Safety and Efficacy of Topical Essential Oil as Steroid-Sparing Agent in the Treatment of Atopic Dermatitis in a Community Outreach Care Program of New Era University Second Year Medical Students, Randomized Double Blind Placebo Controlled Trial*

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ABSTRACT

Background: The high rates of atopic dermatitis among children, treatment failures and treatment costs have created the search for new therapies to control flares of atopic dermatitis.

Objectives: We compared the efficacy and safety of topical essential oil (German Chamomile) versus topical steroids (hydrocortisone 1%) in controlling flares of atopic dermatitis.

Method: We randomly selected 60 children diagnosed of AD or children that qualified to the criteria of AD. They we're randomly grouped into three. Twenty for Essential Oil (EO) group, twenty for Steroid group (SG) and Twenty for placebo (distilled water) group. They were advised to apply medicine kept in uniform brown plastic bottles 3x a day for 4 weeks. Data were recorded weekly using the EASI (Eczema Score Index) scoring. Other topical medications such as emollients and moisturizers were continued.

Results: At week 4 control of flaring was achieved; 42% for EO group and 55% for steroid group. The differences in treatment effects were not statistically significant.

Conclusion: Essential oil was comparable in cure rate to mild topical steroid. Essential oil can be safe and affordable. However further study in a wider scale is recommended.

KeyWords: Atopic Dermatitis, Barrier Function, Eczema, Essential Oils, Roman Chamomile, Jojoba oil, Chamazulene

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INTRODUCTION

Childhood atopic dermatitis is an increasing common condition in young children. The worldwide incidence according to Annals of Nutrition and Metabolism in 2015 is about 20% of children and studies showed that steady increased is most likely to happen for low-income developing countries. Atopic Dermatitis is an interplay of dysfunctional epidermal barrier in genetically predisposed individuals and harmful environmental antigens. Recent studies showed that the focus of treatment of Atopic Dermatitis has shifted from treating symptoms of inflammation to Skin barrier repair. In fact, skin barrier alterations and reduction of innate immune mechanism are now considered the hallmarks of AD. Therefore, barrier repair therapies with steroid-free substances is an important alternative in managing AD.

Essential oils (German Chamomile) and pure carrier oils (jojoba oil) are great option for treating AD. Jojoba oil mimics the oil moisture of the human skin and according to the International Journal of Molecular Science of 2014, this oil effectively increases the absorption of topical drug because of its high content of wax ester. On the other hand, chamazulene is an active agents extracted from German/Roman chamomile flower which according to Pub Med has a good natural anti-inflammatory property. In the study of Safayhi et all published in the Article in Plants Medica (Nov. 1994), they demonstrated in vivo experiments that chamazulene inhibits the Leukotriene B4 in intra cells which blocked the chemical peroxidation of arachidonic acids thus preventing inflammation. The experiments also showed the reduction of TNF alpha in mice and the presence of high concentration of AgNPs/CE5x in chamazulene which has an anti-bacterial activity by inhibiting the H2O2 generated free radicals from fibroblast.

AD poses a significant burden to parents and patients. The chronicity of symptoms (pruritus, sleep deprivation, on and off flares), the financial costs and the deterioration of the quality of life have heightened the interests of researchers, scientists and physicians in the identification of newer and cost effective treatment alternatives.

Methodology:

A double-blind, randomized, interventional parallel assignment and placebo-controlled clinical trial was conducted over a ten (10) months period beginning August 2017 to June 2018 in three multi-center OPD clinics of three (3) collaborative PDS dermatologists (most are done in NEGH).

Sixty three (63) patients, ages 2-17 were recruited and referred by volunteer second year medical students of New Era University from their Community Outreach (Brgy. San Jose, Rodriguez Rizal). They were subsequently invited to seek OPD consults to dermatology consultants involved in this research.

The inclusion and exclusion criteria were as follows.

