the end of the observation, preterm infants in the control group experienced worsening of skin condition scores, from the median value (IQR) 3 (3-4) to 4 (4-4) at the end of the study. The group that received topical VCO had a stable median value (IQR) at the beginning and end of the study, which was 3 (3-3). The median value (IQR) was obtained from the correspondence between the researcher and the author of the article. The estimated mean ± SD of the research data is searched using the formula x = (a+2m+b)/4; using the median (m), the range of the lowest (a) and the highest (b).

The mean value of NSCS in Konar's study in the two groups both decreased, but the results showed that the group that received VCO experienced better skin integrity improvement, where there was a

decrease in the mean NSCS from 4.9 ± 1.1 to 3.9 ± 0.7, while in the control group 5 ± 1 became 4.8 ± 1 at the end of the treatment. Two other studies, Nangia et al., and Salam et al., used topical corn oil in the intervention group and only assessed skin condition at the end of the intervention [4,5]. Even so, both showed better skin condition scores in the treatment group than the control group, as seen from the number of preterm babies with impaired skin integrity in the intervention group compared to the control group at the end of the study. The research of Nangia showed good results in both groups, with the best score obtained being 1 and the worst being 3, where significantly better skin scores were obtained in the group that received oil. Preterm infants who received corn oil mostly (54.05%) showed a score of 1 at the end of the study, while the highest score obtained in the control group was 2 (70.27%). Scores of 1-3 in SCGS Lane and Drost means a dry skin condition accompanied by the presence of scales, where the value is 1 if there is a small amount of scale, 2 if the scale is moderate, and 3 if there is a lot of scale. Salam et al. also assessed skin integrity based on clinical observations with a score range of 0–3, where 0 means the skin is intact, 1 means there is erythema, 2 if there are scales or prick marks, and 3 if there are bruises or skin abrasions. Both of the studies were using dichotomous data, in which the outcome were grouped based on the given number and category, in order for the processing meta-analysis data to be carried out in search of the risk ratio. The results obtained from clinical assessment in both studies were then characterized into two different groups; the first one being the preterm infant with mild to moderate-severe skin integrity discorders with a clinically dry skin along with moderate scales, and the second being the ones who has prick marks, bruises, and abrasions, in which categorized as moderate-severe. Looking at Nangia et al. study, a total amount of 17 preterm infants from the intervention group were categorized as the moderate-severe, which consist of 16 infants who has dry skin within moderate scale, and one infant with a huge amount of scale. Meanwhile, in the control group, a total of 33 infants were found to be 26 of them having dry kin with moderate scale and seven of them with multiple scales. Research by Salam et al. reported that in the intervention group there were 4 infants with clinical signs of scales and prick marks and 2 infants with complaints of bruising or skin abrasion at the end of the study, while in the control group there were more, namely 20 infants with complaints of scales and prick marks, and 3 infants with bruises and abrasions on their skin.

In order to assess the risk of the incidence of moderate-severe skin integrity disorders between the two groups, a meta-analysis was conducted in both studies. As the result, there was a remarkably lower risk of skin integrity disorders for the group of preterm infants who received oil compared to the control group, P=0.01. This result indicates that even though corn oil containt a smaller amount of lauric acid than VCO, the protective effect towards preterm infant's skin still shows a better result compared to the routine care. Its effect as an emollient also plays a role in maintaining or increasing the barrier function of premature babies' skin with its high polarity and ability to retain water so that it can reduce the amount of fluid lost from the skin surface and increase SK hydration. The fatty acids contained in it can be used actively in the metabolism of keratinocytes so that they can improve skin structure and function, replenish intracellular lipids, and smooth and soften the skin.

Some studies previously mentioned also showed another results from the assessment of the skin integrity. Nangia et al., examined the effect of topical application of the corn oil on TEWL values, which resulted that the intervention group showing critically lower TEWL values at all measurement points starting from 12 to 168 hours of age. The mean TEWL value of the oil group indicates that the result is significantly lower. As it were 15.67 ± 8.67 compared to the control group, 25.64 ± 26.43. Comprehensively, this is due to the correlation between the skin barrier function and the TEWL value being incontrovertible. As can be seen that TEWL is the amount of water passively evaporated by the cause of the pressure from the water vapor from both sides of the skin barrier through the skin to the external environment. The presence of an intact or restored skin barrier was considerably indicated by a low value. This is in accordance with the results of the study where the group of preterm infants who received corn oil had better skin integrity conditions than the control group, in line with the TEWL value which was also lower in the intervention group compared to the control.

The incidence of nosocomial infections was also investigated by looking at the results of skin swabs, the presence or absence of sepsis, the incidence of HABSI, and the number of incidences of nosocomial infections. Nangia et al. swab the skin of preterm infants on the seventh day after treatment. Culture examination of skin swab samples showed sterile results in 81% of infants in the corn oil group and in 43% of infants in the control group. Seven infants in the oil group showed growth of gram-positive coccus bacteria, while in the control group, growth of gram-positive coccus bacteria was found in 16 infants, gram-negative bacilli in 4 infants, and mixed colonization in 1 infant. This statistically significant difference shows the effect of the protective properties of corn oil on the occurrence of bacterial colonization on the skin with its antimicrobial activity, which comes mainly from monolaurin. The monoglyceride form of lauric acid works by disrupting microbial membranes and has been shown to have activity against various bacteria, fungi, and viruses that have a lipid envelope.

