A Pilot Study on the Safety and Efficacy of Abelmoschus Esculentus (Okra) 5% Extract in the Treatment of Non-Bullous Impetigo among Paediatric Patients at Jose R. Reyes Memorial Medical Center, Department of Dermatology*

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INTRODUCTION

Impetigo is a common, contagious, superficial skin infection most commonly presenting as erythematous crusting papules and pustules on the face and or extremities. The pathogens usually implicated in this skin disease are gram- positive organisms including Staphylococcus aureus, and less frequently, group A β-hemolytic Streptococcus pyogenes. In JRRMMC, Department of Dermatology, this disease always ranks in the top 10 most common skin diseases annually. Treatment options for this disease include topical and oral antibiotics depending on the condition's severity. Mupirocin and Fusidic acid are considered as gold standard in the treatment of impetigo.[1]

Abelmoschus esculentus or more commonly known as Okra is readily available in the Philippines and is assumed to have medicinal properties like antioxidant antispasmodic, demulcent, diaphoretic, diuretic, emollient, and stimulant. An in- vitro study has proven its broad anti-bacterial property[2] and that maybe due to its palmitic and stearic acid component[3]. Development of an alternative topical treatment option that may be more accessible to the majority of the population due to its cheaper price could create a positive impact in the cure and prevention of common cutaneous bacterial infections. This has led to the idea of challenging the hypothesis if Okra 5% extract can be effectively used in-vivo for superficial bacterial skin infection like impetigo.

OBJECTIVES

General: To determine the safety and efficacy of Abelmoschus esculentus (Okra) 10% extract for the treatment of non-bullous cases of impetigo.

Specific:

1. To determine the efficacy of Okra 5% extract in the treatment of non- bullous impetigo.
2. To determine the safety of Okra 5% extract when treating cases on non-bullous impetigo.

Review of Related Literature

Impetigo frequently occurs in children. Worldwide it represents the most common bacterial skin infection in this group. It is extremely contagious, spreading rapidly via direct person-to-person contact or through fomites. Factors including a warm ambient temperature, high humidity, poor hygiene, an atopic diathesis, skin trauma, and participation in contact sports predispose a patient into developing this skin condition.

Several treatment options may be employed in the management of this disease. In few superficial lesions with no systemic manifestations, the recommendation is giving of either Mupirocin 2% ointment or Retapamulin 1% ointment in combination with daily local wound care. The extent of involvement, co-morbid conditions, patient's immune status and local drug-resistance patterns should be taken into account when deciding whether topical, oral or intravenous therapy is most appropriate.

High and low level resistance against Mupirocin has been elucidated and has been attributed mainly due to the unrestricted over-the-counter usage of this medication.[4] Resistance is a major concern for our part as medical practitioners

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as this would mean less efficacy of our more commonly used topical anti-bacterials.

Several scientific studies have already proven its anti-oxidative effect[5], anti-diabetic[6] anti-cancer[7] and broad anti-microbial properties.[2,8]

The lipid fraction of the okra gum, namely palmitic and stearic acid were found to be the compounds responsible for the antibacterial properties[3]. Usage has been diversified into its usage as a moisturizing component of a hand-sanitizing gel in one study as well[9]

The in-vitro studies have already established its efficacy on both gram-positive and gram-negative pathogenic organisms.[2,7] Although this is a significant breakthrough, no studies have been made yet to apply this new discovery in vivo.

As Okra is readily available in markets and can easily be cultivated even in our own backyard, this study aims to seek a possible alternative topical medication for superficial bacterial skin infections like impetigo.

METHODOLOGY

Study Design:

The study design was an Experimental, Prospective Study

Sampling Design:

Patients considered in the study were those of primary, non-bullous cases of Impetigo in the 2-17 years of age seen at the JRRMMC Department of Dermatology, OPD.

Sample Size:

The researcher had 30 subjects for the study.

Primary Outcome Measure: The proportion of subjects with *Clinical success* or *improvement* and / or bacteriologic cure from baseline.

Secondary Outcome Measure: The proportion of subjects with side - effects noted like erythema, burning/stinging sensation or pruritus.

