

Antimicrobial and Barrier Repair Properties of Virgin Coconut Oil And Mineral Oil in Pediatric Atopic Dermatitis Patients, A Randomized, Double-Blind, Control Trial*

Claudine Joy M. Ramos, MD¹

ABSTRACT

Background: Atopic dermatitis (AD) is a chronic relapsing skin disease in childhood, managed by topical therapies. In the Philippines, use of affordable, widely available and effective alternative therapies such as mineral oil (MO) and virgin coconut oil (VCO), are practical especially in the far-flung areas.

Objectives: This study compares the antimicrobial and barrier repair properties of MO and VCO in mild to moderate atopic dermatitis, using SCORAD (SCORing for Atopic Dermatitis), bacterial culture, tewameter, mexameter and corneometer.

Methods: This is a randomized controlled double-blind trial conducted in two tertiary hospitals. Bacterial colonies, transepidermal water loss (TEWL), level of hydration and erythema were determined at baseline and after 4 weeks using bacterial culture, tewameter, corneometer and mexameter, respectively. SCORAD and adverse effects were also determined at baseline, 2nd and 4th week of treatment.

Results: Baseline patient demographics were similar for both treatment groups. The SCORAD, TEWL and level of erythema were significantly decreased throughout the 4-week duration for both treatment groups, but much lower in the VCO group. The hydration level was significantly increased throughout the 4-week duration but much higher for the VCO group. Lastly, there is more proportion of cultures with "no growth" after the 4-week treatment duration in VCO group.

Conclusion: The antimicrobial and barrier repair properties of VCO are very important alternative which is affordable, readily available, safe and effective for children with mild to moderate AD.

Key Words: dermatitis, atopic, virgin coconut oil, mineral oil, Philippines

INTRODUCTION

Atopic dermatitis (AD), a common skin disease in childhood, especially in 3-6 months old infants is diagnosed by modified Hanifin major criteria of a history of chronic and relapsing course; pruritus; pattern of facial and extensor eczema and xerosis at a younger age, becoming flexural at adult age; and frequent association with a family history of AD. Approximately 60% of patients develop flares in the first year of life and 90% by 5 years of age.¹

There is a rapidly increasing AD prevalence trends reported, in the U.S. at 11.3–12.7% and 6.9–7.6% in children and in adults, respectively², and in other temperate countries, at 10% to 20% in children, and 3% in adults.³ Likewise, the 12-month prevalence of AD in the Asia Pacific region in children aged 13 to 14 years is reported at 9% in Malaysia and Singapore. In the Philippines, there is a 47% prevalence of atopic dermatitis from 2011 to 2018 according to the Philippine Dermatological Society – Health Information System as shown in Figure 1.⁴

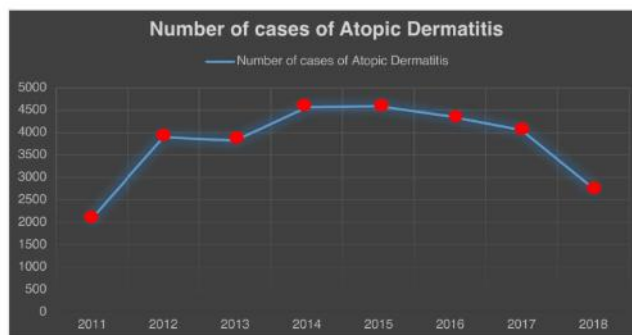


Figure 1. Prevalence of atopic dermatitis from the Philippine Dermatological Society Health Information System (2011-2018)

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¹Resident, Quirino Memorial Medical Center, Quezon City

On the other hand, the Philippine Pediatric Society reported 1,005 cases from January 2010 to September 2019, mostly seen at NCR (49.55%) as shown in Figure 2.⁵

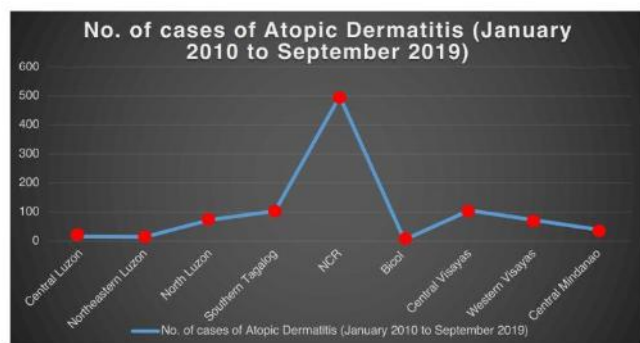


Figure 2. Prevalence of atopic dermatitis from the Philippine Pediatric Society (January 2010 to September 2019)