Salam et al., assessed the incidence of HABSI at the end of the study, where it was found that the incidence was higher in the control group than in the intervention group [5]. A total of 38 preterm infants were recorded as having HABSI, with the most common etiology being coagulase negative *Staphylococcus spp* and *Acinetobacter spp*. Four neonates were known to be infected by *Klebsiella pneumoniae*, 3 neonates each by *Pseudomonas spp* and *Staphylococcus aureus*, 2 neonates each by *Enterococcus spp* and *Candida albicans*, and 1 neonate by *Streptococcus spp*. The treatment group showed lower HABSI overall, in which only 22 neonates developed infection. Three of them were caused by *Acinetobacter spp*, 2 by *Klebsiella pneumoniae*, while the other 4 were caused by coagulase negative *Staphylococcus spp, Enterococcus spp, Candida albicans*, and *Staphylococcus aureus*,

respectively. Some of these pathogenic bacteria which are normal flora on the skin include Coagulase negative *Staphylococcus spp, Pseudomonas spp, Streptococcus spp*, and *Candida albicans*. The infection is indicated by the bacteria's presence in the bloodstream or in the surface of the skin.

Strunk et al., made a report of zero mortality rate (0) in the treatment group, while the control group was 4 (11,1). Late onset sepsis during the intervention period in the intervention group was only found in 1 infant (2.8%) with the causative organisms *S. marcescens, E. faecalis, S. warneri*; while the control group had 4 infants (11,1) caused by *E. cloacae, E. faecalis, S. capitis, S. epidermidis*, and *S. aureus*. Some of these pathogens which are normal flora of the skin include *S. wareri, S. epidermidis*, and *S. aureus*. One of the factors that can cause this process is the presence of poor skin barrier integrity in the skin of preterm babies. Neonatal skin generally begins to be colonized by various types of microorganisms, including potentially pathogenic ones, within a few days after birth. The presence of poor skin integrity is a problem that is often encountered in preterm infants and can be associated with an increased risk of nosocomial infections, because it can be a port of entry for various pathogens. The lower incidence of HABSI in the treatment group proves the antimicrobial activity of corn oil, which can also improve the skin barrier structure of preterm babies so that they can carry out the skin barrier function correctly.

Salam et al.'s research showed that the use of corn oil on the skin of preterm infants can help the process of skin maturity in addition to preventing hypothermia. These findings can be based on the effect of using emollients in providing essential fatty acid supplementation that can help the skin maturation process, and prevent the process of invisible water loss by reducing latent heat so that it will reduce the incidence of hypothermia. Thereby reducing the incidence of late-onset neonatal sepsis, indicated by a decrease in the incidence of late-onset sepsis in this study after the use of corn oil in the treatment group, although the results were not statistically significant.

Another study related to the effectiveness of topical corn oil on the skin integrity of preterm infants was also conducted by Bautista et al., 2009 with a different outcome, namely the incidence of nosocomial infections in the form of sepsis, both clinically diagnosed and supported by bacteriological examination results. Nosocomial infection was defined as the incidence of localized or systemic infection with onset after birth, excluding the type of infection known to have been transmitted through the placenta or infection that started within 24-72 hours after birth. This means that in most cases of bacterial infection, symptoms and signs will begin to appear within 48 hours or so after the baby is started. Clinically diagnosed sepsis (clinical sepsis) is defined as the appearance of a number of signs and symptoms including instability of body temperature (hypothermia or hyperthermia), signs of organ hypoperfusion such as hypotension, slow capillary refill time, reduced urine volume or the presence of significant metabolic acidosis, apnea and/or bradycardia, leukocytosis or leukopenia, or thrombocytopenia, with negative blood culture results. Sepsis supported by bacteriological examination results was defined as the appearance of various signs and symptoms above plus the discovery of a specific pathogen on one or more blood culture examinations, without finding other possible causes of infection. This study reported that the incidence of nosocomial sepsis in the control group who only received routine skin care, showed higher results when compared to the group receiving topical VCO, namely 12 of 28 (43%) compared to 9 of 24 infants (38%). However, this difference was not statistically significant, P=0.695. The mortality rate showed relatively similar results between the two study groups; where the group that received routine skin care showed a mortality rate of 14% and the topical VCO therapy group showed a mortality rate of 12%, with a P value = 0.851. The occurrence of nosocomial infections in preterm infants was still closely related to the fragile factor of the skin barrier which was not fully developed so that It has the potential to be one of the entrances for various pathogenic bacteria. It is well known that the application of corn oil can accelerate the maturation of the skin barrier and improve its function so as to reduce the risk of infection. The results that were not significantly different between the treatment and control groups in this study could be influenced by other factors, such as the sample size being too small compared to other studies.

All of the studies discussed above presented an improvement in the skin integrity in preterm infants as shown from the better score of the skin condition in the treatment group compared to control group, a significantly decreased TEWL in the treatment group, a better result in skin swab culture, a lowered number of HABSI incidence, as well as the lowered incidence of nosocomial infections in the group who received corn oil.

Conclusion

The results of a systematic review and meta-analysis showed that the application of corn oil can significantly reduce the risk of impaired skin integrity on preterm infants.

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