Operational Definition

1. Clinical success is defined by sufficient resolution of signs and symptoms of infection of the target lesion such that no additional antimicrobial therapy is required to treat the impetigo, as evidenced by the Skin Infection Rating scale (SIRS) score of 0 each for exudate/pus, crusting and pain and 0 or 1 each for erythema/inflammation and itching.[10]
2. Bacteriologic cure - defined as elimination of Staphylococcus aureus and Streptococcus pyogenes or response was such that no culture material would be available and therefore evidence of pathogen eradication at the end of treatment visit.
3. Clinical Improvement – is determined by a SIRS score of 0 for exudate/ pus, which does not meet all the criteria for clinical success. [10]
4. Clinical failure is determined by a SIRS score of 1 or greater for exudate/pus.[10]
5. Unevaluable was recorded when a valid clinical assessment could not be made.

Inclusion Criteria

The study included 30 patients clinically diagnosed as cases of Primary, Non-bullous Impetigo with a score of at least 4 and a maximum of 15 in the SIRS and without systemic manifestations like fever, lymphadenopathy, or abscess formation. Lesions had a maximum of 5 per patient on only one area of the body.

Exclusion Criteria

The study did not include patients with extensive lesions (bullous form, extension to delicate areas of eyes, cellulitis), with fever of at least 24 hours duration, lymphadenopathy, with other co-morbid conditions like scabies and lesions that were already treated previously with topical and oral antibiotics.

Stopping Guidelines:

Any patient that reported worsening of lesions, systemic symptoms like fever or

lymphadenopathy that would develop during the course of the treatment were asked to discontinue the tested extract and were given the appropriate oral medication upon assessment.

Materials:

Okra used in the study was the Native White variety that is very accessible to most people in the markets of Manila. This variety is described to be yellow-white fruit color with a more long and slender fruit pod and a slightly bended tip. The okra was placed in white-capped round "latitas" and stored at room temperature. (25^0C)

Study Intervention:

1. Upon consent, base line photos and microbiologic samples were taken from the lesions to be applied with the test ointment.
2. General instruction included application of the tested medication on the lesions twice a day for 2 weeks in combination with local wound care – daily cleaning with mild soap and water and saline compression twice a day and with open dressing. All participants were advised not to self- medicate with any other topical or oral medication during the interim of the study.

Clinical Assessment:

1. Index grading for the impetigo lesions were based on the SIRS scale and was done by an independent assessor at baseline, day 7 and day 14.
2. Lesions were graded according to pre-determined parameters of the SIRS including Blistering, Exudate, Crusting, Erythema and Pruritus/Pain. Grade would range from 0 – absent, 1-mild, 2-moderate and 3-severe. Total score can start at 4 up to 15 depending on severity.
3. Patients were asked to follow-up at day 7 and 14 with re-evaluation of the SIRS grade and update on patient's photos.
4. The same independent assessor took note of the primary and secondary outcome measures at day 7 and 14.

Bacteriologic Sampling and Culture:

Samples were taken from cleaned, unroofed crusts and placed in Trypticase Soy Broth tubes and incubated for at least 24 hours. The broth was then evaluated for growth and compared to McFarland standard. If seen comparable to the standard, the broth is swabbed onto 5% Sheep's Blood Agar Plate and incubated for another 24 hours.

Culture plates with growth was gram stained and checked for presence of cocci in clusters (Staphylococcus sp.) and/ or cocci in chains (Streptococcus sp.).

Statistical Analysis

Data analysis were encoded and tallied in SPSS version 10 for windows. Descriptive statistics were generated for all variables. For nominal data, frequencies and percentages were computed. For numerical data, mean ± SD was generated. Analysis of the different variables was done using the following test statistics:

Repeated Measures ANOVA was used to compare more than two groups with numerical data that were dependent.

Paired T-test – was used to compare two groups with numerical data that are dependent.

Friedman Test - a non-parametric equivalent of the Repeated Measures ANOVA.

Wilcoxon Signed Rank-test – pairwise comparison after Friedman test (non- parametric test.

LIMITATIONS OF THE STUDY

The patients included in the study were the ones seeking consult at the Jose R. Reyes Memorial Medical Center, Department of Dermatology for non-bullous type of impetigo. Bacteriologic identification was limited to culture in Blood Agar plate and gram stains only.