Management is geared towards the prevention of flares based on current knowledge of its complex pathogenesis.⁶ Barrier disruption due to filaggrin deficiency leading to dry skin and inflammation with secondary bacterial infection, are often addressed with the use of topical therapies such as steroids.⁷ However, topical steroids are known for its side effects and its absorption especially in children may have greater adverse effects. Moisturizers were used as primary treatment for mild atopic dermatitis and as adjunctive therapy for moderate to severe atopic dermatitis, which are safe for children. Petrolatum and MO were known as the old standard of care for AD. MO mainly acts a humectant because its thin film infiltrates the extracellular domains of the stratum corneum, therefore, the oil smoothens the dry, curled edges and fills the gaps between the desquamating keratinocytes.⁸ On the other hand, the traditional topical use⁹ and many clinical studies show virgin coconut oil (VCO) to have barrier repair, emollient, occlusive, anti-inflammatory and antibacterial properties¹⁰⁻¹¹ that have found use in the treatment of AD and xerosis.¹²⁻¹³ VCO is composed of three fatty acids attached by ester linkages to the carbon atom of glycerin. Glycerin is known to retain water, hence the oil's humectant property.⁸ In a study comparing MO and VCO, VCO decreased the mean SCORAD indices by 68.23% from baseline up to 8 weeks as compared to 38.1%

decrease in MO. There is also a greater decrease in transepidermal water loss (TEWL) from 26.68 at baseline to 7.09 after 8 weeks in the VCO group as compared with MO group with baseline and post-treatment TEWL values of 24.12 and 13.55, respectively. Lastly, there is a greater increase in skin capacitance in the VCO group from 32.0 at baseline to 42.3 after 8 weeks as compared to the MO group with increase from baseline of 31.31 to 37.49.¹⁴

The increasing prevalence of AD in the country, with its chronic, unremitting course of intractable pruritus is a great burden that interferes with quality of life not just of the patient¹⁵ but also the entire family.¹⁶ In a developing country like the Philippines, there is a lack of access to health care services and medicines, especially in the far-flung areas. As shown in Figure 2, most of the cases are seen in NCR (49.55%); however, the sum of cases in the provinces is higher (50.45%) than NCR and does not account to under-reported cases. Hence, there is a need for an affordable, widely available and effective alternative therapy. Therefore, this study's primary objective is to compare the antimicrobial and barrier repair properties of VCO and MO in pediatric patients with mild to moderate AD. The specific objectives, is to determine the SCORAD level, TEWL, level of hydration and erythema, as well as antimicrobial properties using tewameter, corneometer, mexameter and bacterial culture, respectively.

MATERIALS AND METHODS

Study Design

This is a two-arm parallel randomized, controlled, double-blind trial comparing the antimicrobial and barrier repair properties of VCO & MO in mild to moderate atopic dermatitis in pediatric patients in two tertiary hospitals.

Population

Patients 18 years old and below coming in for consult or referred to the two tertiary hospitals, who were recently or previously diagnosed with mild to moderate AD based on Hanifin major criteria

were included in the study. Exclusion criteria were grossly infected lesions, other diagnoses aside from AD and use of any topical or oral steroids or antibiotics for at least 2 weeks before enrollment. A certificate of approval from the Hospital Ethics Committee was obtained before the trial was initiated. Informed consent from the parents and assent form for children ≥ 9 years old were obtained.

Sample Size

The sample size was calculated using a power of 80% and 0.05 level of significance, using the formula for computing the difference between two proportions. The improvement of SCORAD indices of VCO and MO were set at 70% and 40%, respectively, based on another study [14]. The computed sample size was 39 for each study arm.