1. Male or female paediatric patients ages 2-17 years old with history of Atopic dermatitis and stable disease for at least one (1) month according to parents/caregivers.
2. No clinically significant and relevant abnormalities in medical history or upon physical examination.
3. Patients with mild to moderate atopic dermatitis with Physician Global Assessment of 2 or 3.
4. Patients affected between 5% to 40% Body Surface Area (BSA).
5. Volunteer should understand and be willing to fully comply with all study procedures and restrictions.
6. Demonstrates understanding of the study and willingness to participate as evidenced by voluntary written parent's informed consent.
7. Female of childbearing potential, using an effective contraceptive method for at least one month before the beginning of the study, and willing to use throughout the study.

<u>Exclusion Criteria</u>

1. Volunteers having recent history (within 1 year) of alcohol or other substance abuse as determined by medical history.

2. Participation in another clinical study or received of an investigational drug within 30 days of the screening visit.
3. Previous participation in similar study with similar products.
4. Volunteer has any visible skin disease at the site of application that, in the opinion of the investigator, will interfere with the skin assessments.
5. Volunteer has current or relevant previous history of serious, severe or unstable physical or psychiatric illness or medical disorders, such as hepatic or renal disease.
6. Volunteer or patient has a history of hypersensitivity of tropical oils.
7. Volunteer receiving systemic steroids in the last 3 months.
8. Any skin disorder at the site that the investigator's judgement can affect the reading of test results.
9. Pregnant or any plan of having pregnancy during the study.
10. Any concomitant medications that in the investigator's judgment can confused or alter test results.

Intervention:

The 63 subjects were requested to undergo a primary irritancy test, on which the investigators put one drop of the solution in the right arm and sealed with tegaderm plaster and were requested to have a 24-hour patch test. They were requested to return on the following day for the investigators to record the results. Subjects who did no show primary irritancy were deemed eligible for the study.

The subjects were randomly distributed to the study groups EO (Essential Oil Group), SG(Steroid group) and PG (Placebo group) using randomized code generated from CLINSTAT software.

They were instructed to apply the given solution three times a day over eczematous lesions for four weeks. They were instructed to report immediately if any irritation were noted. They were also told to come for follow up weekly for four weeks.

Outcome Measures:

The primary outcome measures are the lowering of EASI (Eczema Assessment Severity Index) to 50% at week 4 and at least a 2- point improvement in the PGA (Physician Global assessment at week 4. The PGA is a standard 5-point overall severity assessment using the following scoring 0-clear,1-almost clear,2-mild flare, 3-moderate flare,4-severe flare.

Standard Analysis:

All statistical was conducted using SPSS software. Demographic variables and other baseline characteristics were summarized by descriptive statistics. The Chi-Square test without continuity connections was used to analyse discrete variables, and analysis of variables was used for continuous variables to assess comparability among the three treatment groups. Further, the Fisher's exact test was used to test the difference. All statistical tests were two-tailed with a significance level alpha = 0.05.

Results:

A total of 63 patients were recruited for the clinical trial but only 55 completed the treatment protocol and were included in the analysis. The patients were randomized to receive placebo (0.9NaCl) solution, Hydrocortisone 1% lotion and Essential Oil (German Chamomile EO diluted with Jojoba oil at 2% concentration).

Table 1 Demographics

Gender	EO	SG	PG	P value
Male Female	9 9	9 11	10 7	.857
Mean Age	7.4	6.6	8.2	.675

Legend: EO9Essential Oil group); SG (steroid group); PG (placebo group)

Table 1 showed that the demographics data have no significant differences among the treatment groups with regards to gender and age.