RESULTS AND DISCUSSION

Table 1: Baseline Characteristics of patients included in the Study

A total of 30 subjects were included in the study. Table 1 shows the distribution of subjects according to demographic characteristics. Their age ranged from 0 to 10 years with majority (93.3%) at the 0-5 years old category. An almost equal distribution of males and females was noted. More than 75% of the subjects impetigo lesions were located on the head.

Table 1. ***Demographic Characteristics of Subjects***

	Frequency (n=30)	Percentage
Age (in years)		
0 – 5	28	93.3
6 – 10	2	6.7
11 – 15	0	0
16 – 17	0	0
Gender		
Male	16	53.3
Female	14	46.7
Localization		
Head	23	76.7
Trunk	5	16.7
Limbs	2	6.7

Table 2: Skin Infection Rating Scale (SIRS) comparison for Baseline, Day 7 & 14

Table 2.1 ***Comparison of Blistering Grade from Baseline Until Day 14***

	Baseline (n=30)	Day 7 (n=30)	Day 14 (n=30)
Swelling			
3 – Severe	0	0	0
2 – Moderate	0	0	0
1 – Mild	1 (3.3%)	0	0
0 - None	29 (96.7%)	30 (100%)	30 (100%)
Mean ± SD (Median)	1.03 ± 0.18 (1)	1 ± 0 (1)	1 ± 0 (1)
*p value		0.36	

** p-values >0.05- Not significant; p-values ≤0.05-Significant*
Friedman Test

Table 2.1 shows the comparison of blistering grade from baseline until day 14. The result showed that there was no significant difference noted as proven by the p value of 0.36. At baseline, only 1 (3.3%) had mild blistering was noted. None of the subjects had blister development at day 7 and 14.

Table 2.2 ***Comparison of Exudate from Baseline Until Day 14***

	Baseline (n=30)	Day 7 (n=30)	Day 14 (n=30)
Size of Lesion			
3 – Severe	17 (56.7%)	9 (30.1%)	4 (13.3%)
2 – Moderate	12 (40.0%)	7 (23.3%)	4 (13.3%)
1 – Mild	1 (3.3%)	13 (43.3%)	10 (33.3%)
0 – None	0	1 (3.3%)	12 (40.0%)
Mean ± SD (Median)	3.72 ± 0.68 (4)	2.96 ± 1.18 (3)	2.10 ± 1.26 (1)
****p value***		<0.0001	

** p-values >0.05- Not significant; p-values ≤ 0.05-Significant*

Table 2.2 shows the comparison of the exudate of lesion from baseline until day 14. The result showed that there was a significant difference noted as proven by the p value of <0.0001. The exudate significantly decreased until day 14.

Table 2.3 ***Comparison of Crust Grade from Baseline Until Day14***

	Baseline (n=30)	Day 7 (n=30)	Day 14 (n=30)
Crust			
3 – Severe	21 (70.0%)	2 (6.7%)	0
2 – Moderate	8 (26.7%)	8 (26.7%)	4 (13.3%)
1 – Mild	1 (3.3%)	16 (53.3%)	2 (6.7%)
0 – None	0	4 (13.3%)	24 (80.0%)
Mean ± SD (Median)	4.16 ± 0.95 (4.5)	2.26 ± 0.79 (2)	1.33 ± 0.71 (1)
****p value***		<0.0001	

** p-values >0.05- Not significant; p-values ≤0.05-Significant*
Friedman Test

Table 2.3 shows the comparison of crust grade from baseline until day 14. The result showed that there was a significant difference noted as proven by the p value of <0.0001. The median crust grade significantly decreased until day 14.

Table 2.4 ***Comparison of Erythema Grade from Baseline Until Day14***

	Baseline (n=30)	Day 7 (n=30)	Day 14 (n=30)
Erythema			
3 – Severe	30 (100.0%)	7 (23.3%)	4 (13.4%)
2 – Moderate	0	15 (50.0%)	1 (3.3%)
1 – Mild	0	8 (26.7%)	13 (43.3%)
0 – None	0	0	12 (40.0%)
Mean ± SD (Median)	4.60 ± 0.50 (5)	3.06 ± 0.90 (3)	96. 1.16 (2)
***p value**		<0.0001	

** p-values >0.05- Not significant; p-values ≤0.05-Significant*
Friedman Test

Table 2.4 shows the comparison of erythema grade from baseline until day 14. The result showed that there was a significant difference noted as proven by the p value of <0.0001. The median erythema significantly decreased until day 14.