Interventions

VCO was sourced from FRV USDA-Certified Organic Coconut Farm in Barrio Sto. Nino, Leyte and was manufactured without heat under sterile laboratory conditions that followed standard GMP. On the other hand, commercially available MO from a Philippine drug store was used. The high quality pure oils were sourced and repackaged in uniform medicinal opaque plastic bottles with a small opening to mask the color and scent of both oils. Test bottles were coded (X or Y) by the pharmacist. Patients were given 2 bottles (7mL) of the assigned oil and were instructed to apply and massage 0.5 mL (using 1 cc syringe) to the chosen site twice a day immediately after bathing for 5 to 10 minutes. Application of the assigned oil was done for 2 weeks and were asked to follow up to be given refills. They were given the same mild soap.

Outcomes

At baseline and after 4 weeks treatment, severity, transepidermal water loss (TEWL), level of hydration, and erythema for involved areas were determined using SCORing for Atopic Dermatitis; tewameter, corneometer and mexameter (Courage + Khazaka electronic GmbH Mathias-Bruggen-STR. 91 50829 Köln, Germany), respectively. Baseline photographs were also obtained with consent from the parent and patient.

Swabs were collected from clinically uninfected involved sites that were identified by the investigator, each with an easy to identify anatomic landmark. Starting at the center of the site, cotton swabs soaked with sterile normal saline solution were swept over the chosen site (one swab per site); cotton swabs were submitted to the medical technologist at the microbiology department of a hospital laboratory. After 4 weeks of treatment, cotton swab samples were taken again from the same sites of the first cultures and were sent to the same microbiology laboratory.

Both patient and physician-reported adverse effects were assessed after 2 and 4 weeks of treatment.

Randomization, treatment allocation, and blinding

Recruited patients were randomly allocated to the treatment groups by computer generated random numbers. The assigned test bottle was dispensed by the resident who were blinded to the codes. The codes were not disclosed to the investigators until the end of the study. Patients however, can differentiate VCO from MO through its smell, so they were not blinded and were asked not to disclose their assigned treatment to the investigators nor to the resident.

Statistical Analysis

Descriptive statistics was presented using mean and standard deviation for quantitative data and frequency and proportion for qualitative data. For baseline demographics, independent t test was used to compare quantitative data between the two treatment groups, while Chi-square test was performed to compare qualitative data between two treatment groups, provided that the assumptions of Chi-square test were met. Otherwise, Fisher's exact test was performed.

For the outcome measures, data analysis was done using Two-way repeated measures anova for the quantitative data, with data representation using line graphs. For qualitative data, Chi-square test was performed.

The level of significance was set at p values <0.05 . Statistical analysis was done using Stata version 13.

RESULTS

Participant Flow

A total of 80 patients were recruited and enrolled to the study using the inclusion and exclusion criteria from October 2018 to September 2019. 40 patients were allocated for each treatment arm. In between the first and second treatment week, 1 patient from MO group dropped out from the study because the patient had measles. On the other hand, there was no dropout in VCO Group. All patients for each group were analysed and intention to treat analysis was done for the dropout in MO Group using last observation carried forward.

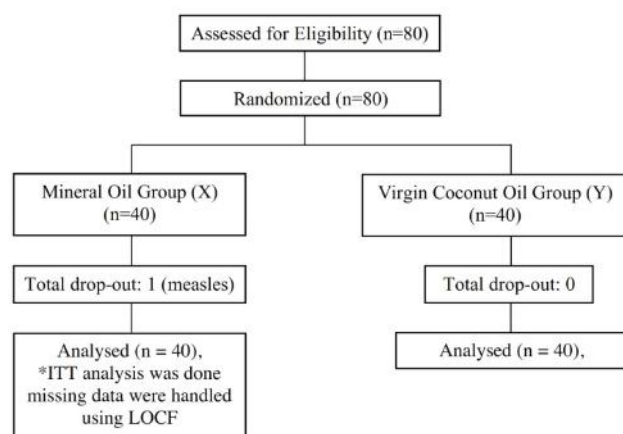


Figure 3. Participant Flow for the Duration of the Study

Patient Demographics

Patient demographics are reported in Table 1. A total of 80 patients were recruited from October 2018 to September 2019. There is no significant difference in the mean age, sex and duration of AD at baseline in between the VCO and MO group. The mean age for patients in the MO and VCO group is 6.8 and 7.25, respectively. There are more females than males, with 55% in the MO and 57.5% in the VCO group. Lastly, all patients were noted to have chronic history of AD with mean of 25.75 and 27.17 months in the MO and VCO respectively. Baseline parameters were also shown in Table 1 with no significant difference between the treatment groups.