Table 2 Physician Global Assessment Score

Duration of Treatment	EO (mean PGA score)	SG (mean PGA score)	PG (mean PGA score)
Day 1	2.9	2.45	2.40
Week 1	2.5	2.10	2.35
Week 2	2.0	1.45	2.25
Week 3	1.1	1.10	2.10
Week 4	1.0	0.65	2.0

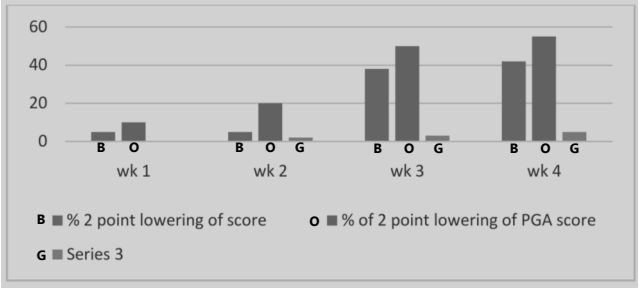
X^2 = 16.816, Ho – PGA Score is independent with duration of treatment; Rejected

Graph A

Legend: Series 1 EO, Series 2 SG, Series 3 PG

The patients were evaluated on the severity of skin redness, welting up, rash, oozing skin and symptoms of itchiness. Table 2 showed the significant improvement of lesions in the SG (steroid group) as early of 2 weeks of treatment duration, while significant improvement was noted on the 3rd and 4th week in the EO group.

Graph B Percentage of 2-point Lowering of PGA Score



Legend Blue – EO, Orange –SG, Grey -PG

Graph B showed that at week 4 around 40-48% of patients achieved the 2-point lowering of their PGA scores in the EO group while around 55-62% achieved the 2-point lowering in the steroid group. No significant changes were seen in the placebo group.

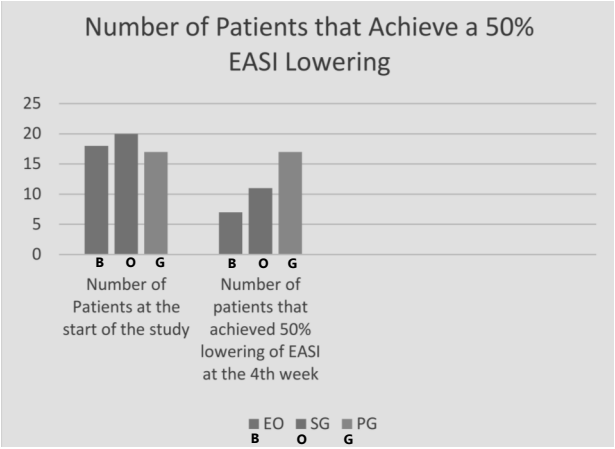
Table 3. Lowering of EASI (mean score)

Duration of treatment	EO EASI mean score	SG EASI mean score	PG EASI mean score
Day 1	38.2	23.4	28
Week 1	32.6	22.4	29
Week 2	24.2	19.2	29
Week 3	20.4	14.0	27.6
Week 4	19.2	11.0	26.35

X^2 = 10.0, Ho –EASI is independent with the duration of treatment, Rejected

Table 3 showed that there was a significant lowering of EASI score to about 50% on both EO and SG. Although, the lowering of EASI score in the SG is higher than in the EO group yet no significant differences between the two were noted. The Placebo control group showed no significant lowering of EASI score.

Graph 3. Number of Patients that achieved 50% lowering of EASI Score



Graph 3 showed that 8 out of the 17 (42%) panellists showed 50% lowering of EASI score in the EO group and 11 out 20 (55%) showed 50% lowering of EASI score in the SG.

Conclusion:

This study demonstrated that German-Chamomile essential oil diluted to Jojoba oil in a 2% concentration, used as topical anti eczema solution have no skin contact sensitization potential. The results of the 10 months' clinical study demonstrated the significant efficacy in lowering Atopic dermatitis lesions severity and showed significant lowering of EASI score to about 50% in almost half of the sample size. Both EO and SG showed no significant difference. The utility of German Chamomile Essential oil diluted with Jojoba oil is very promising as it is well tolerated, easy to make, safe and can be compared to mild potent topical steroids.

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