Table 2.5 ***Comparison of Pain/Itch Grade from Baseline Until Day14***

	Baseline (n=30)	Day 7 (n=30)	Day 14 (n=30)
Number of Lesion			
3 – Severe	0	0	0
2 – Moderate	4 (13.3%)	1 (3.3%)	0
1 – Mild	26 (86.7%)	24 (80.0%)	11 (36.7%)
0 – None	0	5 (16.7%)	19 (63.3%)
Mean ± SD (Median)	2.13 ± 0.34 (2)	1.86 ± 0.43 (2)	1.36 ± 0.49 (1)
***p value**		<0.0001	

** p-values >0.05- Not significant; p-values ≤0.05-Significant*

Table 2.5 shows the comparison of the pain/itch from baseline until day 14. The result showed that there was a significant difference noted as proven by the p value of <0.0001. The pain/itch significantly decreased until day 14.

Table 2.6 ***Comparison of TOTAL Score from Baseline Until 14***

	Baseline (n=30)	Day 7 (n=30)	Day 14 (n=30)
Total Score			
Mean ± SD	10.67 ± 2.04	7.17 ± 2.78	0.77 ± 3.34
(Min - Max)	11 – 13	7 – 9	0 – 3
***p value**		<0.0001	

** p-values >0.05- Not significant; p-values ≤0.05-Significant*
Repeated Measures ANOVA

Table 2.6 shows the comparison of the total score from baseline until day 14. The result showed that there was a significant difference noted as proven by the p value of <0.0001. The mean total score significantly decreased until day 14.

Table 2.7 ***Comparison of Erythema Grade from Baseline Until Day14***

	Blistering	*Exudate*	*Erythema*	*Crust*	*Pain/Itch*
Baseline vs Day 7	0.32	<0.0001	<0.0001	<0.0001	<0.01
Baseline vs Day 14	0.32	<0.0001	<0.0001	<0.0001	<0.0001
Day 7 vs Day 14	1.00	<0.0001	<0.0001	<0.0001	<0.0001

** p-values >0.05- Not significant; p-values ≤0.05-Significant*
Wilcoxon Signed Rank Test

Table 2.7 shows the pairwise comparison of erythema grade, crust grade, swelling grade, size of lesion and number of lesion from baseline until day 14. Supporting the results in tables 2.1 to 2.5, there were significant decreases noted at day 7 when compared to baseline (p<0.0001) and even until day 14 (p<0.0001) except for blistering (p>0.05).

Table 3 shows the distribution of subjects according side effects. There were 8 (26.7%) with erythema and 6 (20.0%) with pruritus, none had burning sense

Table 3 ***Distribution of Subjects According to Side Effects***

	Frequency (n=30)	Percentage
Erythema	8	26.7
Pruritus	6	20.0
Burning Sensation	0	0

Table 4 shows the distribution of subjects according to the growth assessed from the samples taken from their lesions at baseline. There were 10 (33.33%) with growth of *Staphylococcus epidermidis*, 8 (26.67%) with *Staphylococcus aureus* and 12 (40%) of lesions sampled had *Streptococccus pyogenes*.

Table 4 ***Distribution of Subjects According to Bacteria Isolated***

	Frequency (n=30)	Percentage
Staphylococcus epidermidis	10	33.33
Staphyloccocus aureus	8	26.67
Streptococcus pyogenes	12	40

Table 2.1 showed a non-significant difference in the blistering of the lesions from baseline to day 14. The reason for that being the sample population gave priority in choosing non-bullous impetigo and that 1 patient was included with an isolated mild blistering grade because the patient had other lesions counted for the study. The average of the total scores obtained by the study patients using the SIRS showed significant reduction from baseline to day 7 and day 14.

During the course of the treatment, some of the patients complained of erythema and pruritus however all of the said symptoms eventually subsided after completion of the 14-day period.

CONCLUSION

This pilot study has showed that an ointment-based 5% extract of Abelmoschus esculentes (Okra) is effective in the treatment of Non-bullous impetigo. All parameters showed significant improvement even only after 7 days. Mild side- effects noted like erythema and pruritus were observed in some of the patients however, these symptoms dissipated upon completion of the 14-day treatment.