Table 1. Baseline Patient Demographics

	Mineral Oil Group (n=40)	Virgin Coconut Oil Group (n=40)	p value
Age (mean, SD)	6.80 (5.19)	7.25 (5.59)	0.71 T test
Sex (number, percent)	F 22 (55%) M 18 (45%)	F 23 (57.5%) M 17 (42.5%)	0.82 Chi-square test
Duration in months (mean, sd)	25.75 (17.39)	27.17 (19.05)	0.73 T test
Baseline SCORAD (mean, sd)	31.12 (4.69)	30.8 (5.42)	0.78 T test
Baseline mexameter erythema (mean, sd)	341.85 (11.40)	317.55 (10.88)	0.13 T test
Baseline tewameter (mean, sd)	26.49 (1.77)	24.45 (1.27)	0.35 T test
Baseline corneometer (mean, sd)	29.40 (1.77)	26.07 (1.33)	0.14 T test
Culture (number, percent)	S. aureus 39 (97.5%) P. aeruginosa 1 (2.5%)	S. aureus 40 (100%) P. aeruginosa 0	>0.9999 Fisher's exact test

SCORAD Index

SCORAD is a standard tool developed by the European Task Force on Atopic Dermatitis to assess the severity of the extent and intensity of lesions and severity of pruritus and sleep loss. A decrease in SCORAD means that there is an improvement in both subjective and objective AD symptoms. There is a significant decrease in mean SCORAD indices for both treatment groups throughout the 4-week study duration (p value of 0.006) as shown in Table 2. Though the mean SCORAD between groups was comparable at baseline, the mean SCORAD at week 4 was significantly different, with VCO Group having significantly lower mean SCORAD than MO Group (Figure 4).

	Baseline	Week 2	Week 4	p value
Mineral Oil Group	31.12 (4.69)	22.65 (6.13)	14.24 (6.85)	Between treatment groups: 0.006
Virgin Coconut Oil Group	30.8 (5.42)	20.4 (4.21)	9.20 (3.94)	
p value	Across time: <0.0001			

Table 2. Mean SCORAD Indices from baseline up to 4 weeks for MO and VCO Group

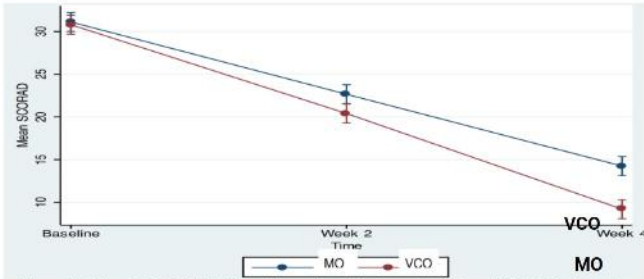


Figure 4. Mean SCORAD Indices throughout the 4-week MO and VCO Treatment

Transepidermal Water Loss (TEWL)

TEWL or insensible water loss is the movement of water from the stratum corneum into the atmosphere, which is significantly increased in AD patients. A decrease in TEWL corresponds to improvement of the skin barrier's function of retaining hydration. There is significant decrease in TEWL as measured by tewameter for both treatment groups throughout the 4-week study duration (p value of 0.04) as shown in Table 3. Though the mean tewameter readings were comparable at baseline, at week 4 they were significantly different, with VCO group having significantly lower mean reading than MO group (Figure 5)

Table 3. Mean tewameter readings from baseline up to 4 weeks for MO and VCO Group

Tewameter (mean, sd)	Baseline	Week 4	p value
Mineral Oil Group	26.49 (1.77)	21.38 (11.38)	Between groups: 0.04
Virgin Coconut Oil Group	24.45 (1.27)	15.31 (3.91)	
p value	Across time: <0.0001		

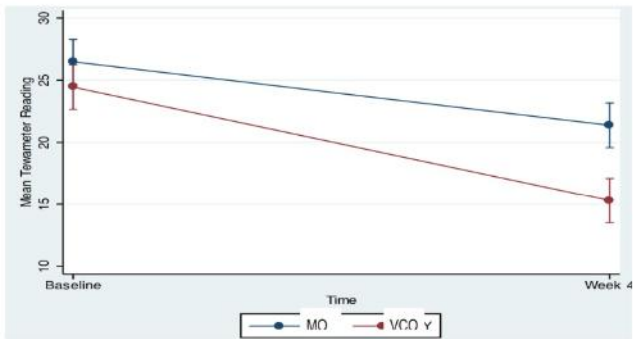


Figure 5. Mean Tewameter readings throughout the 4-week MO and VCO Treatment

Level of Erythema

Erythema is one of the characteristics of the involved areas of the skin in AD and an indicator of inflammation and measured by mexameter. A decrease in the level of erythema is an indicator of improvement with less inflammation. Table 4 shows that the level of erythema is decreased for both treatment groups (p-value 0.01). Though the mean mexameter erythema readings were comparable at baseline, at week 4, they were significantly different, with VCO having significantly lower mean erythema reading than MO (Figure 6).

Table 4. Mean mexameter erythema readings from baseline up to 4 weeks for MO and VCO Group

Mexameter erythema (mean, sd)	Baseline	Week 4	p value
Mineral Oil Group	341.85 (11.40)	307.30 (69.22)	Between groups: 0.01
Virgin Coconut Oil Group	317.55 (10.88)	260.32 (51.02)	
p value	Across time: <0.0001		

Figure 6. Mean Mexameter erythema readings throughout the 4-week MO and VCO Treatment

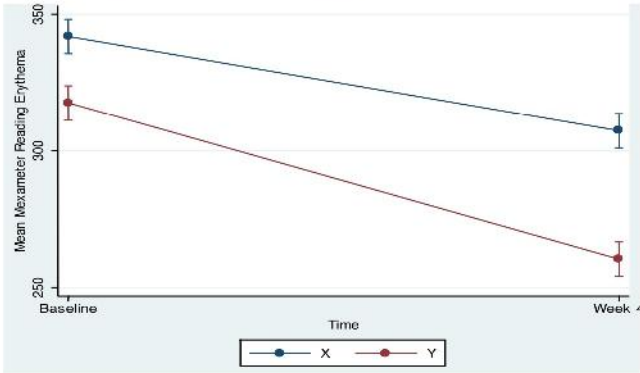


Figure 7. Patient in VCO group at baseline (A) and after 4 weeks treatment (B). Note the significantly decreased erythema after 4 weeks application of VCO

Level of Hydration

Due to impaired skin barrier secondary to filaggrin deficiency, the skin of AD patients were not able to hold moisture, hence, dry. Corneometer measures the hydration level of the stratum corneum, which indicates that the higher the reading, the higher level of hydration. The level of hydration in both treatment groups were significantly increased (p value of 0.88) as shown in Table 6. Moreover, there is significant interaction or change in direction, in that, at baseline, the mean corneometer reading was higher for MO Group, which, at week 4, became lower (Figure 8).

Table 5. Mean corneometer readings from baseline up to 4 weeks for MO and VCO Group

Corneometer Reading	Baseline	Week 4	p value
Mineral Oil Group	29.40 (1.77)	36.05 (7.56)	Between groups: 0.88
Virgin Coconut Oil Group	26.07 (1.33)	39.97 (9.88)	
p value	Across time: <0.0001 Interaction: 0.002		

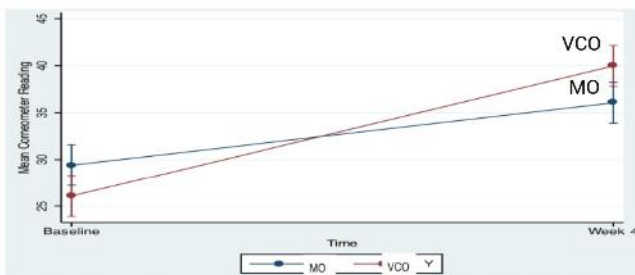


Figure 8. Mean corneometer readings throughout the 4-week MO and VCO Treatment

Bacterial Culture

VCO is currently studied for its antimicrobial effect. The baseline culture was comparable between the two groups, in which most of the patients were positive for *Staphylococcus aureus* colonization. However, one patient in the MO group is positive for *Pseudomonas aeruginosa* colonization. At week 4, there is a significant difference, with significantly higher proportion of subjects with no growth in VCO Group compared with MO Group (Table 6).