RECOMMENDATION

The author recommends that a more accurate microbiologic documentation be done before, during and after the treatment period to specifically identify the organisms in the patient's lesions. The appearance of new lesions was not monitored after the 14-day treatment. Follow up after 1 month of treatment may be employed for this reassessment. A clinical trial with a bigger sample size should be done to further test its efficacy in a wider range of superficial skin infections. A comparison with a positive control and I or a placebo should be done to further solidify its effectivity.

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APPENDIX

Figure 1. Philippine Lady Finger (Native Variety)

Sign/ symptom	Score	Definition
Blistering	0=Absent	No evidence of blisters
	1=Mild	Few raised vesicles present on close evaluation
	2=Moderate	Fluid filled vesicles are obvious and are bothersome to the patient
	3=Severe	Extensive area covered with many vesicles which may include large bullous vesicles
Exudate/pus	0=Absent	No evidence of exudate or pus
	1=Mild	Small amounts of fluid/pus coming from the lesions
	2=Moderate	Exudate/pus infected area is moderate
	3=Severe	Extensive areas infected and there is draining exudate
Crusting	0=Absent	No evidence of crusting
	1=Mild	A few areas have some evidence of crusting lesions
	2=Moderate	Crusting is present throughout the infected area
	3=Severe	Thick crusting appears over the entire impetiginous area
Erythema/ inflammation	0=Absent	Skin tone and color are normal; no signs of erythema or inflammation
	1=Mild	Skin is pink with minimal signs of inflammation
	2=Moderate	Skin is red with definite signs of inflammation
	3=Severe	Skin is red and severe inflammation is present
Itching/pain	0=Absent	No signs of itching or indication of pain
	1=Mild	Some evidence of scratching or rubbing the area is evident and patient reports minor discomfort
	2=Moderate	Evidence of scratching and patient reports bothersome, painful lesions
	3=Severe	Evidence of extensive scratching and patient reports pain that interferes with daily activities or sleep.

Figure 3. Patient 1

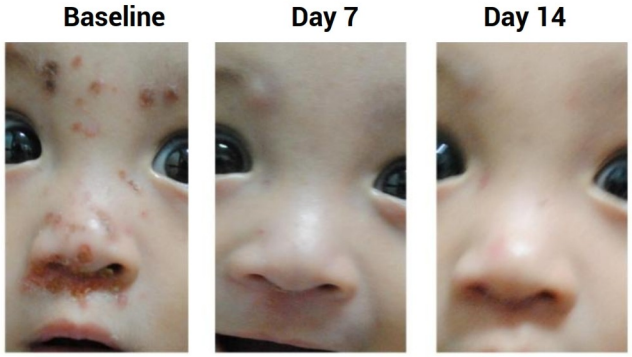

Figure 4. Patient 2

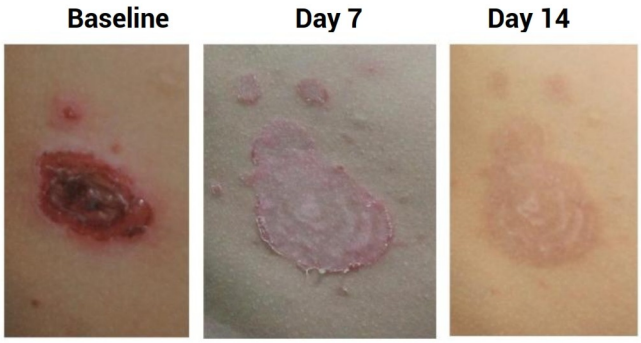

Figure 5. Patient 3

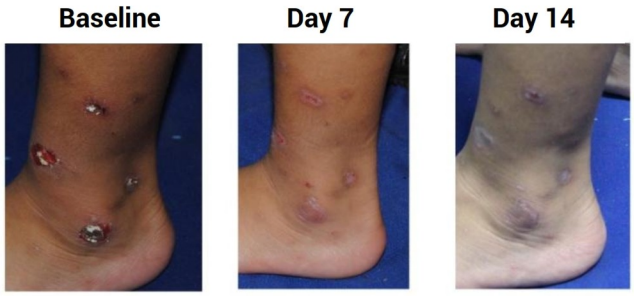

Figure 6. Patient 4