Table 6. Bacterial Cultures from baseline up to 4 weeks for MO and VCO Group

	Mineral Oil Group	Virgin Coconut Oil Group	
Week 4 Culture (number, percent)	S. aureus 39 (97.5%) No growth 1 (2.5%)	S. aureus 7 (17.5%) No growth 33 (82.5%)	<0.0001 Chi-square test

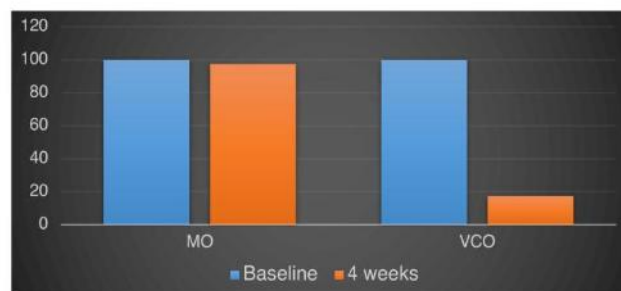


Figure 9. Positive cultures at baseline and after 4 weeks treatment of VCO and MO

Adverse Effects

No adverse effects were reported from both treatment groups

DISCUSSION

The factors that contribute to the complex pathophysiology of AD are genetic predisposition, epidermal barrier disruption, and dysregulation of the immune system. Patients with AD have homozygous mutations in FLG with higher risk of severe AD and earlier onset, longer duration with secondary bacterial infections.² Filaggrin is very important in maintaining the barrier and protective function of the stratum corneum minimizing TEWL and minimizing the penetration of foreign antigens. It is also important in maintaining the acidic pH of the skin by releasing free amino acids in the upper stratum corneum, inhibiting bacterial growth.¹⁷

Immune pathway dysregulation is also important, particularly the T-helper (Th) type 2 signaling pathway, causes increased expression of IL-4 and IL-13 further lowering FLG expression, leading to skin barrier defects.² In other studies, both TH type 1 and 2 are involved in the pathogenesis of AD. Environmental and microbial triggers prime an array of antigen presenting cells in the skin causing skin inflammation.¹⁷ Pruritus,

which is a prominent feature of AD is caused by the release of IL-31 which was reported to enhance the release and production of brain-derived natriuretic peptide leading to release of cytokines and chemokines inducing pruritus.

SCORAD index, developed by the European Task Force on Atopic Dermatitis, is a standard tool to evaluate AD which takes into account the extent, intensity of symptoms (erythema, lichenification, excoriation, edema, oozing/crust and dryness) and subjective symptoms of pruritus and sleep loss.¹⁸ This tool also classifies AD into mild (SCORAD of 0 - 24), moderate (25 - 50) and severe (>50).¹⁹ It can be also used to monitor improvement after treatment. A decrease in SCORAD throughout the treatment duration, as seen in this study, is an indicator of improvement for both objective and subjective symptoms of AD. This also indicates that the treatment used is effective. This study showed that VCO lowers the SCORAD more significantly than MO, indicating the anti-inflammatory and barrier repair properties of VCO.

TEWL or insensible water loss, is directly associated with the permeability barrier of the skin. This is significantly increased in both the involved and uninvolved areas in AD patients. This barrier defect is the effect of decreased ceramide content in the stratum corneum, which is an important lipid of the intercellular lamellae. Therefore, a decrease in TEWL after treatment, as seen in this study, indicates that the therapeutic management applied is able to repair the barrier defect and retain moisture. This study showed that VCO is more significant than MO in decreasing the TEWL. MO was known to have occlusive effect because of its hydrophobic and non-lamellar palisade, which is able to penetrate intercellularly to prevent water loss, but not completely as compared with VCO. VCO is much better than MO as an occlusive since it is composed of fatty acids (65%) of the same length and 92% are saturated and more compact preventing the evaporation of water from the skin.¹¹

Corneometer measures the level of skin hydration by measuring the capacitance of the dielectric medium through the difference between dielectric constant of water and other substances. It

is composed of two electrodes with different electrical charges forming an electromagnetic field to determine the dielectric constant of the stratum corneum. Corneometer measurements range from 0 to 130 arbitrary units (AU) and in standard conditions ($T^{\circ}= 20-22^{\circ}\text{C}$, humidity 40-60%), values of skin hydration varies from very dry (<30 AU), dry (30 - 45 AU) and sufficiently hydrated (>45 AU).²⁰ The skin of patients with AD were not able to attract and bind water due to the decreased content of osmotically active amino acids in the keratinocytes. Their skin also has defective lamellae in the stratum corneum which is not able to trap moisture causing decrease in the hydration level.¹⁷ In this study, both treatment arms were noted to have significant increase in the level of hydration, with VCO group having more significant increase than MO. MO is not known to be a humectant, therefore, it is not able to draw moisture from the environment. On the other hand, VCO is composed of triglycerides which is hydrolyzed by lipases when topically applied, becoming free fatty acids and glycerin same as that of the skin composition. Glycerin contains three carbon hydroxyl functional groups which binds with water, absorbing moisture from the environment and the lower layers of the skin, increasing its hydration level.¹¹ This accounts for the greater increase in corneometer readings for the VCO group as compared with MO group.

Erythema is a prominent feature of the involved areas in AD, indicating the presence of inflammation. Erythema is measured by mexameter by means of two specific wavelengths (green: 568 nm and red: 660 nm), corresponding to the spectral absorption peak of hemoglobin and to avoid other color influences such as bilirubin.²¹ Topical treatments that decrease the erythema are ideal for patients with AD. This study showed that both MO and VCO reduced the erythema with more significant reduction in the VCO group. This anti-inflammatory effect of VCO in the skin was studied and results showed that VCO inhibits TNF- α , IFN γ , IL-6, IL-5 and IL-8 with associated improvement in the barrier property of the skin by increasing the expression of AQP-3, filaggrin and involucrin mRNA expression and also by protecting against UVB irradiation²², hence more significant reduction in the erythema level.

Lastly, bacterial cultures were used to monitor the antimicrobial properties of both arm which showed that the VCO group has higher rates of cultures with no growth compared with the MO group. In patients with atopic dermatitis, the most common bacteria that are present is *Staphylococcus aureus*.²³ The results of the study showed that *Staphylococcus aureus* was 97.5% and 100% isolated by bacterial culture from the MO and VCO groups, respectively. Antibiotic peptides belonging to the dermcidin family in sweat causes *Staphylococcus* colonization in the skin. *Staphylococcus* sp. are speculated to produce exotoxins and lipase that may cause irritation and change the physiologic condition of the skin.²³ VCO is currently being studied for its antimicrobial properties. In a similar study, the antimicrobial property of VCO was compared to virgin olive oil (VOO) and results showed that the VCO group has more significant reduction of 95% in *Staphylococcus aureus* colonization as compared with VOO (50%). This is attributed to the monolaurin and other medium chain fatty acids present in VCO. The skin's microbiota produces lipases which hydrolyzes the triglycerides in VCO producing 82% medium-chain fatty acids, mostly C-12 (C-6 to C-14) fatty acids, as compared with VOO which is hydrolyzed into long chain fatty acids mostly C-18 (C-16 to C-24, except for 0.1% C-14). Because medium chain fatty acids in VCO are smaller, this allows greater penetration through the bacterial cell membrane and inhibit the enzymes necessary for energy production and transfer of nutrients which leads to irreversible changes that causes bacterial death.¹² Another important product of triglyceride hydrolysis is monolaurin which is a monoglyceride from lauric acid and comprises 50% of the VCO fat content. In studies, monolaurin is known to penetrate the lipid membranes of the bacteria such as *Propionibacterium acnes*, *Staphylococcus aureus*, and *Staphylococcus epidermidis* causing bacterial death.²⁴

These antimicrobial and barrier repair properties shown by VCO is a very important treatment strategy for children with mild to moderate AD. VCO provides an affordable, readily available, safe and effective treatment for children with AD with less side effects.

LIMITATIONS AND RECOMMENDATIONS

There are two limitations of this study that could be further addressed in future studies. First is that the study is conducted for a 4-week treatment duration. Future studies may extend the duration to 8 weeks to see the results after longer application of the oils. Another limitation is that the microbiologic cultures are qualitative with no colony forming units. This is because the medical technologists of the hospital laboratory cannot measure the colony forming unit of the culture. Providing the colony forming units may further express the decrease in the number of bacterial colonies after treatment.

CONCLUSION

The antimicrobial and barrier repair properties of VCO are very important alternative which is affordable, readily available, safe and effective for children with mild to moderate AD.

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